MEDICAL SCIENCE AND BIOETHICS: ATTACK OF THE CLONES?

HEARING

BEFORE THE

SUBCOMMITTEE ON CRIMINAL JUSTICE, DRUG POLICY AND HUMAN RESOURCES

OF THE

COMMITTEE ON GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

ONE HUNDRED SEVENTH CONGRESS

SECOND SESSION

MAY 15, 2002

Serial No. 107–194

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MEDICAL SCIENCE AND BIOETHICS: ATTACK OF THE CLONES?

WEDNESDAY, MAY 15, 2002

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON CRIMINAL JUSTICE, DRUG POLICY AND HUMAN RESOURCES,
COMMITTEE ON GOVERNMENT REFORM,
Washington, DC.

The subcommittee met, pursuant to notice, at 1:05 p.m., in room 2154, Rayburn House Office Building, Hon. Mark E. Souder (chairman of the subcommittee) presiding.

Present: Representatives Souder, JoAnn Davis of Virginia, Weldon, and Cummings.

Staff present: Chris Donesa, staff director and chief counsel; Roland Foster, professional staff member; Conn Carroll, clerk; Julian A. Haywood, minority counsel; and Earley Green, minority assistant clerk.

Mr. SOUDER. The subcommittee will now come to order.

We will start with my opening statement. Good afternoon and thank you all for being here today. Today's hearing will examine the scientific, medical, and ethical issues related to human cloning, and examine the need for Federal law in this area.

Scientists stunned the world 5 years ago when they announced the creation of the world's first clone, a sheep named Dolly. In the short time since, cattle, goats, mice, rabbits, and a cat have also been cloned. Efforts are now underway in the United States and elsewhere to create a cloned human being.

The President, the public, religious leaders, and many scientists have all expressed their disapproval of efforts to conduct human cloning for any reason, and the House of Representatives overwhelmingly approved legislation last year, authored by Dr. David Weldon, a member of this subcommittee, to prohibit all human cloning.

Opposition to human cloning is based upon both ethical and scientific considerations. All clones so far have been found to suffer from severe abnormalities, premature aging, and early death. In addition to these problems, cloning also poses significant health risks to the mother of a clone and to the women from whom the eggs necessary for cloning are harvested.

These dangers have not, however, deterred some from attempting to produce cloned humans. We know scientists, such as Dr. Panos Zavos, who is with us today, are pursuing cloning as a means of producing live human offspring, while others seek to create cloned human embryos in order to destroy them for scientific research,

with the hopes that such research may potentially yield treatments or cures.

Regardless of the goals of those who are attempting to manufacture human clones, the fact is that cloning, for whatever purpose, creates human life.

There is no difference between a cloned human embryo created for procreation or for research purposes. Whether or not the newly created embryo is implanted with the intent of reproduction or destroyed for the purpose of research is irrelevant to the fact that a cloned human being has been created. Therefore, a prohibition on cloning that is limited only to preventing the implantation of a cloned embryo, as some have suggested, in effect legalizes human cloning, and raises additional ethical dilemmas.

A ban that permits embryonic clones to be created but forbids them to be implanted in utero legally requires the destruction of human life and criminalizes efforts to preserve and protect such life, once created.

Under a partial ban that permits the creation of cloned embryos for research, human embryos would be manufactured in numerous laboratories around the country. Once cloned embryos are available, it would be virtually impossible to monitor or control what is done with them.

Stockpiles of embryonic human clones could be produced, bought, and sold. Implantation of cloned embryos, an easy procedure, could take place out of sight, and not even the most elaborate and intrusive regulations and policing could detect or prevent the initiation of a clonal pregnancy.

Scientists agree that once begun, a clonal pregnancy would be almost impossible to detect or differentiate from a routine pregnancy, and if detected, what could the government do? Would a woman with a clonal pregnancy be forced or coerced with severe penalties to abort the child? Allowing human cloning for research brings us further down the slippery slope that devalues the sanctity of human life.

Not even a year ago, this subcommittee held a hearing on research involving the destruction of human embryos. At that time, supporters of embryonic stem cell research, which requires the destruction of a human embryo, found "extremely troubling" the announcement that embryos were being created in order to conduct stem cell research. There was a consensus among opponents and supporters of embryonic stem cell research that embryos should never be created solely and specifically for research. But now that is exactly what the proponents of research cloning are demanding.

If we now permit the manufacturing of human embryos for research, where do we draw the line? Do we allow cloned embryos to grow for 5 days before they are destroyed in the process of extracting their stem cells? What about removing tissues from 5-week-old embryos? Should we consider harvesting the organs from 5-month-old fetuses? What will those who support destructive research next claim is necessary in the name of research?

We must finally draw the line that stops the exploitation of any form of human life. Cloning, regardless of intent, reduces human life to a commodity that is created and destroyed for convenience. And despite the claims to the contrary, there is no evidence that

cloning can or ever will cure diseases. Such statements are purely speculative, and pursuing cloning merely diverts limited resources away from more promising research that is already producing promising results.

It is clear that a ban that applies only to reproductive cloning is a false ban, which merely creates an illusion that human cloning has been prohibited. The fact is that all cloning is reproductive cloning, and therefore human cloning for any reason should be banned.

Thank you all for being here today. We look forward to hearing the testimony of each of our witnesses.

[The prepared statement of Hon. Mark E. Souder follows:]

Opening Statement
Chairman Mark Souder

"Medical Science and Bioethics: Attack of the Clones?"

Subcommittee on Criminal Justice, Drug Policy,
and Human Resources
Committee on Government Reform

May 15, 2002

Good afternoon and thank you all for being here today.

Today's hearing will examine the scientific, medical, and ethical issues related to human cloning and examine the need for federal law in this area.

Scientists stunned the world five years ago when they announced the creation of the world's first clone, a sheep named Dolly. In the short time since, cattle, goats, mice, rabbits and a cat have also been cloned. And efforts are now underway in the United States and elsewhere to create cloned human beings.

The President, the public, religious leaders, and many scientists have all expressed their disapproval of efforts to conduct human cloning, for any reason. And the House of Representatives overwhelmingly approved legislation last year authored by Dr. David Weldon—a member of this Subcommittee—to prohibit all human cloning.

Opposition to human cloning is based upon both ethical and scientific considerations. All clones so far have been found to suffer from severe abnormalities, premature aging and early death. In addition to these problems, cloning also poses significant health risks to the mother of a clone and to the women from whom the eggs necessary for cloning are harvested.

These dangers have not, however, deterred some from attempting to produce cloned humans.

We know scientists-- such as Dr. Panos Zavos, who is with us today—are pursuing cloning as a means of producing live human offspring while others seek to create cloned human embryos in order to destroy them for scientific research with the hopes that such research may potentially yield treatments or cures.

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A ban that permits embryonic clones to be created but forbids them to be implanted in utero legally requires the destruction of human life and criminalizes efforts to preserve and protect such life once created.

Under a partial ban that permits the creation of cloned embryos for research, human embryos would be manufactured in numerous laboratories around the country. Once cloned embryos are available, it would be virtually impossible to monitor or control what is done with them.

Stockpiles of embryonic human clones could be produced, bought and sold. Implantation of cloned embryos-- an easy procedure-- could take place out of sight, and not even the most elaborate and intrusive regulations and policing could detect or prevent the initiation of a clonal pregnancy.

Scientists agree that once begun, a clonal pregnancy would be virtually impossible to detect or differentiate from a routine pregnancy. And if detected, what could the government do? Would a woman with a clonal pregnancy be forced, or coerced with severe penalties, to abort the child?

Allowing human cloning for research brings us further down the slippery slope that devalues the sanctity of human life.

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If we now permit the manufacturing of human embryos for research, where do we draw the line? Do we only allow cloned embryos to grow for 5 days before they are destroyed in the process of extracting their stem cells? What about removing tissue from 5-week-old embryos? Should we consider harvesting the organs from 5-month-old fetuses? What will those who support destructive research next claim is necessary in the name of research?

We must finally draw the line that stops the exploitation of any form of human life.

Cloning, regardless of the intent, reduces human life to a commodity that is created and destroyed for convenience. And despite the claims to the contrary, there is no evidence that cloning can, or ever will, cure diseases. Such statements are purely speculative and pursuing cloning merely diverts limited resources away from more promising research that is already producing promising results.

It is clear that a ban that applies only to "reproductive" cloning is a false ban, which merely creates an illusion that human cloning has

been prohibited. The fact is that all cloning is reproductive cloning, and therefore human cloning for any reason should be banned.

Thank you all for being here today. We look forward to hearing your testimony.

Mr. SOUDER. I yield to Dr. Weldon for an opening statement.

Dr. WELDON. Thank you, Mr. Chairman, and thank you for calling this very important hearing.

As a physician who still sees patients on a regular basis, I have a keen interest in developing cures for diseases that plague so many of my patients. We all have family members who suffer from diseases, and we all hope for cures for these conditions.

I have been and remain a supporter of the NIH, and I have been pleased to take an active role in doubling the funding for NIH so we can pursue the necessary cures.

Scientists have announced they are working to clone human beings. Today we will hear testimony from one such researcher. The complete ban on human cloning passed the House on last July and was supported by a wide bipartisan margin, 265 to 162. It was supported by liberals, progressives, conservatives, pro-life, pro-choice Members, and many supporters, I will note, of embryo stem cell research.

Clearly, the support for a complete ban on human cloning is very broad-based support. Why is that so? Because human cloning is a threat to society. Human cloning moved from science fiction to reality when researchers in 1997 cloned Dolly the sheep. For the first time, we had the power to redesign human beings at a basic level.

Human cloning is not about procreation, it is about baby manufacture. It does not produce a child with two parents, it creates a duplicate of an existing human being. Human cloning is not a reproductive right, it is about eugenics and depriving children of their genetic individuality.

No one has the right to alter the human species in such a fundamental way. No one has the right to turn human procreation into baby manufacture, and no one has the right to create children to their own specifications.

This is why it is very important that the other body pass a complete ban like the ban that passed the House. This is why the Senate needs to stop delaying and act on this very, very important issue.

I just want to underscore a very, very important point that I think we need to make. I was hoping that we would have a Justice Department witness at this hearing today. As I understand it, they were unable on the short notice to provide someone, but they have provided us a statement. I think this is a very, very important point, Mr. Chairman.

There are several proposals in the other body that are similar to some of the ideas that were floated here in the House of Representatives last year that entailed various bans on just so-called reproductive cloning, banning the implantation of a cloned embryo into a woman, but allowing unfettered embryo cloning for either scientific purposes or other purposes.

The concern that I have had—and I have a statement from the Justice Department validating this—is that these proposals, such as proposal S. 2439 introduced by Senators Specter, Feinstein and Kennedy, along with others, are essentially unenforceable.

Specifically, what the Justice Department talks about in their statement is that what they attempt to make illegal, the implantation of a cloned embryo into a woman for reproductive purposes, is

actually a procedure that is occurring daily all over the country on a regular basis in fertility clinics, where these fertility clinics are taking sexually fertilized embryos and implanting them in women.

Let me just quote from the statement from the Justice Department. "hence, there is no visible difference between the prohibited activity and the permitted activity, both of which would presumably be conducted within the privacy of a hospital or medical office. Entrusted with enforcing such a limited ban, law enforcement would be in the unenviable position of having to impose new and unprecedented scrutiny over doctors and fertility clinics and/or research facilities to ensure that only fertilized embryos were being transferred to would-be mothers."

This is a very, very critical point, and a point I made in argument and debate in the House, and it is an important point that the supporters of the Kennedy-Feinstein approach have not really successfully addressed: How on Earth would law enforcement enforce such a ban as they are proposing?

Mr. Chairman, I would just like to ask that we strongly consider the possibility of having a second hearing next month and bringing the Justice Department in here to elaborate on this. As I understand it, the vote in the Senate has been put off again, so this issue I think is still very, very timely and very much worth discussion.

Mr. SOUDER. I thank the gentleman from Florida. We will certainly work hard on the calendar to see if we can accommodate both the Justice Department and possibly HHS in an enforcement hearing.

Dr. WELDON. I thank the chairman. Might I also ask unanimous consent to insert this statement in the record.

Mr. SOUDER. Hearing no objection, so ordered.

Before proceeding, I would like to take care of a couple of procedural matters.

First, I ask unanimous consent that all Members have 5 legislative days to submit written statements and questions for the hearing record, and that any answers to written questions provided by the witnesses also be included in the record.

Without objection, it is so ordered.

Second, I ask unanimous consent that all exhibits, documents, and other materials referred to by Members and the witnesses may be included in the hearing record, and that all Members be permitted to revise and extend their remarks.

Without objection, it is so ordered.

If each of the witnesses on the first panel could stand and raise your right hand, I will administer an oath. This is an oversight committee, so it is standard practice that everyone has to take the oath.

[Witnesses sworn.]

Mr. SOUDER. Let the record show the witnesses have each answered in the affirmative.

Witnesses will each be asked to now summarize your opening statements. You have 5 minutes for testimony. Your full statement will be included in the record as well as any other materials that you wish to submit.

At this time, we will start with Dr. Usala.

STATEMENTS OF ANTON-LEWIS USALA, M.D., BRODY SCHOOL OF MEDICINE, EAST CAROLINA UNIVERSITY; BRYAN COWAN, M.D., DEPARTMENT OF OB/GYN, UNIVERSITY OF MISSISSIPPI MEDICAL CENTER; AND PANAYIOTIS ZAVOS, THE ANDROLOGY INSTITUTE OF AMERICA

Dr. USALA. Chronic disease states, such as Type 1 diabetes, Parkinson's Disease, and spinal cord injury result from the destruction of specific cells. Replacement of these tissues may provide immense relief, and possibly cure of the disease. One approach to replace these tissues is to find acceptable transplantation sources and implant donor cells into a patient. If these cells are derived from a source other than the patient, there will be problems with rejecting the foreign transplant material. Cloned patient cells, that is, cells that are induced to replicate with the same DNA template as the patient's, do not have foreign markers and theoretically would not be rejected. However, cloned cells, as well as other cells, still must overcome the problem of appropriate integration into the transplant site in order to replace the function of the destroyed tissues.

Shortly after conception, the human being has a unique DNA template from which all other cells are generated. A differentiated heart cell has the same DNA template as a differentiated skin cell, and they both have the same DNA template as the undifferentiated cells currently in embryogenesis.

Different areas of the DNA template are promoted and repressed, resulting in different cell functions. Which area of the DNA template is promoted and repressed is largely determined by environmental factors outside the cell. Thus, it is hypothetically possible to induce any cell to become any other kind of cell if the right environment were provided.

The mass of cells that begins this replication and differentiation, either shortly after conception or induction through nuclear transfer, defines the beginning of any mammal's life. The continuum of human life thus starts at the beginning of the complex, explosive process of cellular DNA differentiation during embryogenesis and continues throughout a person's life until death. One cannot stop the continuum at any one point and say it is not human life simply because it lacks the ability to do certain functions.

When the mass of cells has feelings or reason is subject to debate. When it begins as human life is a biologic fact. The developing embryo is surrounded by different proteins and factors than later in development, but the DNA template remains the same throughout the person's life.

My hypothesis was that if the correct embryonic environment could be duplicated, a patient's cells may be able to be induced to regenerate within a given site, as they rapidly did earlier in the patient's life, during embryogenesis. This would result in totally compatible, integrated replacement tissue for the disease being treated.

I tested this concept in an FDA-monitored feasibility study. Human patients with diabetic foot ulcers were injected with an artificially made copolymer I designed that resembled early embryonic proteins. It needs to be emphasized that no cells were transplanted into the patients. Their ulcers were injected only with the copolymer protein structure.

If I could have the first slide.

Shown here is the first large animal which I injected the copolymer into. This was a spontaneously diabetic dog that was brought to a veterinarian for euthanasia. After 2 months of IV antibiotic therapy and efforts at surgical closure, the dog's diabetic ulcers persisted. This is very similar to what we see in human patients with diabetic foot ulcers. After many years of diabetes, the circulation is damaged and healing can no longer take place effectively.

Up on the left panel we see the ulcer. That was there for 2 months. You can see part of the elbow bone poking through. That was before the injection, which we injected around the periphery and through the center. Two days later, as you can see, the ulcer became very, very erythematous but not swollen. This was not inflammation. We knew from earlier studies that we induced rapid, explosive growth of new blood vessels with new red blood cells in them.

By 6 days, the animal's chronic ulcer was completely closed, and you can see the new hair follicles growing. Again, no cells were injected. This was just induction of what each one of our cells contains: the power to regenerate if put in the proper environment.

Next slide, please.

After review, the FDA allowed us to try a feasibility trial. We took six patients with chronic diabetic foot ulcers at the University of North Carolina at Chapel Hill to their chronic wound care center.

This is a photo of an ulcer that was 4 years in duration. This patient was treated every 2 weeks for 4 years in an attempt to get this ulcer to close.

Next slide, please.

This is the ulcer 15 minutes after the initial injection of the copolymer matrix. You can see it looks a little different. You can see the spots where the needle was placed to inject one time this scaffolding.

Next slide, please.

Here you have 7 days. You can see what happened, the explosive regeneration that has filled the ulcer that was there for 4 years. This is very delicate tissue, and it is highly vascularized. How do we know? The surgeon poked it and you can see the blood exuding out.

Next slide, please.

This was day 14. It continued to grow with the keratinization occurring.

Next slide.

This was at 1 month.

Next slide.

The same patient at 2 months.

There he was at 3 months.

Four weeks later, this man was able to dance at his daughter's wedding. He was not able to walk for the previous 4 years.

Transplantation strategies, whether derived from foreign donors or cloned cells from the patients themselves, are clearly not the only approach to replace damaged tissue. Other avenues are much further along in clinical trials and should be considered as a first approach for study.

Claims that only human embryonic stem cells or cloned tissues can overcome problems of rejection are false. Indeed, the patient's existing cells provide the most rational source for fully integrating replacement tissue, as occurs during embryogenesis.

Thank you.

Mr. SOUDER. Thank you very much.

[The prepared statement of Dr. Usala follows:]

Anton-Lewis Usala, MD

TISSUE REGENERATION, NOT TRANSPLANTATION, TO CURE HUMAN DISEASE

Chronic disease states such as Type 1 Diabetes, Parkinson's Disease, and Spinal Cord Injury result from the destruction of specific cells. Replacement of these tissues may provide immense relief, and possibly cure, of the disease.

One approach to replace these tissues is to find acceptable transplantation sources and implant donor cells into a patient. If these cells are derived from a source other than the patient, there will be problems with rejecting the "foreign" transplant material. Cloned patient cells (cells that are induced to replicate with the same DNA template as the patient) do not have foreign markers and theoretically would not be rejected. However, cloning by the transfer of somatic nuclei into unfertilized eggs requires a dramatic remodeling of chromosomal architecture. Many proteins are specifically lost from nuclei and others are taken up from the egg cytoplasm. These proteins determine which DNA genes are promoted and expressed, and which DNA genes are repressed.

Since cellular transplant material obtained from developing embryos must overcome the problem of appropriate integration into the transplant site in order to replace the function of the destroyed tissue, scientifically it may make more sense to induce the patient's own tissues to replicate at the desired site as the communication and integration networks are mostly in place. Embryonic stem cell transplantation has repeatedly been shown to be ineffective in large animal models largely because they are not capable of integrating into mature host structures. Even if the stem cells are obtained from cloned embryos, and subsequently are not rejected on the basis of immunologic compatibility, the transplanted stem cells still are not capable of forming the complex integrative network that many structures require.

The developing embryo is surrounded by unique proteins and environmental factors. Once the embryo reaches a more mature fetal stage, the cells are surrounded by more mature proteins and growth factors, leading to more highly differentiated cell functions. Throughout this process, the DNA template that codes for the expression of all cell functions remains the same. One hypothesis states that if the correct embryonic environment could be duplicated, a patient's cells may be able to be induced to regenerate in a given site, as they rapidly did earlier in the patient's life during embryogenesis. This would result in totally compatible, integrated, replacement tissue for the disease being treated.

I would like to share with the committee the preliminary results of a product I developed to induce regeneration of a specific kind of tissue in animal and human patients. My hypothesis was that exposing cells derived from the mesodermal embryonic germ layer to an embryonic scaffolding structure, the patient cells originally derived from this germ layer would be induced to behave as they did during embryogenesis. Mesodermally derived cells give rise to such differentiated structures as blood vessels, deep skin structures, bone and cartilage. The artificial embryonic scaffolding was made from long chain naturally occurring biopolymers that I modified to inject into patients wounds to

induce explosive regeneration of skin, blood vessels, and supporting structures. This embryonic scaffolding contained no cells, only structures for the patient's cells to bind to.

The results I am about to show have been presented at several scientific meetings, but have not yet been published in full manuscript form. Shown is an example of the rapid wound healing induced in a dog that had naturally occurring diabetes and developed multiple full thickness skin ulcers. The dog had undergone multiple courses of antibiotics and surgical closure procedures, but the ulcers would not heal because of the chronic destruction of blood vessels commonly seen with long standing diabetes. After a one-time injection of the embryonic scaffolding, the dog's wound's healed with regenerated tissue. The new tissue resulting from exposure to the embryonic like matrix was determined to be structurally identical to non-wounded areas, without the usual scarring that is normally seen with healing lesions. Further large and small animal studies confirmed our finding, and a six patient feasibility study was approved by the Food and Drug Administration to examine the effect of a one-time injection in patients with chronic diabetic foot ulcers refractory to conventional therapy.

Within days of a one-time injection, all the patients experienced rapid diminution of ulcer size, with apparent regeneration of skin, blood vessels, and surrounding structures. Since the new tissue derived from the patients' own tissue, there was seamless integration with no evidence of rejection. Further study is required to determine if this particular product is safe and effective, but clearly the large animal and human patient studies suggest cellular transplantation is not necessarily required to replace damaged tissue.

Destroying a human embryo to obtain cellular material does in fact destroy a human life, not a potential human life. Shortly after conception, a human being has a unique DNA template from which ALL other cells are generated. The process by which cells become specialized is called differentiation. A differentiated heart cell has the same DNA template as a differentiated skin cell, and they both have the same DNA template as the undifferentiated cells early in embryogenesis.

The mass of cells that begins this replication and differentiation, either shortly after conception or induction through nuclear transfer, defines the beginning of any mammal's life. This differentiation process continues until death. The continuum of human life thus starts at the beginning of the complex, explosive process of cellular DNA differentiation during embryogenesis and ends at death. One cannot stop the continuum at any one point and say it is not human life because it lacks the ability to do certain functions. When the mass of cells has feelings or reason is subject to debate. When it begins as human life is a biologic fact.

All laws are based on precedent. The difference between a just and an unjust society is the precedent the society accepts to base its jurisprudence upon. In my view, the United States is a uniquely just society because it is the first government in the history of humankind in which the right of the individual supersedes the perceived right of the state, thus defining the individual as society's most valued entity. The first ten amendments to our constitution explicitly prevents government, even if so desired by the majority, from

violating these individual rights. As a developing embryo, whether cloned or naturally obtain, is scientifically a human being, the United States must not set the precedent of allowing individuals to be sacrificed for the illusion of a greater good.

Transplantation strategies, whether derived from foreign donors or cloned cells from the patient themselves, are clearly not the only approach to replace damaged tissues. Other avenues are further along in clinical trials, and should be considered as a first approach for study. Indeed, the patient's existing cells provide the most rationale source for fully integrating replacement tissues, as occurred during embryogenesis.

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Dr. Cowan.

Dr. COWAN. Good afternoon, Mr. Chairman and members of the committee. Thank you for holding this important hearing and for inviting us to participate.

I am Dr. Bryan Cowan, professor of obstetrics and gynecology at the University of Mississippi Medical Center in Jackson, Mississippi. I am here today representing the American Society of Reproductive Medicine, ASRM. ASRM is a national professional organization whose nearly 9,000 members are dedicated to advancing knowledge and expertise in reproductive medicine and biology and treating infertility. Our membership is made up of physicians, reproductive biologists, laboratory directors, nurses, and mental health professionals, all of whom are dedicated to advancing the cause of reproductive medicine.

ASRM supports a ban on reproductive cloning at this time but endorses somatic cell nuclear transfer for research. And let me tell you why. ASRM is on record as opposing attempts at human reproductive cloning since the announcement of the successful cloning of a sheep in 1997. In November 2000, our ethics committee released a very thoughtful report on somatic cell nuclear transfer, both therapeutic and reproductive cloning, and concluded that human reproductive cloning was not safe and efficacy of the procedure had not been established.

We have learned how to use cloning with microscopic organisms, and any of us who gardens knows how cloning works. Some species of animals, such as frogs and mice, can be cloned quite successfully. It appears that in larger, more complicated animals, cloning can be made to work but is not yet reliable. Cows and sheep have been cloned, but there have been many problems that, while unfortunate in animals, are completely unacceptable in human beings.

Until there are better results in animals, we have no business even considering reproductive cloning in human beings. Thus, we feel it would be entirely appropriate for the Congress to make human reproductive cloning illegal. We are concerned, however, that much of the proposed legislation, including the bill passed by this body last summer, simply goes too far.

Research using somatic cell nuclear transfer holds tremendous promise. If we take an egg, remove its nucleus and thus the genetic material, replace that nucleus with the DNA from the donated somatic cell, spark that cell to artificially begin cell division and use the resultant stem cell, we may unlock the cures for diabetes, Parkinson's Disease, cardiovascular disease and spinal cord injury, just to name a few conditions. This science is in its infancy. To slam the door shut before we understand it would be unconscionable.

This view, to prohibit reproductive cloning but to allow research into somatic cell nuclear transfer, is not just my view and not just the view of the ASRM. Rather, it is without question the view of nearly every serious scientific and medical group that has examined the issue.

The ASRM is a founding member of the Coalition for the Advancement of Medical Research, a coalition that supports this view. Members include the American Society for Cell Biology, the American Association of Neurological Surgeons, the Congress of

Neurologic Surgeons, the American Society of Hematology, and the American Medical Association, just to name a few.

In addition, the National Academy of Sciences, a Blue Ribbon Commission in California, and a letter signed by 40 Nobel Laureates, concluded that the scientific and medical communities are clear: reproductive cloning should be banned, but research utilizing related techniques must be allowed to go forward.

Yes, there are individual scientists who would defend reproductive cloning, as well as individuals who would support a prohibition even on related research, but there is a clear consensus in the mainstream scientific community that the potential advantages of somatic cell nuclear transfer are so great that the ethical concerns of a minority must not be used to prohibit it. Instead, we should develop wise policy decisions that can solve these ethical concerns.

We have seen firsthand in the United States how fear and unwise policy decisions can make it extremely difficult for us to improve the treatments we have available to offer our patients. The decision to deny Federal funds for research involving human IVF has harmed the millions of Americans suffering from infertility. History is replete with examples of government attempts to block scientific and medical advancement, almost always with negative results.

In the 17th century, Galileo was arrested for arguing that the planets revolved around the sun. In the 19th century, the Church of England argued that providing anesthesia during childbirth violated Biblical tenets, and attempted to outlaw it. Today, organ transplantation and IVF were hugely controversial upon their introduction, and we were greeted with the same objections raised here against cloning. Thankfully, this knowledge was not made illegal, and today we can successfully use these advances to help patients every single day.

There have also been concerns raised about the use of donated eggs for therapeutic cloning. We have been using egg donation to assist reproduction for more than 10 years. To date in the United States, more than 15,000 children have been born into loving families using this important therapy.

Over the years, the ASRM has developed a strict set of guidelines on how to go about egg donation and how to protect egg donors. There is no reason these standards cannot be applied to all eggs used for somatic cell nuclear transfer research and guarantee patient privacy and protection.

The real goal of most of this research would be to develop a better understanding of how an egg works. Once we know how an egg deregulates the DNA after somatic transfer, this knowledge would obviate or even eliminate the need for more eggs to be used to develop stem cells. Any claims as to the number of eggs that would be needed are, frankly, speculation.

I am fearful that a negative decision may be made on somatic cell nuclear transfer that will cause needless suffering for patients with heart disease, diabetes, Parkinson's, or others. Please do not make their situations worse by enacting a new and unneeded prohibition on research just because those techniques might allow reproductive cloning to occur. As a physician, I must tell you how important hope is to our patients. By outlawing this very promising

research, you would be denying hope to millions of Americans and their loved ones.

I thank you for your time, and would be happy to answer any questions. Thank you.

Mr. SOUDER. Thank you.

[The prepared statement of Dr. Cowan follows:]

A Responsible Prohibition on Human Reproductive Cloning

Testimony before the
Subcommittee on Criminal Justice, Drug Policy and Human Resources
Subcommittee
Committee on Government Reform
U.S. House of Representatives

Presented by Bryan Cowan, MD
Director
American Society for Reproductive Medicine

And
Professor of Obstetrics and Gynecology
University of Mississippi Medical Center

May 15, 2002

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Good afternoon Mr. Chairman and members of the committee. Thank you for holding this important hearing and for inviting us to participate.

I am Dr. Bryan Cowan, Professor of Obstetrics and Gynecology, at the University of Mississippi Medical Center in Jackson, Mississippi. I am here today representing the American Society for Reproductive Medicine (ASRM). ASRM is a national professional organization whose nearly 9,000 members are dedicated to advancing knowledge and expertise in reproductive medicine and biology and treating infertility. Our membership is made up of physicians; (ob/gyns, reproductive endocrinologists, and urologists), reproductive biologists, laboratory directors, nurses and mental health professionals, all of who are dedicated to advancing the cause of reproductive medicine.

ASRM has been on record as opposing attempts at human cloning since the announcement of the successful cloning of a sheep in 1997. In November of 2000, our ethics committee released a very thoughtful report on somatic cell nuclear transfer (cloning) (SCNT), again concluding that because the safety and efficacy of the procedure had not been established, it would be unethical at this time to attempt human cloning.

We have learned how to use cloning with microscopic organisms and any of us who gardens know cloning works with many plants. Some species of animals, such as frogs and mice can be cloned quite successfully. It appears that in larger, more complicated animals, cloning can be made to work, but it is not yet reliable. Cows and sheep have been cloned, but there have been many problems that, while unfortunate in animals, are completely unacceptable in human beings. Until there are better results in animals, we have no business even considering it in human beings.

We feel it would be entirely appropriate for the Congress to make human reproductive cloning illegal. However we are concerned that much of the proposed legislation, including the bill passed by this body last summer simply goes too far.

Research using somatic cell nuclear transfer holds tremendous promise. Taking an egg, removing its nucleus and thus the genetic material, replacing that nucleus with the DNA from a donated somatic cell, sparking that cell to artificially begin cell division, and using the resultant stem cells may allow us to unlock cures for diabetes, Parkinson's disease, cardiovascular disease

and spinal cord injury just to name a few conditions. This science is in its infancy; to slam the door shut on it before we understand it would be unconscionable.

This view, to prohibit reproductive cloning, but to allow research into somatic cell nuclear transfer to move forward is not just my view, and not just the view of the ASRM. Rather, it is without question the view of nearly every serious scientific and medical group that has examined the issue.

The ASRM is a founding member of the Coalition for the Advancement of Medical Research (CAMR), a coalition whose members include the American Society for Cell Biology, American Association of Neurological Surgeons/Congress of Neurological Surgeons, American Society of Hematology and the American Medical Association to name just a few. In addition, the National Academy of Sciences, a blue ribbon commission in California, and a letter signed by 40 Nobel Lauretes, the conclusion of the scientific and medical communities is clear: Reproductive cloning should be banned, but research utilizing related techniques must be allowed to go forward.

Yes, there are individual scientists, and this committee seems to have found them, who would defend reproductive cloning as well as individuals who would support a prohibition even on releated research. But there is clear consensus in the mainstream scientific community that the potential advantages of somatic cell nuclear transfer are so great that the ethical concerns of a minority must not be used to prohibit it.

However, we have seen first hand in the U.S., how fear and unwise policy decisions can make it extremely difficult for us to improve the treatments we have available to offer our patients. The decision to deny federal funds for research involving human IVF has harmed the millions of Americans suffering from infertility. Unfortunately, history is replete with examples of government attempting to block scientific and medical advancement, almost always with negative results. In the 17th century Galileo was arrested for arguing that the planets revolved around the sun. In the 19th century, the Church of England argued that providing anesthesia during childbirth violated Biblical tenets and attempted to outlaw it. In the 20th century, organ transplantation and IVF were hugely controversial upon their introduction, with many of the same actors raising the same objections they raise today

against cloning. Thankfully, this knowledge was not made illegal, and today we can successfully use these advances to help patients every single day.

There have also been concerns raised about the use of donated eggs for therapeutic cloning. We have been using egg donation in assisted reproduction for more than 10 years. To date in the U.S., more than 15,000 children have been born into loving families using this important therapy. Over the years, the ASRM has developed a strict set of guidelines on how to go about egg donation, and how to protect egg donors. There is no reason these standards could not be applied to any eggs used for SCNT research.

Moreover, the real goal of much of this research would be to develop a better understanding of how the egg works. Over time this would obviate or even eliminate the need for eggs to be used to develop stem cells. Any claims as to the numbers of egg donors that would be needed are frankly, speculation.

I am fearful that a negative decision may be made on somatic cell nuclear transfer that will cause needless suffering for patients with heart disease, diabetes or Parkinson's disease. Please do not make their situations worse by

enacting a new and unneeded prohibition on research just because those techniques might allow reproductive cloning to occur. As a physician I can tell you how important hope is to patients. By outlawing this very promising research you would be denying hope to millions of Americans and their loved ones.

I thank you for your time and will be happy to answer any questions.

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ETHICS COMMITTEE REPORT

Human somatic cell nuclear transfer (cloning)

The Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

Within 2 years of the announced birth in 1997 of Dolly, the lamb cloned from the mammary cells of an adult ewe, research groups announced that they had cloned mice and calves by using differentiated somatic cells (1–3). In the cloning technique used to produce Dolly, the nucleus of a somatic cell of the ewe was transferred to a sheep oocyte from which the nucleus had been removed, and the cells were fused through electrofusion to produce offspring that shared the genome of the original ewe. Research into the science of reproductive somatic cell nuclear transfer (SCNT) is proceeding as investigators clone additional species by using the original and related methods.

The prospect of using reproductive SCNT to produce human beings has evoked extensive debate among lawmakers, academicians, religious leaders, international and national agencies, professional societies, and others. Whether human reproductive SCNT will ever be undertaken will depend on such factors as the safety and efficacy of the procedure, presence or absence of governmental regulation, perceptions of procreative rights, adherence to a voluntary moratorium against human cloning, consumer interest, and the intensity and extent of ethical objections. Reproductive SCNT in laboratory animals has heretofore been inefficient in that relatively few births have resulted from many attempts. It also has been associated with harmful side effects in calves and with high fetal and neonatal death rates (4, 5). Although concerns about fetal and neonatal safety alone would make reproductive SCNT unethical for humans at present, improvements in animal cloning indicate that safety concerns may be only a temporary barrier to reproductive SCNT in humans. Moreover, researchers have proposed using SCNT to generate embryonic stem cells for persons who need tissue or organ transplants, which raises issues not addressed in this report (6). If undertaken, the development of SCNT for such therapeutic purposes, in which embryos are not transferred for pregnancy, is likely to produce knowledge that could be used to achieve reproductive SCNT (7).

Although consensus about the ethical acceptability of reproductive SCNT does not and may never exist, it is appropriate to think prospectively about the ethical issues that reproductive SCNT would raise if preclinical data suggested the procedure were safe and effective and researchers sought to conduct human trials (8). Ongoing debates about the ethics of reproductive SCNT have revealed that some observers regard human reproductive SCNT as morally unacceptable in all circumstances, others see merit in reproductive SCNT in certain circumstances, and still others await more information before making judgments about the ethical status of the procedure.

REPRODUCTIVE SCNT AS UNETHICAL

One position holds that reproductive SCNT is unethical in all situations. This belief has contributed to the passage of restrictive laws in several nations and to proposals for restrictive legislation in the United States. According to this perspective, reproductive SCNT violates deeply cherished values and traditions. With natural conception or forms of assisted reproduction other than reproductive SCNT, a child is conceived through the mixing of two lineages. With reproductive SCNT, on the other hand, a child would be created in an asexual procedure and would be given a known genome. This represents a dramatic departure

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from natural or assisted conception, and it can be compared with the production of a child to serve the needs of adults. Under this view, reproductive SCNT is more accurately seen as a form of replication than of reproduction (9).

According to this perspective, reproductive SCNT would devalue the genetic distinctiveness of each individual. It would deprive the child of a sense of mystery or right to ignorance about his or her origin (9). Moreover, it would amount to unethical experimentation on the child, who cannot consent to be conceived in a manner that poses risks to her or his health throughout life that cannot completely be addressed. For those who subscribe to this perspective, no situation would justify reproductive SCNT because the act itself is considered immoral. Some of those who object to reproductive SCNT believe that reservations about human cloning should be respected as a barometer of what is intuitively unacceptable (10).

REPRODUCTIVE SCNT AS ETHICAL

Another position defends the use of reproductive SCNT in medically based circumstances, provided that the safety of the procedure can be guaranteed (11, 12). According to this perspective, reproductive SCNT differs only in degree from other assisted reproductive technologies, and it is ethically defensible for two groups of patients: infertile couples who cannot otherwise be treated and couples at risk of passing a serious genetic disease on to their children. In the case of infertile couples, in which one or neither partner can produce gametes, two situations might apply. If the male partner cannot reproduce with his spermatozoa, reproductive SCNT with his somatic cell would enable him to have a genetic tie with the child. His partner would have a biological tie if she donates the recipient oocyte or gestates the child. If the female partner cannot reproduce with her ova, transferring the nuclear DNA from her somatic cell to an enucleated donor oocyte would allow her to have a genetic relation to the child, although her partner would not. In these situations, reproductive SCNT would allow infertile couples to conceive children who are genetically related to them, a reason that couples seek ART services. According to this perspective, reproductive SCNT would meet an infertile couple's desire to participate biologically in the development of a new human being, and it could nurture the emotional bond between the partners. If conceiving a child with the genes of at least one partner is highly important for infertile couples, or if they have reservations about using the gametes of anonymous donors, reproductive SCNT would be a welcome alternative.

In the case of couples at genetic risk, reproductive SCNT could be used to avoid passing a serious genetic disease on to their offspring. If both the male and female partners are carriers of autosomal-recessive disease traits, one partner's somatic cell could be used to conceive. If one partner has an autosomal-dominant disease, the unaffected partner's somatic cell could be used. Reproductive SCNT would offer an alternative for at-risk couples who decline to transfer only unaffected embryos after preimplantation genetic diagnosis or to terminate a pregnancy after prenatal testing and a positive result for the disease in question.

REPRODUCTIVE SCNT AS ETHICALLY UNCERTAIN

Other perspectives fall somewhere between the positions discussed above. Persons who withhold judgment about reproductive SCNT pending further information generally presume that reproductive SCNT is unethical at present because of the risks posed to the fetus and child, but they are not yet ready to approve or bar the procedure (5). They voice concern about the potential impact of reproductive SCNT on offspring, families, and society, and they are as yet unpersuaded that reproductive SCNT would serve a valid family or reproductive need.

Impact on Children

If reproductive SCNT were available, its impact on offspring would presumably vary depending on family dynamics and other features of each situation. The effect could be inconsequential, or it could be positive if the child proudly shared the genome of a beloved parent and enjoyed a special kinship with that parent. Although the child would share the parent's nuclear DNA, the child would be an individual in his or her own right because the child would experience unique circumstances of gestation, rearing, and education. In addition, the child would grow in a singular uterine environment and inherit the mitochondrial DNA of the ooctye donor. Barring unforeseen effects resulting from the use of an adult genome, such as premature aging, reproductive SCNT would probably produce a healthy child if healthy adults were somatic cell donors (13).

The effect of reproductive SCNT may also be harmful for children. Despite counseling to the contrary, rearing parents might harbor undue expectations about the child's personality or believe that the child should be identical to the somatic cell donor. This risk is more likely if a fertile couple sought reproductive SCNT to replicate a person's genome because the couple values the donor's genetic traits, but it is also a risk if reproductive SCNT were used by infertile couples. In either case, harmful typecasting might result. Reproductive SCNT might also give children who know the traits of their genome donors too much information or unrealistic expectations about the future, which would be an especially acute problem if the older cell source had a genetic illness. If no limits were placed on the justifications for SCNT or on those who might act as genome sources, the issues could multiply. Separate issues would arise if the child were conceived with the cell of an existing child, deceased child or adult, living relative, or anonymous donor. Although the impact on the

child in each situation is unknown, the prospect of unfair pressures and expectations that would hinder the child's emotional growth underscores the importance of considering the child's interests in forging a unique identity when weighing the ethical acceptability of reproductive SCNT.

Impact on Couples and Families

Another set of issues involves the impact of reproductive SCNT on couples and families. The birth of a long-awaited child for couples experiencing infertility or genetic risk might have positive effects in families in which genetic relatedness is highly valued. On the other hand, reproductive SCNT would create the new relationship of a person being raised by a genetic twin who is also the social parent. Although this need not be injurious, the birth of a child who shares the genome of one parent might contribute to feelings of inadequacy among siblings who do not share a parent's genome or feelings of superiority by the child who does.

A situation in which partners have different degrees of genetic relatedness to a child may or may not be troublesome. This is not unlike situations in which a family's children have different genetic backgrounds because of remarriage or conception with gamete donation. This new possibility, however, underscores the unknown impact of reproductive SCNT on the family. Reproductive SCNT also raises questions about who is related to whom and about privileges and responsibilities in the event of divorce. Although these outcomes could be addressed through contract or legislation, they would raise additional complications beyond those that exist in gamete donation, embryo freezing, and surrogacy.

Additional concerns would arise if the procedure were widely used in various settings. Reproductive SCNT might be sought by fertile persons who lack a reproductive partner and prefer not to use donor gametes. Individual persons or couples who have no medically based reason for using reproductive SCNT might seek the technique to select a particular somatic cell donor with traits they admire. Depending on the numbers of procedures performed, SCNT might have unsettling effects on relations between the sexes and on families if people had the option of not combining their genes with those of another person. Although some see procreation by unmarried persons as a welcome and justified extension of procreative liberty, others are dismayed by what they perceive as the erosion of the two-parent family. Widely accessible reproductive SCNT might accelerate this erosion.

Impact on Society

If SCNT were limited only to couples who were infertile or at genetic risk, it might be done so infrequently as to have little societal impact. Demand for what would likely be a labor-intensive and costly procedure might be low, especially given advances in other forms of infertility treatment.

On the other hand, there is no guarantee that the use of reproductive SCNT would be carefully constrained. Its use on a broad scale would touch fundamental values that would warrant careful exploration before any clinical application is attempted. An often expressed concern is that prospective parents would seek somatic cell donors on the basis of their exemplary traits and that potential donors would market themselves as high-caliber genome sources. The seeking and offering of genomes might introduce an additional element of marketing to procreation. The eugenic practice of deliberately seeking persons who are perceived to be superior gene sources might promote a genetic determinism that devalues the unique capacity of each individual for personal growth. Reproductive SCNT might also perpetuate an undue emphasis on genetic relatedness. If done on a wide scale, some suggest, it could restrict genetic diversity and impair the ability of humans to adapt to a changing environment (14).

SUMMARY

Given the breadth and intensity of ethical concerns expressed globally about reproductive SCNT, it is important that caution be exercised before clinical use of this procedure is considered, even if safety concerns are adequately addressed. Even if a successful argument could be made for reproductive SCNT in particular situations, it is not clear that offering reproductive SCNT generally would be justified. Nevertheless, it does not necessarily follow that the procedure should be foreclosed permanently. There is not yet clear consensus that reproductive SCNT in cases of infertility serves a compelling need. If there were, additional problems would still need to be addressed, such as the need for counseling of couples and decisions about what to disclose to the child. Nor is there clear consensus on a compelling need to bar the technique.

As long as the safety of reproductive SCNT is uncertain, ethical issues have been insufficiently explored, and infertile couples have alternatives for conception, the use of reproductive SCNT by medical professionals does not meet standards of ethical acceptability. This situation does not, however, preclude research into therapeutic SCNT that does not involve transferring embryos to the uterus, provided that ethical procedures for conducting research are followed (15). Nor does a moratorium on reproductive SCNT remove the need to study more carefully the ethical implications of cloning, especially for infertile couples.

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ETHICS COMMITTEE REPORT

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Financial incentives in recruitment of oocyte donors

The Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

During the last decade, oocyte donation has increasingly been accepted as a method of assisting women without healthy oocytes to have children. Besides coordinating the voluntary and unpaid donation of oocytes from friends and relatives, a number of programs offer financial incentives to prospective oocyte donors. These remunerations take the form of monetary payment to donors or reduced IVF fees to women undergoing IVF who agree to provide oocytes to others. Programs also provide services to couples who have recruited their own donors through offers of payment.

The use of financial incentives raises two ethical questions: [1] do recruitment practices incorporating such incentives sufficiently protect the interests of oocyte donors? and [2] do financial incentives devalue human life by treating oocytes as property or commodities?

When oocyte donation first became clinically available, clinicians expected that donor oocytes would be provided by three groups: [1] women undergoing IVF who produced more oocytes than necessary for their own use, [2] women undergoing ovarian superovulation whose oocytes could be retrieved during an unrelated surgical procedure, and [3] women who agreed to undergo ovarian superovulation and oocyte retrieval to provide oocytes to others.

When embryo cryopreservation became available, however, most women in the first group preferred to have oocytes fertilized and embryos stored for their own future use. In addition, most women in the second group were unwilling to accept the burdens associated with ovarian superovulation and monitoring or were excluded from donating for medical reasons. To secure an adequate supply of donor oocytes, many IVF programs now offer financial incentives to potential oocyte donors in the first and third groups.

TYPES OF INCENTIVES

Two types of financial incentives are common. One is monetary compensation offered to women who undergo superovulation and retrieval procedures for the sole purpose of providing donor oocytes. Another form of financial incentive involves an arrangement known as oocyte sharing. In this arrangement, a woman undergoing IVF is charged a lower fee for that procedure in exchange for providing some of her oocytes to another woman.

A survey published in 1993 found approximately 60% of responding programs offered payment to women undergoing oocyte retrieval solely to provide oocytes to others (1). In 1997, 78% of the 335 assisted reproduction programs reporting to the ASRM/SART registry stated that they offered oocyte donation services and 23% of these programs reported offering the option of oocyte sharing (2).

Although there is some variation in compensation arrangements, they have certain features in common. Programs, infertile couples, and independent agencies recruit women for oocyte donation through advertising, often through notices in college or other local newspapers. By early 1999, some IVF programs reportedly offered as much as $5,000 for one retrieval, although $2,500 appeared to be more common. Regional influences seem to account for these differences. Although these payments have not been verified, much higher sums—$50,000 or more—have been offered in print and Internet advertisements placed by couples or entrepreneurs seeking oocytes from women with specific physical characteristics and intellectual abilities.

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Few detailed descriptions of U.S. oocyte-sharing programs have been published. It seems that IVF patients in these sharing arrangements generally donate up to half the oocytes retrieved in a single cycle to another patient, in return for a 50%–60% reduction in the total costs of the IVF cycle (3). Oocyte-sharing programs reportedly exist in a number of other countries, including the United Kingdom, Israel, Denmark, Australia, Spain, and Greece (4).

ETHICAL CONCERNS RAISED BY FINANCIAL INCENTIVES

Both types of financial incentives create the possibility of undue inducement and exploitation in the oocyte donation process. College students and other women may agree to provide oocytes in response to financial need. High payments could lead some prospective donors to conceal medical information relevant to their own health or that of their biological offspring. Patients undergoing IVF who cannot afford a full procedure may, because of their overwhelming desire to have children, consent to share oocytes without careful consideration of risks and burdens. With both types of financial incentives, there is a possibility that women will discount the physical and emotional risks of oocyte donation out of eagerness to address their financial situations or their infertility problems. Financial incentives also could be challenged on grounds that they conflict with the prevailing belief that gametes ought not become products bought and sold in the marketplace.

Concerns Raised by Payment

Women undergoing retrieval purely to provide oocytes to others are exposed to physical and psychological burdens they would not otherwise face. There is some risk of unintentional pregnancy, because hormonal contraceptives must be discontinued for donation to occur. Donors also are exposed to morbidity risks and a remote mortality risk from superovulation and oocyte retrieval. Although the data are unclear at this time, it is possible that fertility drugs and oocyte donation procedures could increase a woman's future health risks, including the risk of impaired fertility (5). Young women may be prone to dismiss the potential psychological consequences of donation, particularly those that could arise if they later experience infertility problems themselves. In addition, they may underestimate the psychological and legal consequences of their agreement to forgo parental rights and future contact with children born to oocyte recipients.

Another ethical concern is that payment for oocytes implies that they are property or commodities and thus devalues human life. Many people believe that payment to individuals for reproductive and other tissues is inconsistent with maintaining important values related to respect for human life and dignity. This view is reflected in state and federal laws prohibiting direct payment to individuals providing organs and tissues for transplantation. Yet such laws generally permit organ and tissue donors to receive reimbursement for expenses and other costs associated with the donation procedure. In biomedical research, another practice with some similarities to oocyte donation, human subjects exposed to physical and psychological risks are often reimbursed for expenses. Moreover, they may receive additional payments to compensate for the time and inconvenience associated with study participation.

Compensation based on a reasonable assessment of the time, inconvenience, and discomfort associated with oocyte retrieval can be distinguished from payment for the oocytes themselves. Payment based on such an assessment is also consistent with employment and other situations in which individuals are compensated for activities demanding time and physical effort.

As payments to women providing oocytes increase in amount, the ethical concerns increase as well. The higher the payment, the greater the possibility that women will discount risks. High payments, particularly for women with specific characteristics, also convey the idea that oocytes are commercial property. Moreover, high payments are disturbing because they could be used to promote the birth of persons with traits deemed socially desirable, which is a form of positive eugenics. Such efforts to enhance offspring are morally troubling because they objectify children rather than assign them intrinsic dignity and worth. Finally, high payments could make donor oocytes available only to the very wealthy.

Concerns Raised by Oocyte Sharing

Women participating in oocyte-sharing programs undergo ovarian superovulation and oocyte retrieval for their own benefit and to assist the oocyte recipient. Yet oocyte sharing presents the possibility of added burdens to such women. In some cases, few oocytes may be produced. Donors with few oocytes available for the initial IVF cycle may have their chances of pregnancy reduced. All donors will have fewer oocytes to create embryos for their own possible later use; thus, some may need to undergo additional superovulation and retrieval procedures.

Donors in oocyte-sharing programs also may be required to undergo the additional medical and psychological screening required of oocyte donors. They also may experience extra psychological burdens. A donor who remains childless may feel added distress based on her knowledge that another couple may become the parents of a child genetically related to her. In a 1997 British survey, 8% of 79 donors who failed to become pregnant reported experiencing such distress (4).

Oocyte sharing also raises concerns related to commodification of human life. Women undergoing IVF with the hope of having their own children receive a financial benefit in exchange for providing oocytes to others. Critics of oocyte

sharing argue that it involves "an indirect form of egg—and ultimately child—buying" (6).

Women undergoing IVF who agree to share oocytes accept the added time, inconvenience, and discomfort associated with the enhanced medical and psychological screening accompanying oocyte donation. It could be argued that the reduction in their IVF costs is payment for these and other added burdens entailed in sharing oocytes, rather than for the oocytes themselves. This characterization is somewhat strained, however. The preferable approach is to acknowledge the potential for commercialization inherent in such arrangements and to consider whether the benefit of expanded access to IVF is sufficient to override this moral concern.

JUSTIFICATIONS FOR PERMITTING FINANCIAL INCENTIVES

Although potential harm must be acknowledged and addressed, financial incentives may be defended on ethical grounds. First, providing financial incentives increases the number of oocyte donors, which in turn allows more infertile persons to have children. Second, the provision of financial or in-kind benefits does not necessarily discourage altruistic motivations; indeed, in surveys of women receiving such benefits, most reported that helping childless persons remained a significant factor in their decisions to donate (4, 7). Third, financial incentives may be defended on grounds that they advance the ethical goal of fairness to donors. From this perspective, women who agree to provide oocytes to others ought be given the opportunity to benefit from their action.

The failure to provide financial or in-kind benefits to oocyte donors would arguably demean their significant contribution. Such an approach also would treat female gamete donors differently from sperm donors, who typically receive a financial benefit (albeit a modest one) for a much less risky and intrusive procedure. Fourth, the pressures created by financial incentives do not necessarily exceed and may be less than those experienced by women asked to make altruistic donations to relatives or friends.

Although the physical and psychological risks entailed in oocyte donation are real, they are not so severe as to justify intervention to limit the decision-making authority of adult women. Programs offering financial incentives should take steps to minimize the possibility of undue influence and exploitation by incorporating certain safeguards into the disclosure and counseling process. Programs can also structure the provision of incentives in ways that reduce the likelihood that women will be improperly influenced to donate. Such steps would reflect good ethical practice and reduce the likelihood of later legal action by dissatisfied donors.

DISCLOSURE AND COUNSELING

To discourage improper decisions to donate oocytes, programs should adopt an effective information disclosure and counseling process. Regardless of how prospective donors are recruited, programs should ensure that they receive accurate and meaningful information on the potential physical, psychological, and legal effects of oocyte retrieval and donation. The potential negative health and psychological consequences should be openly acknowledged. Prospective donors should understand the measures they must take to avoid unwanted pregnancy during a stimulation cycle. They also should understand that they could later develop desires to establish contact with genetically related children, desires that may be difficult or impossible to satisfy because of legal or other barriers.

Donor candidates should be encouraged to explore their possible emotional responses, particularly those that could develop if they have infertility problems themselves. To reduce the incidence of subsequent psychological problems, it would be prudent to limit donors to those who are 21 or older and have the emotional maturity to make such decisions (8).

To enhance the likelihood that information relevant to donation will be fully explored, programs are encouraged to designate an individual with psychological training and expertise to counsel prospective donors (9). This individual's primary responsibilities are to ensure that the prospective oocyte donor understands and appreciates the relevant information and feels free to decide against donation if doubts arise at any point before completion of the procedure. The prospective donor's motivation should be explored during the session, with the goal of ascertaining whether she fails to appreciate the full consequences of her donation or is improperly discounting the risks because of her economic status or infertility problems. Counseling also should be provided to donor couples in oocyte-sharing programs to promote informed and voluntary decisions.

Some empirical data show that egg donors may want to know whether children are born as a result of their donations. Others may have preferences about how their donated eggs are used (10). For example, they may not want eggs to be provided to unmarried persons or unused embryos produced with their eggs to be destroyed. Program staff should discuss with prospective donors the amount of information they will be given about whether a birth occurs and any control they will have over oocyte disposition.

THE INCENTIVE STRUCTURE

Payment

Payments to women providing oocytes should be fair and not so substantial that they become undue inducements that will lead donors to discount risks. Monetary compensation

should reflect the time, inconvenience, and physical and emotional demands associated with the oocyte donation process.

A 1993 analysis estimated that oocyte donors spend 56 hours in the medical setting, undergoing interviews, counseling, and medical procedures related to the process. According to this analysis, if men receive $25 for sperm donation, which this analysis estimated as taking 1 hour, oocyte donors should receive at least $1,400 for the hours they spend in the donation process (11). In 2000, the average payment to sperm donors was $60–$75, which this analysis suggests would justify a payment of $3,360–$4,200 to oocyte donors.

The above analysis fails to consider the time spent by sperm donors undergoing interviewing and screening. Even if this additional time is taken into account, however, the lengthier time commitment of women providing oocytes supports substantially higher payments to them than to sperm donors. Moreover, because oocyte donation entails more discomfort, risk, and physical intrusion than sperm donation, sperm donor reimbursement rates may not be a good model for determining payments to women providing oocytes.

It has been suggested that compensation for oocyte donors should be given for the hours spent on medication and on clinic visits, with the hourly rate based on the mean hourly wage of persons with demographic characteristics similar to those of the donor (12). This method of establishing payment rates presents practical difficulties and arguably would be unfair to women from lower income groups.

Although there is no consensus on the precise payment that oocyte donors should receive, at this time sums of $5,000 or more require justification and sums above $10,000 go beyond what is appropriate. Programs recruiting oocyte donors and those assisting couples who have recruited their own donors should establish a level of compensation that minimizes the possibility of undue inducement of donors and the suggestion that payment is for the oocytes themselves.

Payment also should reflect the amount of time expended and the burdens of the procedures performed. Thus, a woman who withdraws for medical or other reasons should be paid a portion of the fee appropriate to the time and effort she contributed. To protect the donor's right to withdraw, oocyte recipients must accept the risk that a donor will change her mind. In no circumstances should payment be conditioned on successful retrieval of oocytes or number of oocytes retrieved. Likewise, donors should never be required to cover the costs of the interrupted cycle. To avoid putting a price on human gametes or selectively valuing particular human traits, compensation should not vary according to the number or quality of oocytes retrieved (8) or the donor's ethnic or other personal characteristics.

Oocyte Sharing

Designing a fair oocyte-sharing program requires attention to a number of issues. As noted above, the general approach is to reduce the donor's total IVF costs by about half, in exchange for a donation of half the oocytes retrieved. This appears to be a reasonable allocation of benefits and costs. Because donors are still responsible for the remaining IVF costs, the difference in fees seems not so extreme as to induce women to accept risks they would ordinarily reject. In contrast, a program that charged no IVF fee to oocyte donors would raise serious concerns about undue inducement.

At minimum, oocyte-sharing programs should formulate and disclose clear policies on how oocytes will be allocated, especially if a low number of oocytes or oocytes of varying quality are produced. If a donor is accepted into an oocyte-sharing program, the reduction in fees should not be conditioned on retrieval of a particular number of oocytes or quality of oocytes retrieved (8).

ADDITIONAL ETHICAL CONSIDERATIONS

Once the donation process begins, oocyte donors become patients owed the same duties present in the ordinary physician-patient relationship. Programs should ensure that every donor has a physician whose primary responsibility is caring for the donor. Oocyte program staff should recognize that physicians providing services to both donors and recipients could encounter conflicts in promoting the best interests of both parties and should create mechanisms ensuring equitable and fair provision of services.

Programs offering either type of financial incentive should adopt and disclose policies regarding coverage of an oocyte donor's medical costs should she experience health complications from the procedure (8). Ideally, programs should ensure that donors will be covered for any health care costs resulting from the procedure. Programs also should consider whether to make psychological services available to oocyte donors who experience subsequent distress related to the procedure.

Programs offering financial incentives should ensure that advertisements for donors are accurate and responsible. If financial or other benefits are noted in advertisements, the existence of risks and burdens also should be acknowledged. Donors independently recruited by prospective oocyte recipients or agencies should undergo the same disclosure and counseling process as donors recruited by the program. If donors have been independently recruited, programs should attempt to ascertain whether excessive or improper incentives were offered. Programs should refuse to participate if prospective oocyte recipients or recruiting agencies have offered excessive payment that could compromise the donor's free choice or have engaged in other ethically inappropriate conduct. Programs should adopt procedures and standards for determining when independent recruitment arrangements involve unacceptable payment.

To limit the health risks of donation and to avoid inad-

vertent consanguinity among offspring, programs should limit the number of times a woman may undergo retrieval procedures purely to provide oocytes to others (8, 13). A good faith effort should be made to avoid accepting women who have already made a high number of donations elsewhere. Finally, all IVF programs offering oocyte donation should encourage further study of the medical and psychological effects on donors. Findings from such research could improve evaluation of risks and benefits and allow programs to provide more accurate information to prospective donors.

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Mr. SOUDER. Dr. Zavos.

Mr. ZAVOS. Good afternoon, everyone. Thank you, Mr. Chairman, for inviting me for this very interesting session.

I am a reproductive specialist and scientist that has dedicated the last 24 years of my life in helping infertile couples have children and complete their biological cycle. I care about couples suffering from infertility. Do you care about infertility?

Infertility affects approximately 10 to 15 percent of the couples of reproductive age throughout the developing world. There are 10 to 12 million infertile couples in the United States alone. Assisted reproductive technologies have played a major role in treating various causes of infertility. In fact, about 65 percent of the couples who seek medical help will eventually succeed in having a child. However, in cases where there are no sperm or eggs present, possibly due to loss of testicular or ovarian function, for those couples, they must go to other options such as sperm donation, oocyte donation, or adoption.

If you care about these unfortunate infertile couples, why are you considering legislation that would make both them and the people that are trying to help them criminals? Criminalizing human reproductive cloning in the United States will only make it less safe and more costly for these infertile couples. They will be forced to travel outside the United States to pursue their dream of creating a family.

After all, according to the Americans with Disabilities Act, infertility is a disability, and reproduction is major life activity for purposes of the ADA. In light of this, it is the right of each and every American citizen to bear a child.

Cloning cannot be curbed. Mr. Chairman, experts state repeatedly, and history proves the point very clearly, that scientists will clone, even if President Bush and the Congress will ban it. The House of Representatives may vote against human cloning, but that will not stop scientists from doing it and people from wanting it.

In the words of an infertility patient who wants her own genetic baby so badly that she would go wherever she had to in order to clone either herself or her husband, "If they called me right now and said, 'We are paying for everything and giving you the chance to have your own genetic child,' I would be on the plane so fast it is not even funny."

In the words of a bioethicist, "The best way to control this research is to fund it by the Federal Government, because then you create rules and regulate it."

In my words, Mr. Chairman, the genie is out of the bottle and it keeps getting bigger every day. There is no way this genie is going back into the bottle. Let us find ways to develop it properly and disseminate it safely.

If you are concerned about the risks of human cloning, the proper approach is to fund it and then institute regulations that will ensure that human cloning is done properly, with a minimum of risks to the baby, just as is done in other medical and drug innovations. This is what our team is working on, and we will not go forward with human cloning until the risks are comparable with other IVF procedures.

We have no intentions of doing this in the U.S.A., whether any legislation is passed for or against this technology. Furthermore, Mr. Chairman, we have no intentions of breaking the laws of this country or any other country to accomplish this. We are law-abiding citizens of this great Nation of ours, but we are a compassionate group of people that wish to help our fellow men and women to have the gift of life, the gift of life that most of us have been so fortunate to have to enjoy and take for granted. Let us not be so uncompassionate and so insensitive to tell those people that we are not willing to listen to them and are unwilling to help them. This is not what our country's Constitution and principles are all about. We believe in creating families, not preventing them. In God we trust.

Reproductive Regeneration as a Means of Infertility Treatment. It is quite evident to us, along with other competent human reproductive specialists, that with further elucidation of the mechanisms involved during the process of embryogenesis, careful tailoring of subsequently developed culture conditions and manipulation strategies, and appropriate screening methods, will eventually allow infertile couples to safely have healthy, genetically related children through somatic cell nuclear transfer methods.

The Opponents of Human Cloning or Reproductive Regeneration. The most prominent opponents to human reproductive regeneration and spokesmen for animal cloning are Drs. Ian Wilmut from the Roslin Institute and Rudolph Jaenisch from the Massachusetts Institute of Technology, MIT, who have misled and have misdirected the public and its leadership for their very own gains, whatever those gains might be.

If one reviews the animal cloning literature, which is so eloquently alluded to as being totally destructive in your opening statements today, Mr. Chairman, I must tell you that one can deduce that the poor cloning success rates noted by "the animal cloners" are mainly due to experiments that are poorly designed, poorly executed, approached, understood, and interpreted, and these experiments were mostly done under nonsterile and uncontrolled conditions and environments and having a hit-and-miss type of an outcome.

According to a recent article in Time Magazine, Wilmut and Jaenisch stated that animal cloning is inefficient and is likely to remain so for the foreseeable future. On the contrary, a number of studies have already demonstrated far higher rates of success, and in some cases, matching or exceeding success noted in human IVF today.

Interestingly enough, and this is especially for the Congressman from Florida to listen, the Roslin Institute scientists who cloned Dolly the sheep and had so many problems with the sheep that they have cloned that they have changed their agenda today on the cloning subject and have stated recently that they plan to seek permission to experiment on cloned human embryos for medical purposes. What are their true motives? What are they?

Animal Cloning vs Human Reproductive Regeneration. It has been very clearly shown that animal cloning and its difficulties appear to be species-specific. The data cannot be extrapolated with a great degree of accuracy to the human species. In a recent study

by scientists from Duke University, it was demonstrated that it may be technically easier and safer to reproduce somatic cell nuclear transfers in humans than in sheep, cows, pigs, and mice because humans possess a genetic benefit that prevents fetal overgrowth, one of the major obstacles in cloning animals.

The Political Status on Cloning. The political situation with cloning in general remains very fluid, Mr. Chairman, today mainly because of the inability of the politicians to understand, comprehend, and act decisively on the issues that cloning presents to society. After all, their inability to act decisively may have a great deal to do with their resistance to debate and face the facts that humans will be cloned.

Recent statements by the President of the U.S.A., Mr. George Bush, in his speech to the American public President Bush made an appeal for a global ban on cloning, whether it may be for therapeutic or reproductive cloning, on the basis that we should not use people for spare parts and we should not manufacture people.

Reproductive cloning, Mr. Chairman, does neither. Quoting President Bush, "Life is a creation, not a commodity. Our children are gifts to be loved and protected, not products to be designed and manufactured. Allowing cloning would be taking a significant step toward a society in which human beings are grown for spare body parts and children are engineered to custom specifications, and that's not acceptable."

And that is not acceptable to us either, Mr. Chairman. We agree with President Bush on the sanctity of human life. Reproductive cloning does not involved a destruction of human embryos, nor does it modify or engineer the genetic code to custom modifications. Reproductive cloning is nothing more than another modality for the treatment of human infertility and giving the gift of life to childless couples that have exhausted all other choices for having a child. What is so wrong about that?

History tends to repeat itself. This is not the first time that the scientific community has had to deal with controversial issues regarding new technologies. Exactly the same thing happened with IVF in the Kennedy Institute in Washington in 1978, when Professor Robert Edwards and Dr. Patrick Steptoe were faced with such criticism; 24 years later, the exact opposite of everything the experts predicted happened: IVF today is synonymous to sliced bread.

In conclusion, Mr. Chairman, I would like to say the following. As Professor Robert Edwards, the great English scientist, who I have great respect for and who helped create the world's first test tube baby, Louise Brown, in 1978, so eloquently prophesied recently, saying the following, "Cloning, too, will probably come to be accepted as a reproductive tool if it is carefully controlled."

It is your responsibility, Mr. Chairman, to control this, with the guidelines via which this can be developed, but it will be developed. Mr. Chairman, science has been very good to us, and we should not abandon it now. Consider why America has the best medical care in the world. It is because we have the freedom to investigate, research, and market the latest medical techniques, all within proper procedures and safeguards.

This is not the time to panic and try to turn back the clock. The genie is already out of the bottle. Let us make sure it works for

us, not against us. Let us do it right, and let us do it here. By banning cloning, America will be showing the world that she is hesitant and/or reluctant to take the lead in this new arena of technological advancement. The world today is looking at the most powerful Nation on Earth for leadership on this issue. And walking away from it, banning it, is not a sign of leadership but cowardice.

Do not let the future of this technology slip away from our fingers because we are too afraid to embrace it. I believe that it is the right of the American people to choose whether or not they want to have this technology available to them. Let us educate ourselves and debate the issues, and not make irrational decisions based upon fear of a new technology.

Banning this technology would not only give our enemies license to use it to their advantage, and that is really pretty much one of the important aspects of it, but let us learn from history, Mr. Chairman and forge ahead in this brave new world as leaders, not spectators. That is the American way. Thank you very much.

Mr. SOUDER. Thank you.

[The prepared statement of Mr. Zavos follows:]

Testimony before the House Subcommittee on Criminal Justice, Drug Policy, and Human Resources

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Introduction

I am a Reproductive Specialist and Scientist that has dedicated the last 24 years of my life in helping infertile couples have children and complete their biological cycle (see Attachment). In January 2001, we have announced the possibility of using reproductive regeneration technologies as a means of treating infertility, and our intention to develop these technologies in a safe and responsible manner. However, we have received great opposition from fellow scientists, news media and the general public. It seems that the great opposition is due to the lack of complete understanding and comprehension of what in actuality human cloning really is all about. The British Medical Association however, has so appropriately stated: "Public hostility to human reproductive cloning may be based on an illogical transient fear of a new technology". Much of the confusion is caused by the variance in opinions coming from different scientific sources, politicians, news media and Hollywood. Due to the limited knowledge of these technological and medical procedures in the Scientific Community, we have organized, hosted and attended meetings involving scientists from all over the world to discuss and debate the issues of human reproductive regeneration (1). We have even presented our intentions before the Congress of the United States last year.

Do You Care About Infertility?

Infertility affects approximately 10-15% of couples of reproductive age throughout the developing world. Assisted Reproductive Technologies (ART) have played a major role in treating various causes of infertility. In fact, about 65% of the couples who seek medical help will eventually succeed in having a child. However, in cases where there are no sperm or eggs present (possibly due to loss of testicular or ovarian function), the only options these couples face are sperm donation, oocyte donation or adoption. These are difficult choices for couples to make and many do not want to use sperm or egg sources other than their own or do not wish to consider adoption. Reproductive regeneration (RR), which is synonymous to reproductive cloning, can therefore play a very real role in the treatment of severe male or female infertility in couples that wish to have their own biological children.

After a lot of time, money and suffering, many of the infertile couples have been able to have children using present IVF techniques. Personally, it has given me great satisfaction to assist them in the creation of their own families. However, some of these infertile couples have not been able to experience the joy of creating their own families because the present technologies are not advanced enough to help them. For them, human reproductive cloning is the only way they can have their own children. As a Reproductive Specialist and a scientist who cares about their plight, I am trying to develop safe techniques of human cloning so they can have the healthy babies they want. Mr. Chairman, am I wrong in wanting to help couples become parents?

If you care about these unfortunate infertile couples, why are you considering legislation that would make both them and the people that are trying to help them, criminals? Criminalizing human reproductive cloning in the United States will

only make it less safe and more costly for these infertile couples. They will be forced to travel outside the United States to pursue their dream of creating a family. After all, according to the Americans with Disabilities Act (ADA), infertility is a disability and reproduction is a major life activity for the purposes of the ADA (Bragdon v. Abbott, 118 S.Ct 2196; 1998). In light of this, it is the right of each and every American citizen to bear a child.

Cloning cannot be Curbed

Mr. Chairman, experts state repeatedly that history proves the point very clearly that scientists will clone even if President Bush and the Congress forbid it. The House of Representatives may vote against human cloning but that will not stop scientists from doing it and people from wanting it. The American Society for Reproductive Medicine (ASRM) of which I am a long standing member of, recently stated that "thousands of years of human experience have shown us that governments cannot bottle up human progress, even when you want to"and that "there is every reason to believe that if passed, this kind of prohibition would not be effective". In another case made by a infertility patient, who wants her own genetic baby so badly that she would go wherever she had to, in order to clone either herself or her husband "if they called me right now and said, 'We're paying for everything and giving you the chance to have your own genetic child,' I would be on a plane so fast it's not even funny," she said. In the words of a bioethicist "The best way to control this research is to fund it by the federal government, because then you create rules," and in my words Mr. Chairman, this Genie is out of the bottle and it keeps getting bigger by the hour. There is no way that this Genie is going back into the bottle. Let us find ways to develop it properly and disseminate it safely.

Banning human reproductive cloning in the United States will not stop human cloning. In fact, the first cloned pregnancy may have occurred already. If you institute a ban, all that will happen is exactly what happened when the first IVF baby was born in 1978. The United States banned IVF when it first came out and then after several years, decided it had made a mistake and spent the next several years catching up with the technology that was advanced in other countries. The only people that suffered were the infertile U. S. couples who were unable to have children or had to travel outside of the United States to receive these treatments. Let us show the proper compassion for those suffering American infertile couples. Let us give them some hope and let us not turn our backs on them. They deserve something better than that.

If you are concerned about the risks of human cloning, the proper approach is to fund it and then institute regulations that will insure that human cloning is done properly with a minimum of risk for the baby just as is done in other medical or drug innovations. This is what our team is working on and we will not go forward with human cloning until the risks are comparable with other IVF procedures. Of course, because of the present political climate in the United States, we have been forced to look elsewhere in the world for a proper venue. We have no intentions of doing this in the USA whether any legislation is passed for or against this technology. Furthermore, Mr. Chairman, we have no intentions of breaking the laws of this country or any other country to accomplish this. We are law abiding citizens of this great Nation of ours, but we are compassionate group of people that wish to help our fellow man and woman have the gift of life. The gift of life that most of us have been so fortunate to have, enjoy and take for granted. Let us not be so uncompassionate and so insensitive to tell those people that we are not willing to listen to them and unwilling to help them. This is not what our Country's constitution and principles are based on. We believe in creating families, not preventing them. In God we trust!

Reproductive Regeneration as a Means of Infertility Treatment

The incidence of developmental abnormalities following natural sexual reproduction in humans is 3% and is significantly higher when maternal age is over 40. As recently reported in the New England Journal of Medicine, the risks are even greater from IVF and other more advanced ART procedures yielding more than 30,000 children per year in the USA. It is vividly clear that thousands of potential parents accept these risks to conceive a child. If human reproductive regeneration is banned as a reproductive technique on safety grounds, then we may find ourselves in the untenable position of having banned all reproductive techniques which suffer equal or higher risks, thereby, possibly even banning natural sexual reproduction with its 3% risk, a situation that the majority of people would consider ridiculous. It appears reasonable to suggest that the incidence of developmental abnormalities as to the safety of human reproductive regeneration is negligible when compared to current risks associated with IVF and other ART procedures.

It is quite evident to us along with other competent human reproductive specialists that with further elucidation of the molecular mechanisms involved during the processes of embryogenesis, careful tailoring of subsequently developed culture conditions and manipulation strategies, and appropriate screening methods, will eventually allow infertile couples to safely have healthy, genetically related children through SCNT methods.

The opponents of Human Cloning or Reproductive Regeneration

The most prominent opponents to human reproductive regeneration and spokesmen for animal cloning are Drs. Ian Wilmut from the Roslin Institute and Rudolph Jaenisch from the Massachusetts Institute of Technology (MIT), who have misled and have misdirected the public and its leadership for their very own gains, whatever those gains might be. They have repeatedly stated that the application of animal cloning technologies to humans, is extremely dangerous, not because of ethical and social implications, but because of the foreseeable possibility that cloning humans might result in a very high incidence of developmental abnormalities, large offspring syndrome (LOS), placental malfunctions, respiratory distress and circulatory problems, the most common causes of neonatal death in animals (2). They also noted that the rate of success as an ART method is extremely low, being only 3%. Furthermore, they state that because since the production of Dolly the sheep in 1995, they have not improve on these technologies themselves, they have concluded that reproductive regeneration is not safe and efficient for use in humans, and would like for the world to believe this. Let us examine the facts as they appear.

If one reviews the animal cloning literature, one can deduce that the poor cloning success rates noted by the "animal cloners" are mainly due to experiments that were (i) poorly designed, (ii) poorly executed, (iii) poorly approached, and (iv) poorly understood and interpreted. These experiments were mostly done under non-sterile and uncontrolled environments and having a "hit-and-miss" type of outcome. Also, when the cloned animals died, no clear view of their cause of death was ascertained. In short, their experimentation methods lacked the seriousness of purpose that is vital when performing similar studies in humans. Furthermore, the same scientists responsible for Dolly, the sheep, now plan to utilize similar crude technologies to experiment on cloned human embryos for medical purposes.

According to a recent article in Time Magazine (3), Wilmut and Jaenisch stated "animal cloning is inefficient and is likely to remain so for the foreseeable future". On the contrary, a number of studies have already demonstrated far higher rates of success and, in some cases, matching or exceeding successes noted in human IVF today. Also, if history is any indicator, one can reasonably expect that further refinements to the cloning process will improve efficiency rates. Scientists have reported success rates of 32% in goats and 80% in cows since 1998, as opposed to the poor 3% success rate Wilmut obtained when cloning Dolly in 1995. Furthermore, scientists at Advanced Cell Technologies in Worcester, Massachusetts, in association with others, have recently produced 24 cloned cows, that were all normal and healthy and have survived to adulthood (4). Despite the overwhelming data that exists showing refinements in the RR technology that yield improving success rates, Wilmut and Jaenisch still insist that it is inefficient based upon their poor success using very crude and uncontrolled experimental techniques , almost seven years ago. One can only but question their motives for their illogical arguments. They do not seem interested in developing and refining techniques, but they rather seem to have immense private interests and want to patent and control the technologies for themselves. Interestingly enough, the Roslin Institute scientists who cloned Dolly the sheep have changed their agenda on the cloning subject and have stated recently that they plan to seek permission to experiment on cloned human embryos for medical purposes. What are their true motives?

Animal Cloning vs. Human Reproductive Regeneration

It has been very clearly shown that animal cloning and its difficulties appear to be species-specific, and the data cannot be extrapolated with a great degree of accuracy to the human species. In a recent study by scientists from Duke University Medical Center, it was demonstrated that it may be technically easier and safer to perform somatic cell nuclear transfer (SCNT) in humans than in sheep cows, pigs, and mice because humans possess a genetic benefit that prevents fetal overgrowth, one of the major obstacles encountered in cloning animals (5).

The genetic benefit is based on the fact that humans and other primates possess two activated copies of a gene called insulin like growth factor II receptor (IGF2R). Offspring receive one functional copy from each parent as expected. However sheep, pigs, mice and virtually all non-primate mammals receive only one functional copy of this gene because of a rare phenomenon known as genomic imprinting in which the gene is literally stamped with marking that turn off its function. Since humans are not imprinted at IGF2R, then fetal overgrowth would not be predicted to occur if humans were cloned. If this theory is correct, the incidence of developmental abnormalities following human SCNT would be significantly lower. Also, the authors concluded that the data showed that one does not necessarily have these problems in humans. This is the first concrete genetic data showing that the cloning process could be less complicated in humans than in sheep.

The political Status on Cloning

In the United States, the House passed in July, 2001the Weldon Bill or the Human Cloning Prohibition Act of 2001 (bill H.R. 2505). This bill would prohibit any person or entity, in or affecting interstate commerce, from (i) performing or attempting to perform human cloning, (ii) participating in such an attempt, (iii) shipping or receiving the product of human cloning, or (iv) importing such a product. The bill currently pending in the US Senate, S 790, written by Sen, Sam Brownback (R Kansas), would criminalize all cloning with a fine of up to $1 million and 10 years in prison and it is almost identical to the bill (H.R. 2505) passed by the House in July 2001. The Council of Europe has introduced a protocol that prevents any abuses of such techniques by applying them to humans, banning "any intervention seeking to create a human being genetically identical to another human being, whether living or dead". Finally, the Protocol leaves it to countries' domestic law to define the scope of the term "human being". In April 24, 2001, England has banned "reproductive regeneration" but not "therapeutic cloning".

The political situation with cloning in general remains very fluid, mainly because of the inability of the politicians to understand, comprehend and act decisively on the issues that cloning presents to society. After all, their inability to act decisively may have a great deal to do with their resistance to debate and face the facts that humans will be cloned.

Recent Statements by President Bush

In his speech to the American public, President Bush made an appeal for a global ban on cloning, whether it be for therapeutic or reproductive cloning, on the basis that we should not use people for "spare parts" and we should not "manufacture people". Reproductive cloning does neither. As opposed to therapeutic cloning which results in the inevitable death of an embryo once the stem cells have been removed, reproductive cloning aims to protect and preserve life in allowing the embryo to grow and be implanted into the uterus for a subsequent pregnancy. From an ethical point of view, there is no destruction of life.

Quoting President Bush: "Life is a creation, not a commodity. Our children are gifts to be loved and protected, not products to be designed and manufactured. Allowing cloning would be taking a significant step toward a society in which human beings are grown for spare body parts, and children are engineered to custom specifications; and that's not acceptable." And that's not acceptable to us either, Mr. Chairman! We agree with President Bush and uphold the sanctity of human life. Reproductive cloning does not involve the destruction of human embryos, nor does it modify or "engineer" the genetic code to custom specifications. Reproductive cloning involves employment of similar technology used for Intra cytoplasmic Sperm Injection (ICSI), which is routinely employed in IVF centers throughout the World. The only difference is that instead of using a sperm cell from the father, scientists can use a somatic cell nucleus and inject it into

the mother's anucleated egg. The resulting embryo would have its genetic makeup from the father, but the expression of the genetic code and characteristics and personality of the baby born will be completely different and unique. Reproductive cloning is nothing more than another modality for the treatment of human infertility in giving the gift of life to a childless couple that have exhausted all other choices for having a child. What is so wrong about this?

Is History Repeating Itself?

This is not the first time that the scientific community has had to deal with controversial issues regarding new technologies. Exactly the same events happened with IVF in the Kennedy Institute in Washington in 1978. Professor Robert Edwards and Dr. Patrick Steptoe were faced with such criticism from hundreds of reporters, senators, judges, scientists and doctors, when they proposed the idea of in-vitro fertilization. The language and accusations were the same as what we face today, including "they ignored the sanctity of life, performed immoral experiments on the unborn", "subject to absolute moral prohibition", "no certainty that the baby won't be born without defect" and to "accept the necessity of infanticide. There are going to be a lot of mistakes" (6-11).

Twenty-four years later, the exact opposite of everything the "experts" predicted happened. IVF has become an acceptable and routine treatment of infertility worldwide. The abnormalities that were expected to have been unacceptable proved to be the same, if not less than with natural conception (11). Ironically, those critics of IVF have become the "pioneers" of IVF. These same critics might have delayed the introduction of IVF but their actions mostly harmed patients, and also the medical and scientific community. I am certain that the reproductive cloning procedures will follow in the same footsteps. Recently, I have had the opportunity to openly debate Professor Robert Winston from the UK, on the issue of human reproductive cloning at an Oxford Union Debate at Oxford University. Ironically enough, he was one of the leaders originally opposed to IVF, and who is currently a leading IVF specialist in Britain. The technology that he was vehemently opposed to, almost twenty-five years ago, is now the very same technology that he uses to earn a living. Once reproductive regeneration is commonplace in the ART treatment market, will he, along with all the other critics, "jump" on the bandwagon and offer this new technology in their own IVF centers? I believe so. They have done it before and they can do it again. Mr. Chairman, we can not afford to behave this way and most importantly wish to repeat the same mistake.

Conclusion

As Professor Robert Edwards, the great English scientist who helped create the world's first test-tube baby in 1978, so eloquently prophesied recently "Cloning, too, will probably come to be accepted as a reproductive tool if it is carefully controlled" (12). No doubt, humans will be produced via reproductive regeneration. Recent scientific and technological progress demonstrates that very clearly. Similar to IVF, the technology of reproductive regeneration will advance, techniques will be improved, and knowledge will be gained. Reproductive regeneration's difficult questions can be answered only through a dedicated pursuit of knowledge and an exercise of our willful rationality, and in the end, the answer to the debate over human nature may be simply that man's nature is the product of his own will.

Mr. Chairman, science has been very good to us and we should not abandon it now. Consider why America has the best medical care in the world. It is because we have the freedom to investigate, research and market the latest medical techniques, all within proper procedures and safeguards. This is not the time to panic and try to turn back the clock. The Genie is already out of the bottle. Let's make sure it works for us, not against us. Let's do it here. Let's do it right.
By banning cloning, America will be showing the world that she is hesitant and/or reluctant to take the lead in this new arena of technological advancement. The world today is looking at the most powerful nation on Earth for leadership on this issue, and walking away from it by banning it is not a sign of leadership, but cowardice. Do not let the future of this technology slip away through our fingers, because we are too afraid to embrace it. I believe that it is the right of the American people to choose whether or not they want to have this technology available to them. Let us educate ourselves and debate the issues and not make irrational decisions based upon fear of a new technology. Banning this technology would only give our enemies license to use it to their advantage. Let us learn from history and forge ahead in this brave new world as leaders, not spectators, the American way.

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Mr. SOUDER. I want to thank each of you for your testimony. Nobody can accuse us of not hearing all sides of debate in the first panel.

I am next going to yield to the ranking member, Mr. Cummings, for his opening statement, and then we will move to questions.

Mr. CUMMINGS. Thank you, Mr. Chairman.

Back in 1995, Congress passed legislation banning the use of Federal funds for human cloning research. Two years later, the birth of Dolly the sheep gave immediacy to the unsettling prospect of thinking, feeling, human clones also walking the Earth.

In recent years, a vigorous debate has ensued over the medical and ethical implications of all aspects of human cloning research. Last July, that debate reached the floor of the House of Representatives. When all was said and done, the House had passed legislation that would render all human cloning research efforts a criminal enterprise, including those aimed not at reproduction but exploring the potential for new medical therapies and cures to human diseases and ailments.

During the House debate, a substantial minority of Members, including myself, questioned whether closing the door to therapeutic or research cloning activity in the United States was timely or prudent. These concerns were expressed through support of a substitute amendment by Representative James Greenwood of Pennsylvania. That substitute amendment failed.

The U.S. Senate is now about to embark on a similar debate in which the same central issue will be aired: should a ban on human cloning extend to therapeutic or reproductive cloning research?

Dr. Zavos, we, too, take it very, very seriously. As a matter of fact, I think it is one of the most wrenching issues that we deal with in this Congress, because we have a debate, and on the one hand—and a lot of it is based upon religion—a lot of people feel you should not interfere with life. There are others who feel that we should try to address the issue and provide, I think as you are talking about, possible cures to diseases and trying to open up the door for research that might very well do a lot of good.

It is a wrenching issue. In this very hearing room not very long ago, we had a couple who testified they had two young children who actually needed certain—or could have benefited possibly from certain research of this nature. And it was clear that they had very little likelihood of surviving without it. They, by the way, were testifying against cloning, and it was very interesting.

On the other hand, we had some folks who felt very strongly that there was—they wanted to allow research to help other people. So this is a tough, tough issue. I do not want anyone here to go for 1 second thinking that we do not consider this matter to be a very, very serious matter.

Those who support a ban on therapeutic cloning raise a variety of objections to this research, ranging from the morality of creating embryos for research purposes to the practicality of the research to whether a partial ban can effectively be enforced.

There are, of course, counterarguments to each of these objections. Today we will hear from witnesses whose views cover the spectrum, as we have already heard, from support for reproductive

cloning at one end to a categorical opposition to all human cloning research at the other.

We will also hear testimony proposing some intermediate approaches not embodied in the current legislative proposals. I hope that the members of the subcommittee and Members of the Senate who may be paying attention will listen with an open mind.

Ultimately, this debate is about whether Congress will close off an avenue of scientific research that some reputable scientists believe may offer immense benefits to millions of people in and beyond this country, ladies and gentlemen, people who are suffering and people who will suffer in the future from a range of life-threatening and severely debilitating diseases and ailments, including diabetes, Parkinson's Disease, and spinal cord injury, to name just a few. This we should not do rashly. I think the House did act rashly last July, and I hope therefore that today's hearing will serve the constructive purpose of establishing a more thorough record that will provide for a more informed and thoughtful debate in the Senate.

To all our witnesses, we thank you. I have often said it is so pleasing to see so many young people in the room, because I have often said that our children are the living messages we send to a future we will never see. This is an issue that they will have to grapple with. We are grappling with it today, but they will grapple with it in future generations, so we have a duty to give it our very, very best thought, our very, very best research, and come to our very, very best conclusions. With that, I thank all of you for being here. Good day.

Mr. SOUDER. Thank you.

Just so you understand, this is being carried over our Government Reform channel, so that Members and their staff can see it in their offices, in addition to later on on C-Span and others. The House is in session, so it is not on regular C-Span right now.

I would like to start the questioning with Dr. Zavos.

Have you as yet produced a cloned human embryo?

Mr. ZAVOS. I'm sorry?

Mr. SOUDER. Have you as yet produced a cloned human embryo?

Mr. ZAVOS. No, sir.

Mr. SOUDER. Do you expect to be capable of impregnating a woman with a cloned human embryo in the future, the near future?

Mr. ZAVOS. The answer to that is yes.

Mr. SOUDER. The near future?

Mr. ZAVOS. There is obviously very high speculation, as you may have read in the news recently, that there may be three women pregnant already with a cloned embryo. Therefore, there might be some children born soon via reproductive cloning, as my former associate, Severino Antinori from Rome, has stated recently.

Mr. SOUDER. Are you saying you have women who are currently impregnated, or just your former colleague from Rome?

Mr. ZAVOS. I have no cloned pregnancies to announce, and I have never produced a cloned embryo as yet.

Mr. SOUDER. Do you expect to be able to do so in the near future?

Mr. ZAVOS. Yes. Our team is ready to carry on the process, and we feel like we are quite confident that we can carry this successfully.

Mr. SOUDER. Do you believe the reports from Rome are true?

Mr. ZAVOS. I'm sorry, with those cameras here——

Mr. SOUDER. Do you believe the reports from Rome are true?

Mr. ZAVOS. I don't believe those reports from Rome, no. Obviously, I have my reasons for that, and you know, obviously, I may have been born elsewhere, outside the United States, but I am still from Missouri.

Mr. SOUDER. The "show me" State, for those who may be too young to know that.

Mr. ZAVOS. Yes.

Mr. SOUDER. Would it be possible to distinguish between natural pregnancy and a clonal pregnancy, in your mind? In other words, how would the government be able to tell the difference?

Mr. ZAVOS. No. To my knowledge, no. The only way, obviously, is to DNA-test the offspring and the DNA donor, if they concede to that, of course.

Mr. SOUDER. So you believe if the bill passed that authorized reproductive cloning, there really would not be a functional way to tell the difference?

Mr. ZAVOS. No, not really. After we create an embryo, after that embryo is cloned or sexually produced via IVF or whatever, they cannot be told apart. Therefore, you know, all this speculation that goes around that we are going to be able to supervise it and do this and do that reminds me of the 1940's, of the Germans, somewhere. I hope that America does not come to that.

Mr. SOUDER. Dr. Usala, do you think the money spent on human cloning takes away research on more realistic and promising avenues for cures that could actually treat a large number of people? We have been having this debate in the halls of Congress and literally meeting in the hall. We have had this debate among a number of Members on the zero sum game. How do you think this plays out?

Dr. USALA. I feel very strongly that it would detract. I feel very strongly that if cloning were allowed, there would be a landslide of funding from the NIH and other sources to only go that route. The reason is that my colleague, Dr. Cowan, was saying, talking about Galileo. Galileo was the odd man out. He was viewed as an extremist.

The way funding really works in this country, those with original ideas do not participate in the funding from government sources.

I was part of a private company that developed this technology. I didn't ask for NIH funding until I didn't need it anymore, and the reason for that is that researchers will go where the review committees will approve grants. If cloning, if human embryonic stem cell research is viewed as a promising area, whether or not it really is, academic scientists will be drawn to it.

As an example, before 1992, the NIH and the American Diabetes Association said that there is no real evidence that type blood sugar control prevents complications in Type one diabetes. Well, we now know that wasn't true.

I have had diabetes since I was 1 year of age, and I am currently 43. The children I grew up with with diabetes are all dead because the scientists that were very respected at the NIH and the American Diabetes Association said that no control doesn't make any dif-

ference, and as a result of that, research wasn't geared for developing therapies that could help keep blood sugars in the normal range.

Now, again, I was viewed as an extremist for taking insulin shots before 10 years of age, but I am alive to tell you about this. But my point is that if we decide as a society that a therapy may be useful, and particularly if the Federal Government allows funding for it, all efforts seem to go in that direction. And it is only, "the extremists," that take others.

I have shown you preliminary data that was reviewed by the FDA, and I can assure you that FDA standards are far more stringent than just the peer review process of article publication. I was only interested in finding a cure of medical therapy for my patients; and as a result, I obtained funding from other sources.

In summation, Mr. Chairman, I think that if we do allow cloning to occur, we will be going down a path that will require years of research on only speculation.

Mr. SOUDER. Thank you.

Mr. Cummings.

Mr. CUMMINGS. Doctor, as I listen to you, I just couldn't help but think that you were the one who fought sort of out of the box; is that right?

Dr. USALA. Correct, sir.

Mr. CUMMINGS. And you would have been viewed as somebody who may have been a little radical; am I right?

Dr. USALA. That's correct.

Mr. CUMMINGS. At 43, you are still here to tell us about it. And I'm just thinking, when I look at Dr. Zavos I think he would be looked at perhaps today as being a little radical. And as I listen to you, you almost make the argument for making sure that we do try to look at things outside the box. And help me with that.

Dr. USALA. Well, I think that the Federal Government might not—it might not be the correct place for it to go down a path that seems to favor one form of therapy or another. Certainly we can't discuss the scientific validity of any of our approaches here. That would take days, weeks, months, years, and we still wouldn't come to a conclusion. But I think what we have to always remember is, is this consistent with our society?

The problem I have with using cloning for research purposes is that a human life is destroyed, and it is as simple as that. And the paradox of creating life and then mandating by law that you have to destroy it to prevent what Dr. Zavos would like to do seems to me total contradictory to the fabric of American society.

So that is my largest objection against the therapeutic cloning issue.

Mr. CUMMINGS. Thank you.

Dr. Zavos, has the existing regulatory framework, namely the FDA, been the reason why you are pursuing cloning outside the United States; and will your plans change if a ban on cloning is made into law?

Dr. ZAVOS. We don't have any intentions of changing our plans at this moment. I think we are not in the business of pitching tents anywhere that people sort of show us to do that. It is the responsible way, I think, for us as a team. We already have two places

that we could be executing this particular type of research and this project. And, therefore, we are not interested, and we have decided that.

And I testified before the Congress last year that we had decided from the beginning that America is not the best place to do this, the reason being that I think our society is the best society in the world to live in. But when it comes to subjects like that, we cannot get the Americans to agree on too many things. Therefore—there is a great deal of diversity in this country, and I don't think that we can unite the Americans on this issue. And I respect that. And we cannot afford to be disrupted by the politics and the so-called "ethical" and other rules and variables that are thrown at us.

Obviously, we remain focused on this subject and that is to clone a human for reproductive purposes, because I think it is time for that to happen. And there is no way of turning back. There are five teams in this world that I know of that are doing this right now; and I think that we—and I happen to believe that, because I know the depth of our team, we're the best ones to do this.

Mr. CUMMINGS. Dr. Cowan, we seem to have some difference of opinion among the scientists here. It gets a little hard for us to sort out these things. You are all the experts and we have to rely on you, and you all are kind of saying different things.

Should we give all of these perspectives equal weight?

Dr. COWAN. In my opinion, the differences that you hear are based on both the extremes and the main frame of research work in the United States. And I think that you have to bring all of this information together to form the opinion, but in fact, pick the straightforward pathway of what the main contingency in the United States brings forward.

The debate that emerges from the outside—no research, no cloning, all the way to cloning and research—allow us to fold this information together. And these debates are very important. It is certainly very important to hear this information, but I think that the main thrust of the information will come from the medical scientific community, yes, sir.

Mr. CUMMINGS. I know you don't have a crystal ball, but if you could, based upon what you hear and see today and the research you have done, what do you see in 20 years?

Dr. COWAN. On this subject, we will be done with embryo cloning. That process will have brought us new technology, so we don't need to take an embryo and try to clone it. We will have developed substantial treatments for our patients. If this research is allowed to go forward, we'll have developed substantial treatments for our patients.

Mr. CUMMINGS. Thank you all very much.

Mr. SOUDER. Dr. Weldon?

Dr. WELDON. Thank you, Mr. Chairman.

Dr. Cowan, you said in your testimony on page 2, human reproductive cloning would be wrong at this time—I am quoting you there—at this time.

Dr. COWAN. That's correct.

Dr. WELDON. On page 3 you said, "Until there are better results in animals, we have no business even considering it in humans."

The gentleman to your left has no problem with trying with humans right now. Am I reading and understanding your testimony correctly to say that the society you represent feels that once the proper research is done and that this could be developed safely in humans, that your professional association would support reproductive cloning?

Dr. COWAN. I do not know what the professional society will ultimately recommend. At the present time, however, we know only a small part of cloning from animal work, and that work tells us that it is not safe. We have no controls in place, and we do not recommend it for clinical care.

Dr. WELDON. You are the president; is that right?

Dr. COWAN. I am sorry?

Dr. WELDON. You are the Director of the American Society of Reproductive Medicine.

Dr. COWAN. No, sir, I am not. I am on the board of directors.

Dr. WELDON. But you kind of leave the door open. That's the impression I get. You say, at this time, until there are better results in animals; I can't help but conclude that at least in your opinion and the position of many members of your professional association that you may come out ultimately in support of Dr. Zavos' position that we should allow reproductive cloning.

Dr. COWAN. Yes, sir. It is a difficult position. Certainly, at this time though, we don't recommend it; but times can change. Times have changed for all of us, and we may very well see the position for reproductive cloning in the future. Rather than close this door, we would prefer to say, leave it open until we know more about it.

Dr. WELDON. Would you not agree that this would raise some very serious ethical issues that extend far beyond the original debate associated with IVF, issues of paternity, who's the mother, who's the father, inheritance, legal issues, whole hosts of moral and ethical issues.

Dr. COWAN. Yes, Dr. Weldon, I would.

Dr. WELDON. You further made statements about tremendous potential for cures. You know, I am a physician, and I'm sure you're aware of that. I treat persons with diabetes and Parkinson's disease.

I remember the great debate we had in this country back in the early 1990's about the so-called tremendous potential of fetal tissue research and all of the attempts at transplanting neuronal tissues to treat Parkinson's disease were a dismal failure. Why are you coming as a physician before this committee contending that there is great promise in this arena?

I read the New England Journal of Medicine every month—it comes out every week; I read the JAMA every week. I haven't seen any articles that suggest that there is the great potential that you claim in your testimony.

Where are you coming from on this? Are you doing research that we don't know about?

Dr. COWAN. No, sir, I am not doing any stem cell research or somatic transfer research at all. But I do believe that this research is a very important tool for us to investigate and learn the answers to the questions that you're asking—will it help us treat these patients?

If we fail, we fail, but it offers hope to our patients for the treatments of the diseases.

Dr. WELDON. I want to interrupt you on that. You say it offers hope. In my opinion, it offers false hope because there are millions of people who listen to these debates and hear what people like you are saying, and they think this is around the corner.

But I met with the—I think he is the president of the Research Division of the Juvenile Diabetes Foundation, a Dr. Goldstein, I think his name was. They have over $100 million budget. They're spending zero on cloning.

You get the impression out there that there's all these great breakthroughs that are on the horizon when you say, we have to do this research. And, you know, what I'm saying to you is you could just as easily make the argument that you're creating blatant false hopes.

And, you know—I was so intrigued by your testimony, Dr. Usala. I can't tell you how many diabetic ulcers I have treated. And the outcome of your kind of research is really fantastic. It is cutting edge, it's on the horizon. I assume you can use this product in other tissues; it is not limited to diabetic ulcers. You can do research in heart tissue and neuronal tissue to stimulate growth; is that correct?

Dr. USALA. This particular product, Dr. Weldon, induces regeneration of mesenchymally derived tissues, deep skin, bone, cartilage and blood vessels. Again, I am just looking to how nature does it. Nature spent several hundred million years coming up with the template for how this works. I have currently formed another company, ECTOcell, trying to find a similar scaffolding that will induce ectodermally derived tissues.

But the concept, I believe, is a valid one because we all know as scientists the chaperone proteins really modulate the expression of the DNA template. And those chaperone proteins are modulated by cytoplasma factors which are modulated by the external environment. During embryogenesis there are particular proteins that come into play naturally, and what I am trying to do is find artificial analogues of those to induce the same effect.

In answer to your question, this, I believe—and we have—the company that I left has data to support that tissues derived from the mesodermal layer can be induced to regenerate with this material.

Dr. WELDON. I know my time has expired with you, but could you explain to the people on this committee what you're talking about, "mesoderm" and "ectoderm," because I know what you're talking about, but——

Mr. SOUDER. I have no idea.

Dr. WELDON. I yield back after he answers that question.

Dr. USALA. There are three basic germ layers that evolve during embryogenesis, mesoderm which gives rise to kind of connective tissue structures, like blood vessels, bone, cartilage, deep skin, ectoderm, which gives rise to all of your neural tissue and the outer layer of skin; and endoderm, which gives rise primarily to the internal organs.

And basically all these cells from the different germ layers, have the same DNA. Well, why is it that they differentiate into different

things? And so what I try to do is to mimic what I thought was the structure that surrounded the different tissue layers, to tell those cells to become blood vessels, to tell those cells to become nerves.

I think I hit it right with the mesodermal layer; at least in the feasibility trial, when I left, it—you could call Dr. Bill Morriston at the University of North Carolina. It was pretty spectacular stuff.

And we don't have to go through the mental "what if" or we don't have to go through the—perhaps with enough funding, on a very limited budget, we were able to bring this to human clinical trials and achieve good results.

Mr. SOUDER. Next we go to Congresswoman Davis of Virginia.

Mrs. JO ANN DAVIS OF VIRGINIA. Thank you, Mr. Chairman.

And, gentlemen, I apologize. I wasn't here to hear your testimony, but I was chairing another committee.

Dr. Zavos, I did come in in time to hear that I think you said: You haven't already impregnated a woman with a cloned embryo, but you would expect to in the future. Can you tell me when?

Dr. ZAVOS. No. I can't answer that, obviously. We are doing this, but it's our plan and we obviously are not ready to release that. And when? Sometime in the future.

Mrs. JO ANN DAVIS OF VIRGINIA. I have had people in my office telling me that China has already cloned humans. Have you heard anything to that effect?

Dr. ZAVOS. I am familiar with what the Chinese are doing, the Russians are doing, the Europeans are doing. I know of several teams that are making a great deal of progress on this issue, and their goal is to clone a human being; so there's obviously no shortcut on this one. And the Chinese will obviously be successful in probably—by passing us very significantly.

And I wanted to refer to Congressman Weldon's comment in reference to, why are we keeping the doors open? There is a reason why we keep doors open, until we can see quite vividly that this technology is a total disaster or it holds a great deal of promise.

My question is why are the British legislating in favor of therapeutic cloning? Why did the Australians just pass a law allowing that? And that is a very big issue.

Mrs. JO ANN DAVIS OF VIRGINIA. I don't mean to cut you off, but I have limited time, and I would like to ask some more questions.

I am not sure who this would be for, but how many eggs have to be harvested to clone a human embryo?

Dr. ZAVOS. We don't know that except to say that our experience with our team doing cloning in mice and cows have yielded a very high success in creating embryos via somatic cell nuclear transfer. The recent events at ACT, Advanced Cell Technology, they have attempted to—out of six anucleated embryo host sites they were able to do two human embryos, which is a 33 percent success rate in creating embryos.

So this technology is developing very fast and it's developing by the day, not by——

Mrs. JO ANN DAVIS OF VIRGINIA. Thank you, Dr. Zavos. I want to go to Dr. Usala now.

Why do you think the adult stem cell research has not gotten the attention that the embryo stem cells have? I mean, it seems to me

that if we are going to set up a bank that you know someone could deposit the stem cells in, why does that not work or why are we not getting the attention there?

Dr. USALA. I am not sure, Congresswoman Davis. It is speculation at best, and I would not be able to speculate for you.

I think that those who have brought the human embryonic stem cell debate to our attention, even the people that really did the initial work on it, do not believe you can grow parts from it. What has happened is, I think this has been taken up by others who are more peripherally involved; and it seems just intuitively that if you take something at an earlier stage of development, you should be able to get it to do what you want. And I think that it's more complex than that, as we found out—the same issues as Dr. Weldon brought up.

In the early 1990's they said, we can cure diabetes if we take fetal islets because they are less developed. They should be easier to take. And we don't hear about it anymore; it is a dismal failure.

I believe the human—in the case of adult stem cells, it is not quite as intuitive that they would work, but in fact, they do. And in fact, the adult stem cells probably will work better because they are in the environment of the actual patient that they are trying to get to induce some tissue replacement with.

So I think it's basically—and I think this is unfortunate to say, but I think it just has to do with the way it has been marketed. And, again, that is speculation.

Mrs. JO ANN DAVIS OF VIRGINIA. And, again, I am just still trying to learn about this, so if I am hearing you right then, adult stem cell has worked and embryonic stem cell has not worked?

Dr. USALA. Human embryonic stem cells, to date, have not worked well. And in animal models they haven't worked—or some of them have worked in small animals; in large animals they really haven't. And there have been some very profound complications, including uncontrolled growth, cancer.

With the adult stem cells we don't seem to see that.

Mrs. JO ANN DAVIS OF VIRGINIA. Thank you, Mr. Chairman.

Thank you, gentlemen.

Mr. SOUDER. Thank you.

We have been joined by the distinguished gentleman from New York, Mr. Gilman.

Mr. GILMAN. Thank you very much. I regret I was delayed at another hearing.

Let me ask the panelists, what is the benefit in scientific research of cloning? Do any of the panelists care to answer that?

Dr. COWAN. I guess I'll take that one.

And the question is, what is the benefit of therapeutic cloning?

Mr. GILMAN. For medical research.

Dr. COWAN. Well, I can't specifically identify any particular disease. We have had some diseases discussed; spinal cord injury, Parkinson's disease, diabetes, these are diseases that are discussed.

The issue for research to me, however, is the ability to probe the cells, probe the therapeutic modalities and develop understanding about the cell process, as well as therapeutic options for our patients. We all dream that we're going to do a therapeutic investigation, but most of these dreams actually do not come forward for us

conducting medical research. Instead we learn just a small piece of that helps us go further and further down the road.

I don't know if that is the answer to your question, but it's what we seem to understand today.

Mr. GILMAN. Do any of the other panelists wish to comment on that?

Dr. USALA. I think that what cloning will do is provide perhaps hundreds of millions of dollars for NIH grants, for career development.

I am not sure I agree with my colleague that oftentimes this does not relate in any therapy. On $6 million, I brought from animal trials into human clinical trials, FDA-monitored, done under the very strict FDA regulations of both product production, clinical protocol.

I think that—well, it is like the movie, Animal House, knowledge is good. And I think sometimes the funding isn't really given for medical therapy, but rather as an end in and of itself. In my view, there really isn't any goal on the horizon of medical therapy. It really would just be interesting knowledge.

Mr. GILMAN. Does any other panelist care to comment?

Dr. ZAVOS. There is no doubt that there is a great deal of potential, and we haven't really sort of touched this topic yet. I think we have a long way to go.

And I think the evidence I can provide, Mr. Congressman, is the fact that governments such as England, Australia and others have already passed legislation regulating the exploitation of this technology, of this science. And there's obviously—are they smaller than we are? I don't think so. They are more opportunistic than we are.

I think we are walking a very tight rope here calling ourselves ethically and morally better than they are, and we are going to pay a hefty price to buy that technology 10, 20 years down the road. And we're making a big mistake.

Mr. GILMAN. Thank you very much.

Thank you, Mr. Chairman.

Mr. SOUDER. Before we move to the second panel, first let me thank each of you for taking the time to come here today. We will have additional written questions from some of us and some follow-up. This has been our second hearing. We're clearly intending to have a third as this issue continues to work. We have oversight of both the Department of Health and Human Services and the Justice Department.

Dr. Zavos, we have asked you a couple of times, and I understand that this isn't the time or place where you want to release any particular announcement, do you have a rough timeframe? When I first asked you the question of when there might be a clonal pregnancy, you suggested that it would be sooner rather than later. Do you have a rough timeframe? Is that 3 months, 1 month?

Dr. ZAVOS. My notion is that it will happen. A pregnancy can take place this year, 2002. A birth will be 2003. So all indication is that 2002 could be the year of the clones.

Mr. SOUDER. Do you think that will be outside the United States?

Dr. ZAVOS. Oh, definitely it will be outside the United States.

Mr. SOUDER. I thank you for coming today and look forward to talking to you.

If the second panel could now come forward.

Each raise your right hands.

[Witnesses sworn.]

Mr. SOUDER. Let the record show that each of the witnesses responded in the affirmative.

As you heard, we ask you to try to summarize your testimony within 5 minutes, and your full statement will be inserted into the record, as well as any other materials.

Dr. James Kelly is a patient advocate, and activist probably, and we would appreciate you starting with your testimony.

STATEMENTS OF JAMES KELLY, PATIENT ADVOCATE; ELIZABETH HOWARD, PATIENT ADVOCATE; AND JUDY NORSIGIAN, BOSTON WOMEN'S HEALTH BOOK COLLECTIVE

Mr. KELLY. Mr. Chairman, I just want to say for the record, I am not a doctor.

Mr. SOUDER. We made you an honorary doctor today. Can you pull the mic a little closer? You are recognized for 5 minutes.

Mr. KELLY. Five years ago——

Mr. SOUDER. Your promotion got you so excited you got distracted there.

Mr. KELLY. Five years ago, I had an auto accident and I became paralyzed with a spinal cord injury.

And right off the bat, because I was a troubleshooter for 19 years for the railroad industry and eventually a train dispatcher, I took Dr. Zavos' advice and I educated myself concerning what it was going to take to get me out of my condition to return my body. And I did this by spending literally thousands of hours a year reading PubMed and MEDLINE, medical journals, in speaking with the leading researchers in the country in neuroscience, to find out just exactly what it was going to take to cure spinal cord injury, because I wanted to support the researchers that were doing the kind of research that was going to lead to the cure that I needed.

I didn't want to just support research, blank research or a blank check on research, because the way that you fix anything, whether it's the way Dr. Usala fixes people with diabetic foot ulcers or the way you fix a diesel locomotive, you do it by finding out what needs to be done and you take care of what has to be done.

With that said, every year 26 million Americans are diagnosed with conditions that stem cells are expected to some day cure. Many more millions already suffer from these life threatening conditions or crippling conditions. Therefore, it is not farfetched to say, even a year's delay in the availability of cures for these conditions will result in millions of Americans needlessly suffering catastrophic impairment or enduring needless misery. Their loved ones will know profound sadness and grief.

Americans are being told that cloning has the potential to play a large part in curing disease. Americans are believing what they are being told, and therefore they are speaking out in defense of their cures.

But in my opinion, the question we should be asking ourselves is not, does cloning have therapeutic potential, but rather, will

cloning—giving cloning research the green light speed the availability of medical cures, or will it slow or block their progress?

After many months of investigation into the—sorry; I am jumping around and I'm losing my place—into the safety, performance and marketing potentials of embryonic stem cells, adult stem cells and cloned embryonic stem cells, I've arrived at a definite conclusion regarding the question that I think we should be asking; and I would like to present what I learned.

I hope each of you will draw your own conclusions from this information and will speak up for your future where you have a chance; but please do so while considering the following points because this issues outcome will soon be a matter of life and death for millions. I want to emphasize that my only intention, or my only priority in getting involved in this investigation was that people with things like cancer, heart disease, spinal cord injury, Parkinson's, Alzheimer's, Rett disease will not have to suffer and die needlessly.

I want the cures that everybody else wants. I want out of this wheelchair. I want Dr. Usala to be cured of Type 1 diabetes. I want Dr. Usala's two children to be cured of Type 1 diabetes. I want you to know what my priorities are.

This is the information I learned about cloning. Embryonic stem cells taken from cloned embryos have safety and performance obstacles that need to be overcome before they can be medically tested in humans, including short- and long-term, genetically patience and reliability, a tendency to form tumors when injected into the host animals, and unexpectedly foreign tissue rejection. In other words, stem cells taken from cloned embryos, even though they have the patient's DNA, can still be rejected.

The whole point is, it's supposed to not be rejected, but it will be rejected as a recent study in cell pointed out, and I will get to that later here if I have time.

Another thing that is a problem with cloned embryonic stem cells is, they may offer questionable benefits regarding the potential to medical conditions with a genetic basis. In his March 5th testimony to the Senate, Dr. Stuart Newman of New York Medical College noted genetically matched cells from cloning may well be useless in treating conditions with a genetic basis, such as juvenile diabetes, for these cells will have the same genetic defect to cause the problem in the first place.

Unfortunately, ma'am, I am sorry to say the same thing is true with Retts disease, because I want the same thing you want. I want your daughter cured. And I hope you understand the points I just said there. Do you?

Cloned embryonic stem cells have yet to play a necessary part in treating any condition that improves a live animal or a human's medical condition. Cloned embryonic stem cells would require 15 million women's eggs to cure all diabetic Americans if attempting—if every attempt to clone was successful. However, most sources now claim that 100 attempts are needed to create a single cloned embryo able to yield usable stem cells, with each attempt needing another egg. Therefore 1.5 billion eggs would be required to use cloning for diabetic uses alone. Heart disease would require five to

seven times more with 21 million new cases of heart disease a year.

There are a couple of quotes here I would like to quote of leading scientists who—where I got this information. Thomas Okarma is the chief executive of Geron Corp., a self-therapy company. He says he has no interest in using cloned embryos to produce customized treatments for disease. The odds favoring success "are vanishingly small," he says. The costs are daunting. Okarma explains that it would take thousands of eggs on an assembly line to produce a custom therapy for a single person. "the process is a nonstarter commercially," he says. In the previously—and that came out of an L.A. Times article.

In the same article, Lutz Giebel, CEO of CyThera, a cell therapy company in San Diego, points out, "Quality control presents another hurdle...the FDA can't regulate it" and "no one could afford the treatment." Giebel calls therapeutic cloning a research tool only.

Also the embryonic stem cells are not expected by scientific supporters to have the potential for leading the medically available cures for a very long time. Scientist Janet Rowley is a pro-cloning member of the President's Council on Bioethics. In speaking of the therapeutic potential of cloned embryonic stem cells, she recently cautioned, "I think it's not fair to say that the promise will not be realized, but I think it is fair to say that the promise may take a very long time." And I want to point out that we began our war on cancer with the notion it was going to be over in 10 to 20 years, and we are far from it.

Mr. SOUDER. Mr. Kelly, we have let you go over some. We will insert into the record your information on adult stem cells, and if you would like to do a conclusion, then we'll draw more out.

Mr. KELLY. What would you like me to do?

Mr. SOUDER. If you want to just make a few concluding comments, then we'll ask you further questions, and we'll put into the record the adult stem cell material.

Mr. KELLY. It was my fault. I am very sorry.

My closing statement, what I would like to say is, I did not look at the ethical or the moral sides of this because my primary and my only concern was what was going to lead to cures faster, OK?

After I came to the conclusion that banning cloning of humans was going to actually keep funds from being diverted from more promising avenues, I was then able to look at the moral and ethical issues involved, and I came to the conclusion that it actually is wrong to use human life at any stage for any purpose, especially if you are using that human life with the idea that you are going to destroy it.

And what I would like to say finally is, most of us are instinctively horrified—what I want to say is, this is a very important—very, very important. This issue is going to determine the life and the quality of life and even the life and death of many millions of Americans. It is actually probably one of the most important issues

that our Senate and our Congress has faced for very many years, and we need to get it right.

We need to understand what is going on and we need to get it right.

[The prepared statement of Mr. Kelly follows:]

Testimony of James Kelly
before the
House Government Reform Committee
Subcommittee on Criminal Justice, Drug Policy, and Human Resources

Subject: Human Cloning

May 15th, 2002

A wise man once said: "For those who perceive, one sign is enough. For those whose minds are closed, a thousand reasons are wasted."

The outcome of the present cloning debate will affect the lives of over a hundred million Americans. This is a cold, hard fact, not wild speculation. Every year twenty-six million Americans are diagnosed with diseases or conditions that stem cells are expected to someday play a major part in curing. Many more millions already suffer from these life-threatening or crippling conditions. Therefore it is not far-fetched to say that even a year's delay in the availability of cures for these conditions will result in millions of Americans needlessly dying, suffering catastrophic impairment, or enduring needless misery. Their loved ones will know profound sadness and grief. Millions more will anxiously await the future with desperate hope. But what if their cures are delayed for three years, five, ten, twenty or more?

Americans are being told that cloning has the potential to play a large part in curing disease. Therefore, many who suffer these conditions (and many able-bodied Americans) support the cause of cloning regardless of the moral questions involved. They believe what they're being told, and they're speaking out in defense of their cures. But in my opinion the question we should be asking is not "Does cloning have therapeutic potential?" Rather, it is: "Will giving cloning research a green light speed the medical availability of cures, or slow or block their progress?"

Because of a 1997 spinal cord injury, I'm paralyzed below the chest. For the past five years I've closely followed medical research, learning the factors involved in curing my condition. Over the last several months I've compared the research progress and technical roadblocks of adult, embryonic, and *cloned* embryonic stem cells for *all* the conditions they're expected to address. I focused on their therapeutic potential as well as safety, performance, and marketing potentials. In weighing these aspects I tried to determine objectively whether cloning research would speed or slow the availability of cures. My only priority is that millions don't needlessly die, and that many others, including myself, regain lost mental or physical functions as quickly as possible.

I have arrived at a definite conclusion, and would like to present what I've learned. I hope each of you will draw your own conclusions, and speak up for your future while you still have a chance. But please do so while carefully considering the following points, for this issue's outcome will all too soon be a matter of life or death for millions.

- Embryonic stem cells taken from cloned embryos:

  - ✓ are projected as a source of embryonic stem cells with the patient's DNA, so that these cells will not be rejected by the body's immune response.

  - ✓ are expected to replace damaged or diseased adult tissues in humans, such as heart cells, nerve cells, insulin-producing islet cells, and others.

  - ✓ have safety and performance obstacles that need to be overcome before they can be medically tested in humans. These include short- and long-term genetic mutations and unreliability (1), a tendency to form tumors when injected into animals (2), and, unexpectedly, foreign tissue rejection. Say the authors of a recent study: "Our results raise the provocative possibility that even genetically matched cells derived by therapeutic cloning may still face barriers to effective transplantation for some disorders" (3).

  - ✓ may be of questionable benefit in terms of treating medical conditions with a genetic basis. In his March 5 testimony before the Senate Judiciary Committee, Dr. Stuart Newman of New York Medical College noted: "Genetically matched cells from cloning may well be useless in treating conditions with a genetic basis such as juvenile diabetes – for these cells will have the same genetic defect that caused the problem in the first place."

  - ✓ have yet to play a necessary part in any treatment that improves a lab animal's or a human's medical condition.

  - ✓ would require fifteen *million* women's eggs to cure all diabetic Americans, *if* every cloning attempt produces a viable embryo and ultimately a cell line. However, most sources claim a hundred attempts or more may be needed to create a single usable stem cell line, with each attempt needing another egg. If that is true, one and a half *billion* eggs would be required to use cloning for diabetic uses alone. Heart disease would require at least five to seven times more (with twenty-one million new cases of heart disease a year).

    Thomas Okarma, chief executive of Geron Corporation, a cell therapy company, has said that he has no interest in using cloned embryos to produce customized treatments for disease, because the odds favoring success "are vanishingly small" and the costs are daunting. Okarma says it would take "thousands of [human] eggs on an assembly line" to produce a custom therapy for a single person. "The process is a nonstarter, commercially," he says. He points out that it would take "100 eggs if you're lucky" to produce an embryo whose stem cells will be usable. His view is shared by Alan Robins, chief scientific officer of BresaGen Ltd., a cell therapy company in Australia and Athens, Georgia. "Where do you source that many eggs?," Robins asks. "Sourcing human eggs is a contentious issue in itself… It is not something we want to get involved in." (4)

  - ✓ are expected by leading scientific supporters to be too expensive to use on an individual patient basis. The April 5, 2001 issue of *Nature* reports that the idea of human

"therapeutic cloning" is "falling from favour" and that "many experts do not now expect therapeutic cloning to have a large clinical impact." James Thomson of the University of Wisconsin, a leading embryonic stem cell researcher, says this approach would be "astronomically expensive." In light of the wastefulness of the cloning process and the damage it does to gene expression, this article notes that "many researchers have come to doubt whether therapeutic cloning will ever be efficient enough to be commercially viable." (5)

In the previously cited L.A. Times article, Lutz Giebel, CEO of CyThera, a cell therapy company in San Diego, points out: "Quality control presents another hurdle. The Food and Drug Administration is set up to sample drugs produced in large commercial lots, not individual cell therapies. It is not commercially viable. Quality control is difficult; the FDA can't regulate it, [and] no one can afford the treatment." Giebel calls therapeutic cloning a "research tool only."

- ✓ are not expected by scientific supporters to lead to medically available cures for "a very long time." Scientist Janet Rowley is a member of the President's Council on Bioethics who supports cloning for research. In speaking of the therapeutic potential of cloned embryonic stem cells she recently cautioned: "I think it's not fair to say that the promise will not be realized, but I think that it is fair to say that the promise may take a very long time. And I just want to point out that we began the war on cancer in 1970 with the notion that it was all going to be over in 10 or 20 years and we're far from it." (6)

- Adult stem cells:
  - ✓ can have the patient's DNA when needed.
  - ✓ have been proven capable of maturing into tissues needed to cure the same conditions that cloned embryonic stem cells are expected to address (7, 8, 9, 10, 11, 12).
  - ✓ are readily available. Recent advances have taught researchers how to harvest multipotent stem cells from the skin, blood, bone marrow, and intestines (13, 14, 15).
  - ✓ are affordable (they've been used for years in humans for certain types of cancers and other illnesses with the backing of health care providers).
  - ✓ are much further advanced towards clinical use. Experimental use of adult stem cells has already led to functional improvements in both animals and humans for the following conditions: Heart Disease (16), Stroke (17), Traumatic Brain Damage (18), Diabetes (19), Spinal Cord Injury (20), Immune Deficiency Syndrome (21), Multiple Sclerosis (22, 23), certain forms of Cancer (24), Parkinson's Disease (25), and others.
  - ✓ require further research to simplify, perfect, and expand their uses.

- The FDA approves clinical testing of new treatments based on their merits *as a whole*, including each of their component steps in context with the rest. Therefore, cloning's potential for causing short- and long-term genetic mutations, tumor formation, and tissue rejection will need to be ironed out *separately* for each of its purported uses. Due to the complexity and magnitude of these obstacles and the number of applications that cloning is projected to address, while its clinical potential in the foreseeable future is completely nil, its potential to divert crucial resources for "a very long time" from other avenues, such as adult stem cells, is enormous.

- Adult stem cell usage is not the only therapeutic avenue closer to providing beneficial treatments than cloning. In fact, for my condition, spinal cord injury, three primary approaches have been identified with the potential to restore lost neural functions (26, 27, 28). These are: bridging the injury site with a growth-permissive scaffolding or neutralizing inhibitory molecules within the site's "glial scar"; inducing robust sprouting of existing axons to cross the injury site; and specialized neural cell replacement. Of the three, stem cells from whatever source (specialized cell replacement) have very little potential to lead to even minimal functional gains in the chronic condition if used alone (29). Overcoming the inhibitory injury site and inducing existing axons to sprout, cross the injury site, and remake broken neural connections offers far greater functional benefits (30, 31, 32, 33).

- In his online spinal cord injury forum, neuroscientist Wise Young of Rutgers recently noted "a growing consensus in the field that the most desirable cells for transplantation are cells that are far enough along the way to differentiating into desirable cells, such as neurons, insulin-secreting cells, radial glial or olfactory ensheathing glial cells, that they have a high likelihood of producing such cells." He was commenting on a recent study using fetal "progenitor" cells -- stem cells that are committed to becoming a specific adult cell type but still retain stem cell characteristics. (34) Embryonic stem cells taken from cloned embryos are the very earliest and least developed of all stem cell types. Without implanting cloned embryos in a woman's womb and then later removing the fetus, medical science has no reliable way to bring stem cells from cloned embryos to this "most desirable" stage. This study also points out that many scientists believe adult progenitor stem cells are equally desirable and are already being clinically tested in humans.

I began my inquiries with a chip on my shoulder. It appeared to me (from media reports of comments made by pro-cloning scientists) that religious groups and moralists might keep me from being cured. Also, I didn't want to consider these moral aspects, in case my inquiries led me to conclude that my best chance of being cured lay in being cloned. Only a daily barrage of facts that conflicted with my preconceptions allowed me to see past my resentment and fear. That I uncovered these facts myself, rather than being told them by others, probably contributed to my gradual acceptance of what I learned.

After uncovering the information presented in this testimony I was able to objectively consider the moral aspects of cloning. Until then, I refused to consider these aspects in case my investigations led me to conclude I needed cloning to regain the use of my body. Once I made my conclusions based on what I'd learned, I *still* didn't give any thought to the moral aspects of

cloning, since my conclusions made its morality a moot point (regarding my own priorities). But as an ex-train dispatcher and ex-locomotive electrician, I tend to see things in black and white. So while attending the President's April 10th speech in support of Senator Brownback's proposed ban on human embryo cloning for any purpose (human somatic cell nuclear transfer), for the first time I looked squarely at the morality of cloning. This is what I saw.

No matter what it's called, an embryo, a blastocyst, or whatever, if implanted into a woman's womb, the living entity made through cloning would someday be an infant. Regardless of whether its eyes are blue or its hair is brown, the infant would have to be human, not a bird, or a dog, or a pig, or a zebra. Simply put, a cloned embryo is certainly a very small and very early stage of human life, but nonetheless it is a valid stage of human existence. So how could I continue to ignore the fact that cloning involves intentionally creating human life with the prior intention of killing it? Or how could I reason that *any* end justifies such a means…even if the end is supposedly to save my life?

The scientific and practical facts presented in this testimony led me to conclude that it's highly unlikely that human cloning will ever be medically useful. Without a doubt it is a highly problematic avenue, requiring the diversion of substantial funds and resources from research avenues that offer more than futile hope. Therefore human cloning research is far more likely to slow the availability of cures than to hasten their development. Because of this and the moral perspective I've just presented, I totally support the Brownback-Landrieu Human Cloning Prohibition Act (S. 1899).

Most of us are instinctively horrified in a deep inner way by fatal sickness, lingering disease, and crippling conditions. Speaking for myself, I know I'm terrified of never regaining my body, or the life I loved. Therefore I can easily understand why we have a strong need to believe the primary goal of researchers is to make us well, or to protect our health, rather than to safeguard their careers, advance their special field, or protect the continued growth of science for the sake of science. But this life and death matter is *much* too important to allow us to choose our course through fear, resentment, trust, ambition, or hope. We need to get it right!

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Mr. SOUDER. We appreciate your passion, and it is personal and it is an addition for people you work with; and we appreciate that passion. Because often we can look at these things in a detached way, and it is important for us to see how you feel it and to see the impact on individuals, as well as for us to theoretically understand it. So I appreciate the emotion that you have brought to it in addition to the personal research that you have done.

Thank you for your testimony.

Ms. Howard.

Ms. HOWARD. Good afternoon, chairman and members of the committee. It is good to see someone from my home State of Virginia here. Thank you for the opportunity to testify on the importance of somatic cell nuclear transfer, also known as therapeutic cloning or regenerative medicine.

My name is Elizabeth Howard, and I am here on behalf of the Coalition for the Advancement of Medical Research. The Coalition consists of over 70 universities, scientific and academic societies, patient organizations and other groups that are dedicated to supporting and advancing stem cell research.

Today, I know I am speaking for millions of Americans living with MS, spinal cord injuries, ALS, Parkinson's disease and many other less known illnesses that are equally as tragic, who may benefit from therapeutic cloning. I entered this debate from the patients' perspective. I do not profess to have a scientific or medical background, but I do have a background in watching suffering without the ability to help.

Almost 3 years ago, I gave birth to a beautiful, healthy girl named Allison, and Allison is with me here today. My pregnancy and delivery were textbook perfect. Everything about Allison checked out fine and there was great joy in my family about this new life and its promise.

Back then, in June 1999, I was oblivious that all expectant mothers are at risk of having a Rett syndrome daughter, that I might be one of those moms who had watched in horror as her happy, healthy baby girl did not develop properly and would lose a few acquired skills from which she derived joy and contact with the outside world.

Rett syndrome strikes girls very early in their development, anywhere between the first 6 to 18 months of life. In 1999, it was discovered that Rett syndrome arises from a noninherited mutation in the MeCP2 gene on the X chromosome. MeCP2 plays an important role in brain growth and function. Because Allison's Rett syndrome onset was particularly early, she has never crawled, walked or talked.

After undergoing numerous tests for over 2 years, involving many big needles, she began continuous compulsive hand-wringing, which is the hallmark of this syndrome. We finally had a diagnosis, but with this, learned that Allison might be trapped at the 6-month developmental level forever at best.

Sadly, it is easier to point out the short list of abilities Allison does have than enumerate the long list of skills that she should have attained by now, but hasn't. She still manages to chew food with assistance. She can no longer use her hands. She can sit up

very slouched, but still falls over. She has a contagious laugh and beams a wonderful smile.

Finally, she makes excellent eye contact. It is with her penetrating blue eyes that Allison speaks to me, urging me to do everything I can to make her life less traumatic and more whole. She compels me to push me for advances in science, like SCNT, that hold promise to protect her from the many, many dreadful manifestations of Rett syndrome. These include seizures that can significantly set back development; breathing abnormalities that can be so intense the girls pass out; GI problems, which typically lead to feeding tubes; curvature of the spine, frequently resulting in complicated scoliosis surgery and/or dying suddenly while sleeping for no obvious or immediate reason.

Despite all the important and vast advances in medical research over the last 20 to 30 years, there is still no cure or treatment for Rett syndrome.

Let me state for the record that the Coalition for the Advancement of Medical Research supports efforts to prohibit human reproductive cloning. However, it is imperative that advancements in SCNT not be stifled or outlawed, since this may be one of the best avenues for ensuring that girls like Allison and the millions of Americans suffering from other disorders might some day live a more meaningful life and future generations of people afflicted by these disorders, perhaps our very own children and their children, might never have to endure what this current generation has suffered through.

It is not my intent to exaggerate the promise or timing of SCNT research, but how can I look into my daughter's sparkling blue eyes and not assure her that scientists and lawmakers are embarking upon an area of research supported by 40 scientific Nobel Laureates that might allow her to have a happier ending.

During the first panel, the American Society for Reproductive Medicine spoke to the science involved in the SCNT process. So in the interest of time, I won't explain it again. But let me just reiterate there is a critical distinction between the use of cloning technology to create a baby, which is reproductive cloning, and therapeutic cloning techniques central to the production of breakthrough medicines, diagnostics and potential vaccines to treat various diseases.

Due to its promise to enhance the quality of life of both the young and the old suffering from various devastating, often life-threatening, disorders, how can we not allow this research to advance? The present momentum in biomedical research and the profound implications of what we are learning will inevitably raise public concerns. Yet an across-the-board ban on all types of human cloning would significantly set back advances in research that offer hope for Rett syndrome girls and the numerous Americans struggling on a daily basis just to make it past another uncontrollable seizure or tremor, to breathe without pain, to use their eyes as the onset of blindness occurs, and to continue walking before the amputation of their legs is required.

On behalf of the Coalition for the Advancement of Medical Research and the countless Americans who stand to benefit from therapeutic cloning and the family members and friends who love them, I again thank the committee for its deliberations and for the opportunity to speak on this issue.

Mr. SOUDER. We thank you for your testimony.

[The prepared statement of Ms. Howard follows:]

TESTIMONY FOR ELIZABETH HOWARD (MOTHER TO TWO-YEAR OLD ALLISON, WHO SUFFERS FROM RETT SYNDROME)

On Behalf of the
COALITION FOR THE ADVANCEMENT OF MEDICAL RESEARCH

Before the
SUBCOMMITTEE ON CRIMINAL JUSTICE, DRUG POLICY, AND HUMAN RESOURCES
GOVERNMENT REFORM COMMITTEE
US HOUSE OF REPRESENTATIVES

May 15, 2002

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Good afternoon Chairman Souder and Members of the Committee. Thank you for the opportunity to testify today on the importance of somatic cell nuclear transfer (SCNT), also known as therapeutic cloning or regenerative medicine. My name is Elizabeth Howard, and I am here on behalf of the Coalition for the Advancement of Medical Research (CAMR). The Coalition consists of over 70 universities, scientific and academic societies, patient's organizations, and other groups that are dedicated to supporting and advancing stem cell research. Today, I know that I am speaking for millions of Americans living with MS, spinal cord injuries, ALS, Parkinson's Disease, and many other less well-known illnesses that are equally as tragic – such as Canavan and Kernicterus -- who may benefit from therapeutic cloning.

I enter this debate from the patient's perspective. Almost three years ago, I gave birth to a beautiful, healthy girl named Allison. My pregnancy and delivery were textbook perfect. Everything about Allison checked out fine, and there was great joy in my family about this new life and its promise. Back then, I was oblivious that *all* expectant mothers are at risk of having a Rett Syndrome daughter. That I might be one of those moms who would watch in horror as their happy, healthy baby girl did not develop properly and would lose the few acquired skills from which she derived joy and contact with the outside world.

Rett Syndrome strikes girls very early in their development, anywhere between the first 6-18 months of life. It arises from a non-inherited mutation

in the MeCP2 gene on the X chromosome. MeCP2 plays an important role in brain growth and function. Because Allison's Rett Syndrome onset was particularly early, she has never crawled, walked, or talked. After undergoing numerous tests for over two years involving many big needles, she began continuous, compulsive hand-wringing, which is the hallmark of this Syndrome. We finally had a diagnosis, but with this learned that Allison might be trapped at the six-month developmental level forever.

Sadly, it is easier now to point out the short list of abilities Allison does have than enumerate the long list of skills she should have obtained by now but hasn't. She still manages to chew food (with assistance since she can no longer use her hands); she can sit up very slouched, but still falls over; she has a contagious laugh, and she beams a wonderful smile. Finally, she makes excellent eye contact.

With her penetrating blue eyes, Allison speaks to me, urging me to do everything that I can for her to make her life less traumatic and more whole. She compels me to push for advances in science – like SCNT – that hold promise to protect her from the many dreadful manifestations of Rett Syndrome. These include seizures that can significantly setback development; breathing abnormalities that can be so intense the girls pass out; gastrointestinal problems, which typically lead to feeding tubes; curvature of the spine frequently resulting in complicated scoliosis surgery; and/or dying suddenly while sleeping for no obvious, immediate reason. For now, there is no cure or treatment for Rett Syndrome.

Let me state here for the record that the Coalition for the Advancement of Medical Research supports efforts to prohibit human reproductive cloning. However, it is imperative that advancements in SCNT, which is distinct and separate from reproductive cloning not be stifled or outlawed since this may be one of the best avenues for ensuring that girls like Allison and the millions of Americans suffering from other disorders might some day live a more meaningful life. And future generations of people afflicted by these disorders – perhaps our own children, and their children -- might never have to endure what this current generation has suffered through. It is not my intent to exaggerate the promise or timing of SCNT research, and I certainly do not profess to have a scientific background. But how can I look into my daughter's sparkly blue eyes and ***not*** assure her that scientists *and* lawmakers are embarking upon an area of research -- supported by 40 scientific Nobel Laureates -- that might allow for her to have a happier ending?

I understand that the word "cloning" has caused many individuals to imagine the worst possible abuses. But allow me to make a critical distinction between the use of cloning technology to create a baby – reproductive cloning - and the therapeutic cloning techniques central to the production of breakthrough medicines, diagnostics, and potentially vaccines to treat diseases like Parkinson's, Alzheimer's, diabetes, heart disease, various cancers, paralysis resulting from spinal cord injury, and perhaps even Rett Syndrome. Therapeutic cloning will not produce a whole human being. Due to its promise to enhance the quality of life the young and old suffering from various devastating, often life-threatening, disorder, how can we not allow this research to advance?

Somatic cell nuclear transfer may prove to be a vital tool in allowing scientists to fully develop the promise of stem cell research. Somatic cell nuclear transfer involves the use of a donor's unfertilized egg and a patient's own cells. Eventually, scientists hope to learn enough about how the egg works to replicate it in a lab and no longer need eggs. The research could allow a patient's own genetic material to be used to develop stem cell therapies specifically tailored to that individual's medical condition, thus not triggering an immune rejection response. In other words, using somatic cell nuclear transfer could repair patients with their own cells. We strongly oppose all efforts to ban therapeutic cloning.

Mr. Chairperson, it is likely that we will continue to be confronted with scientific advances that pose difficult social and ethical questions. It seems to me that we often learn things that frighten us or make us uncomfortable at first. We should not let the fear felt by some of us prevent the rest of us from alleviating suffering. Indeed, we live in a pluralistic society where a number of views can be accommodated. There are Americans who believe research on animals is unethical. I can respect their views, and even allow them not to avail themselves of the fruits of that research. Yet we do not let them keep me or my family from taking advantage of the knowledge gained by that research.

The present momentum in biomedical research, and the profound implications of what we are learning, will inevitably raise public concerns. Yet an across-the-board ban on all types of human cloning would significantly setback advances in research that offer hope for Rett Syndrome

girls and the numerous other Americans struggling on a daily basis just to make it past another uncontrollable seizure or tremor, to breath without pain, to use their eyes as the onset of blindness occurs, and to continue walking before the amputation of their legs is required.

On behalf of the Coalition for the Advancement of Medical Research, the countless Americans who stand to benefit from therapeutic cloning, and the family members and friends who love them, I again thank the Committee for its deliberations and for the opportunity to speak on this issue.

Mr. SOUDER. Ms. Norsigian.

Ms. NORSIGIAN. Thank you, Mr. Chairman, and others on the committee. I am Judy Norsigian, the Executive Director of the Boston Women's Health Book Collective, and coauthor of "Our Bodies, Ourselves," now in its 7 edition. There are now 4.5 million copies in print in over 20 editions around the world with seven more on the way. It is the book that is the mainstay of the global women's health movement.

First, I want to note that we do support embryo stem cell research that utilizes not only existing cell lines, but also embryos originally produced for use in IVF clinics. At the same time, along with other women's health and reproductive rights advocates, we have raised serious concerns about the wisdom of allowing embryo cloning, even for research purposes, at this point in time.

We also believe, after a number of conversations with knowledgeable scientists, that today's most pressing challenges in the field of embryo stem cell research do not require access to embryo cloning. Despite much media hype to the contrary, there really have not been compelling arguments to allow embryo cloning now, especially in light of the serious and profound consequences of developing this particular technology.

I have attached earlier Senate testimony that addresses a number of our concerns.

But today I would like to underscore just two of the reasons that warrant a far more cautious approach than that adopted by the Sector/Kennedy/Feinstein/Hatch bill, permitting embryo cloning for research purposes, and the Dorgan/Johnson bill which does not even totally ban implantation of a clonal embryo. Most importantly, neither bill would adequately protect the women who would be donating eggs for somatic cell nuclear transfer.

First, embryo cloning is a key element in the development of germline genetic modifications including modifications that go far beyond the realm of curing diseases into the world of so-called "designer babies." The matter of germline modification, selecting for traits that would be passed on to future generations, is a separate discussion from human reproductive cloning and must take place before embryo cloning is allowed to go forward, and be refined in an environment with completely inadequate regulation of human germline genetic modification.

Second, there are substantial risks to women's health posed by Lupron, the most common drug used to hyperstimulate the ovaries in the process of gathering eggs for somatic cell nuclear transfer. And unlike situations where individual women might benefit directly from using this drug, as could be the case when undergoing IVF or in treating endometriosis or in treating anemia-associated fibroids, women who take this drug solely for the purpose of providing eggs for research do not benefit personally.

At this point, it is not clear they would be benefiting relatives or loved ones either.

As of the spring of 1999, the FDA, the Food and Drug Administration, had received 4,228 reports of adverse drug effects from women using Lupron. Interestingly, they also received 2,943 such reports from men who used the drug in prostate cancer treatment; and despite the differences in age, sex and indication for use, the

complaints were remarkably similar. 325 adverse events reported for women resulted in hospitalization, and additionally, 25 deaths were reported. Whether these deaths are directly attributable to Lupron remains to be determined, and I have recently asked FDA staff to look into this more carefully.

Although the FDA cannot now provide more detailed data on adverse reports for women over the past 3 years—and there have been thousands—nor data on how many of these problems were long-lasting, rather than transient, FDA staff have indicated they will be reviewing these data in the near future. Our office, meanwhile, has received numerous complaints over the past decade from women who have had persistent joint pain, headaches and other serious problems many months and even years after their last Lupron shot. I am attaching a list of problems that have been reported to the FDA and in the medical literature.

By the way, given our current problems with under-resourced and inadequate IRBs, we cannot now expect most IRBs to protect the women who would be providing eggs for research purposes. Once the FDA has completed its analysis of the many additional adverse reports on this drug, we will certainly have a more complete picture of the risks than we do now. But until such a time when more reassuring data might become available, or different drugs developed with a better safety profile have a longer track record, it is unethical to move forward with somatic cell nuclear transfer.

Parenthetically, I do want to note that scientists in Italy and possibly elsewhere claim to have already perfected techniques for freezing eggs, something I have been told has not yet been done with success in this country. If unused, frozen eggs harvested initially for the purposes of IVF were to become available for subsequent somatic cell nuclear transfer, then of course you would not be exposing those same women to risks for the purpose of research only.

Just at the practical level, it makes little sense to pursue clone cures for the diseases most often mentioned in media reports. Parkinson's and Alzheimer's diseases alone affect 5 million American and would require, minimally, 250 million eggs to produce individualized therapy that would match the patient's own genome. This figure of 250 million assumes that at least 50 eggs would be needed per patient. And since, on average, about 10 viable eggs are likely to be collected from each individual woman who is a donor, 25 million women would be needed as donors, about half of all women of reproductive age, and that is just for these two diseases.

The specter of such massive use of ovarian hyperstimulation, coupled with laparoscopic surgery, makes no sense, especially when other fruitful and less problematic approaches to developing therapies are already under way.

In closing, I would like to note recent articles by Professor George Annas of the Boston University School of Public Health in both the Boston Globe April 21 and the New England Journal of Medicine last week. Professor Annas is not opposed to research cloning, but he does recommend that three features are essential to any bill that would effectively prevent human reproductive cloning: first, a prohibition on the stockpiling of embryos by outlaw-

ing the freezing and storage of research embryos; two, a prohibition on the purchase and sale of human eggs or embryos; and three, disqualifying of, "anyone who is involved in activities related to in vitro fertilization or other infertility treatments" from doing research with cloned embryos.

These three elements are absent from all bills I mentioned earlier that permit embryo cloning for research purposes, and it would seem that their inclusion would have been an obvious thing to do to minimize the likelihood of human reproductive cloning.

Professor Annas also notes that a compromise position which calls for a moratorium on embryo research cloning could also make it possible to pass legislation that would ban human reproductive cloning. Last June, a statement on cloning, signed by over 100 individuals and organizations and posted at our Web site, has called for such a moratorium on the use of cloning to create human embryos for research purposes.

We recognize that no current legislative proposals embody this position, but we do believe that it still remains the best public policy. And during such a moratorium the FDA could more completely analyze the problems with drugs used for ovarian hyperstimulation, and the public could have a more thorough discussion of the scientific, regulatory and ethical issues at stake. This moratorium would be prudent and reasonable policy when faced with a technology of such profound consequence.

Thank you very much.

[The prepared statement of Ms. Norsegian follows:]

Subcommittee on Criminal Justice, Drug Policy & Human Resources
Committee on Government Reform

Testimony of Judy Norsigian,
Executive Director, Boston Women's Health Book Collective
Co-author of ***Our Bodies, Ourselves for the New Century***
May 15, 2002

I am Judy Norsigian, the Executive Director of the Boston Women's Health Book Collective (BWHBC), and co-author of "Our Bodies, Ourselves," now in its 7th edition as "Our Bodies, Ourselves for the New Century." There are now 4 ½ million copies in print in over 20 editions around the world, with over 7 more editions on the way.

First, I want to note that we do support embryo stem cell research that utilizes not only existing cell lines but also embryos originally produced for use in IVF (in vitro fertilization) clinics. At the same time, along with other women's health and reproductive rights advocates, we have raised serious concerns about the wisdom of allowing embryo cloning – even for research purposes – at this point in time. We also believe, after a number of conversations with knowledgeable scientists, that today's most pressing challenges in the field of embryo stem cell research do not require access to embryo cloning. Despite much media hype to the contrary, there really have not been any compelling arguments to allow embryo cloning now, especially in light of the serious and profound consequences of developing this particular technology.

I have attached earlier Senate testimony that addresses a number of our concerns. Today, I would like to underscore just two of the reasons that warrant a far more cautious approach than that adopted by the Sector/Kennedy/Feinstein/Hatch bill permitting embryo cloning for research purposes, and the Dorgan/Johnson bill, which does not even totally ban implantation of a clonal embryo. Most importantly, neither bill would adequately protect the women who would be donating eggs for somatic cell nuclear transfer.

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Second, there are substantial risks to women's health posed by Lupron ™ (leuprolide acetate), the most common drug used to hyper-stimulate the ovaries in the process of gathering eggs for somatic cell nuclear transfer. And unlike situations where individual women might benefit directly from using this drug – as could be the case when undergoing IVF, or in treating endometriosis, or in treating anemia-associated fibroids – women who take this drug solely for the purpose of providing eggs for research do not benefit personally.

As of the spring of 1999, the FDA had received 4228 reports of adverse drug events from women using Lupron ™. (Interestingly, they also received 2943 such reports from men, who used the drug in prostate cancer treatment, and despite the differences in age, sex, and indication for use, the complaints were remarkably similar.) 325 adverse events resulted in hospitalization, and additionally, 25 deaths were reported. Whether these deaths are directly attributable to Lupron remains to be determined. Although the FDA cannot now provide more detailed data on adverse reports from women over the past 3 years, nor data on how many of these problems were long lasting rather than transient, FDA staff will be reviewing this data in the near future. Our office, meanwhile, has received numerous complaints over the past decade from women who have had persistent joint pain, headaches, and other serious problems many months and even years after their last Lupron ™ shot. By the way, given our current problems with under-resourced and inadequate IRBs, we cannot now expect most IRBs to protect the women who would be providing eggs for research purposes.

Once the FDA has completed its analysis of the many additional adverse reports on this drug, we will certainly have a more complete picture of these risks than we do now, but until such a time when more reassuring data might become available - or different drugs developed with a better safety profile - it is unethical to move forward with somatic cell nuclear transfer. (Parenthetically, I do want to note that scientists in Italy and possibly elsewhere claim to have already perfected techniques for freezing eggs- something I have been told has not yet been done with success in this country. If unused frozen eggs harvested initially for the purpose of IVF were to become available for subsequent somatic cell nuclear transfer, this particular safety objection would no longer be relevant. But the matter of germline genetic modification still needs to be addressed.)

Just at the practical level, it makes little sense to pursue clone cures for the diseases most often mentioned in media reports. Parkinson's and Alzheimer's diseases alone affect 5 million Americans and would require minimally 250 million eggs to produce individualized therapies that would match the patient's own genome. (This figure of 250 million assumes that at least 50 eggs would be needed per patient.) And since about 10 viable eggs are likely to be collected from each individual woman who is a donor, 25 million women would be needed as donors - about half of all women of reproductive age. The specter of such massive use of ovarian hyper-stimulation coupled with laparascopic surgery makes no sense, especially when other fruitful and less problematic approaches to developing therapies are already underway.

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who is involved in activities related to in vitro fertilization or other infertility treatments from doing research with cloned embryos (Boston Globe, April 21, 2001). These 3 elements are absent from all bills I mentioned earlier that permit embryo cloning for research purposes, and yet it would seem that their inclusion would have been an obvious thing to do to minimize the likelihood of human reproductive cloning.

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ADDENDUM: Among the most common adverse effects of leuprolide acetate reported to the FDA for women are: rash, vasodilation (dilation of blood vessels), paresthesia (sensation of burning), tingling, pruritis (itching), headache and migraine, dizziness, urticaria (hives), alopecia (hair loss), arthralgia (severe joint pain, not inflammatory in character), dyspnea (difficulty breathing), chest pain, nausea, depression, amblyopia (dimness of vision), syncope (fainting), asthenia (weakness), asthenia gravis hypophyseogenea (severe weakness due to loss of pituitary function), amnesia (disturbance in memory), hypertension (high arterial blood pressure), tachycardia (rapid beating of the heart), muscular pain. bone pain, peripheral edema, nausea/vomiting, asthma, emotional instability, abdominal pain, insomnia, general edema, chronic enlargement of the thyroid, liver function abnormality. vision abnormality, anxiety, myasthenia (muscle weakness), and vertigo.

Mr. SOUDER. I want to thank each of you.

And once again we have a very diverse panel with different approaches to this same concern, which is how best to help people in this country.

Let me ask Ms. Norsigian, would it be—without the last three restrictions you have, in other words, one of the things that is likely to happen if, in fact, that many women were needed, much like other things, even blood donation, wouldn't this likely also skew to those who are low income as far as donors and often younger people who are needing money?

Ms. NORSIGIAN. Absolutely. There is actually quite a bit of literature on this issue of excessive incentives and in situations of poverty. We have got worldwide examples where women have been exposed to unacceptable research risks or treatment risks because of the incentives that were offered.

There would be an incentive. Mostly low-income women, women of color, would probably be candidates. But I think when you are looking at creating public policy of this sort, I think the safety issues are the paramount issues. And the other ethical issues, this would be a problem.

But there are other examples where we have passed legislation, where we have public policy that lends itself to this. Already, when we look at the situation where women provide eggs for women who are undergoing IVF procedures, young women, coeds across the country are being paid $5,000 on up for providing eggs for IVF clinics.

Some argue those are inappropriate incentives. Others say they are not inappropriate. But in those situations, you can definitely say there is a potential for benefiting somebody.

In the case of research cloning, the individual women who are going to provide the eggs do not have any conceivable chance right now of benefiting someone. It is a very distant prospect of cures given the state of research we have right now.

Mr. SOUDER. What is the potential scale?

Ms. NORSIGIAN. The scale would be enormous, that is true. Of course, there are scientists who are saying ultimately we would do away with cloning. We, of course, would develop better approaches. From a business point of view it doesn't make sense.

But I do not think we justify a path from here to there that is littered with the bodies of women who have been damaged, whose health has been seriously damaged because we think there may be an end point that we cannot guarantee, especially when we have other avenues that, as people today have pointed out, seem to be much more promising.

Mr. SOUDER. Thank you.

Mr. Kelly, we have asked this a couple of different times, and it was suggested in the first panel, as well as our last hearing; and certainly in debate of when we spend the money on human cloning, does that take money from research from more realistic and promising avenues for cures that actually help people with different disabilities such as your own, or different diseases.

Could you elaborate on what you've learned from some of your research?

Mr. KELLY. Thank you for asking me that. I can definitely elaborate on that.

I want to say something right off the bat, OK, if any money—if any money at all is spent on cloning, it will definitely take away money from avenues that could lead to cures for my condition. I can say that without a doubt. And the reason why I can say that is because cloning doesn't offer anything for my condition, all right?

People with spinal cord injury—Christopher Reeve, for example, they are being led to believe that cloning is going to cure them. Cloning is not going to cure a spinal cord injury, because they don't know what it takes to cure a spinal cord injury.

What cloning offers is specialized cell replacement, neurons and oligodendrocytes. Oligodendrocytes are the cells in the central nervous system that remyelinate the central nervous system axons or the nerves in the central nervous system.

Christopher Reeve testified to the Senate that he needs remyelination in order to be cured. He told the Senate that embryonic stem cells are the only way you can do that.

That is not true. There are four adult cell types that remyelinate the central nervous system. Two of them are in clinical trial. One is in a clinical trial at Yale; and the other is going to clinical trial at the NIH, and it's called bone marrow stem cells.

But remyelination is not the main obstacle to curing spinal cord injury. The main obstacle is getting nerves to grow across the injury site. That has nothing to do with specialized cell replacement. Neurons won't grow across the injury site. Oligodendrocytes won't grow across it.

There are dozens of avenues that are being developed to try to get nerves to grow across that lesion. It is called a lesion, and is what's called a gleal scar, and the gleal scar is very inhibitory to nerve regeneration. And cloning in any way cannot help get nerves to go across that lesion. And any money that goes to cloning will definitely impede the progress of research for spinal cord cures.

Now, just to finalize this, the leading researcher in the United States has, per Time Magazine—his name is Wise Young; he is the neuroscience director of Rutgers University, and by the way, he is in favor of anything the NIH is in favor of. He is in favor of cloning because he is in favor of research for the sake of research, I believe—in my opinion.

But he did say on his on-line forum to the SCI community—when asked, what are the prime motivations of researchers, what motivates scientists and researchers, he said, Most scientists that I know of work for recognition by other scientists; we have been trained this way.

Funding is, of course, important to scientists. Many scientists will go to great lengths to get funding from the NIH and other organizations, including changing their experiments and even changing their fields to get funding. The NIH has great influence over science in the United States for this reason.

What many people do not understand is, the NIH runs mostly through peer review, i.e., scientists who decide which applications have sufficient scientific merit to be funded. Only 20 percent of the grants are funded. Therefore, the competition is fierce and publications are important to decide funding. Therefore, if scientists

around the United States and researchers around the United States decide the best way to get funded by the NIH is to fund what they think the NIH wants to fund, they will change their research to do it.

You could have somebody that works on adult stem cells, which are right now very close to clinical trials for many conditions; and if they think—if they turn in a couple grant applications and they get turned down for whatever reason, they think they might be able to get it approved by submitting grant applications for cloning, Dr. Young is saying that they will do it.

And I know that they will do it. I know it because Dr. Young, in 1985, wrote a letter to the FDA—and I have it here also. And in this letter to the FDA, he told the FDA that he was working on an avenue for my condition, spinal cord injury, that resulted in 78 percent of the treated animals being able to walk independently 4 months after having their spinal cords severely crushed. And he pointed out in his letter to the FDA that this was better than anything he had ever seen in his lab, including methylprednisolone and maxillim, which he pointed out was in a multicenter clinical trial by the NIH.

Two months after submitting this letter to the FDA, he abandoned this line of research, which he had been working on for 7 years, because the NIH would not fund it. And he took over the methylprednisolone national clinical trial that the NIH was conducting. And he conducted that clinical trial for 12 years, all right?

The NIH looked into methylprednisolone and that is what they backed for 12 years. And Dr. Young admits that he had a more promising research avenue that was not funded by the NIH and was abandoned because it was not funded by the NIH.

And now in the year 2000, here we are in the year 2000, these scientists publish and they say that the national acute spinal cord injury studies, 2 and 3, which were the NIH clinical trials, often cite as evidence that high dose methylprednisolone is an efficacious intervention in the management of acute spinal cord injury.

Neither of these studies convincingly demonstrates the benefits of steroid. There are concerns about the statistical analysis randomization and clinical end points. Even if the punitive gains are statistically valid, the clinical benefits are questionable. Furthermore, the benefits of this innovation may not warrant the possible risk.

The point is, there are other studies that back this up, and I cited them in my presented paper. The point is, the NIH turned its back on promising research in the past that scientists had compelling evidence was better than what the NIH was backing. And what they did in doing that was they spent 12 years on this other avenue methylprednisolone that scientists now say not only does not improve the condition of people with spinal cord injury, but it causes more damage.

Now what is going to happen—I am telling you this with total certainty of everything that I have put in my paper—I am sorry I am such a poor speaker. What's going to happen is what happened in 1985 that probably led to as many as half of the people paralyzed today being unnecessarily paralyzed. And now what is going to happen in cloning, history is going to repeat itself, but it's not

going to be 300,000 Americans that are going to be affected, it is going to be 100 million Americans.

Mr. SOUDER. Well, thank you for that. I am going to yield to Dr. Weldon in just a minute, but let me reinforce from our end what you have shown in your studies. I know from being in the legislative end—first as a staffer, now as a Member of Congress—and also with friends in different agencies that we get what we ask for.

We get what we ask for. I work not in the health field so much but in the education area; and when we say we want this kind of research and we put that in legislation or when somebody in the department does it or, as in one case in one bill where a Member had gone to a conference and thought this education idea sounded good so it got written in a bill and then the research dollars were diverted to that form of education based on one Member having gone to a conference, that is how the research dollars get driven, from our end.

What you have done is put it in the reverse. In other words, you said here you saw it, that the researchers will respond to where the money flows and that the policies that seem to be asked for out of Congress or are media-driven may not be based on science.

There has been this false dichotomy today that implies that this is a scientific decision that is being made, and I don't believe it is. This is our second hearing, and we have yet to hear, after 20-some years of research in embryonic stem cell research and other things, of anyone seeing any information where we have other promising results. In fact, in talking with a number of my colleagues who favor this type of research, they admit they do not have it.

We are trying to look for a less politically charged way, because they are acknowledging the potential diversion of huge amounts of dollars from things that in fact are working.

This is not science versus nonscience. It is ridiculous to compare it to Galileo about the flat earth, for crying out loud. This is science versus science and where do we put the dollars to most effectively help people like yourself and your daughter and that we are getting caught up in, roughly, name-calling about how best to do this.

I believe ethics are a key variable to this, but particularly when the ethics is debatable, the science is screaming out that there is research on one side, it is baffling to me why we continue to debate this when there is no hope but a false hope. I have not heard anything specific other than that.

Mr. KELLY. Sir, unbelievably, what I am finding, without a doubt, is it is not science versus science, it is science versus cures, OK? There is definitely science out there that offers hope for cures. There definitely is. But cloning is not that science.

It does not offer it for several reasons. Not only does it have huge technical obstacles that are going to take decades to overcome, and the scientists I have quoted in my paper—I am not just pulling these numbers off the top of my head, but it is going to take decades to overcome them, if they can be overcome. And they even say that, that they are not even sure they can be.

But, on top of that, the cost of overcoming these obstacles and the cost of the treatment itself is going to be so astronomically high.

James Thomson—that's where I got that number—is the father of embryonic stem cells. He admits that the cost of many types of therapies that could come from cloning could be astronomically high. Nobody could afford it. And if you cannot afford it, where are people getting the word therapeutic for cloning if there is not going to be any therapy? If I cannot afford it, the government cannot afford it and the insurance companies cannot afford it, who is going to afford it? It is not going to happen.

We are being used. We are being misled. We are—and when I say "we," I mean the disabled communities—we are slitting our own throats by trying to back cloning, and we are doing it out of desperation.

Mr. SOUDER. Thank you very much.

Dr. Weldon.

Dr. WELDON. Thank you, Mr. Chairman.

I want to thank all of our witnesses and Ms. Norsigian in particular. Your testimony was excellent and to the point.

I got the impression that you would like to see a moratorium, but there are no moratoriums currently being debated in the Senate. As you know, we passed a ban in the House. Understanding that, the political reality, of the two bills to come out of the Senate, which one would you prefer, the Brownback-Landrieu version or the Kennedy-Feinstein version of the bill? Which would be better for women's rights, would you say?

Ms. NORSIGIAN. If I had to choose, I would choose the Brownback-Landrieu, because I know if the evidence were to emerge that would convince me that this was a promising line of research, we could revisit the issue.

I know the bill asks for a revisitation of the issue, and new scientific progress or discoveries could be considered, and the ban could be overturned. In the meantime, women would be protected.

I want to caution everybody who might go to an IVF clinic and be told that Lupron is perfectly safe or that it is fine and we do not have problems, it is a bit of a sleeping giant here. I want to use an analogy.

Some of you remember what happened with genetically engineered insulin. You know that it finally caused the animal-based insulin to be taken off the market, and those who were forced to use the genetically engineered insulin had some serious problems. There is a Canadian woman named Colleen Fuller who went into a coma several times. She is not the only one. Many, many people did.

It took a long time before physicians and the government recognized that there really was a problem associated with genetically engineered insulin, and it took the people who suffered quite a long time to have this recognized. In the end, animal-based insulin came back on the market, so those people who could not use the genetically engineered insulin had another choice.

This is not dissimilar in that we have many women—they have formed the Lupron Victims Network. Many of them have been sharing information on the Internet. I have talked to several people who work at IVF clinics who have seen these problems. But, in some cases, the women do not go back to the clinics because they have had such a bad experience with Lupron they do not trust the

physician who gave it to them to begin with, so physicians do not see those women again.

Dr. WELDON. Let me make sure I understand you clearly, though.

Ms. NORSIGIAN. What I am saying is there is a need to protect women from what I think right now are fairly substantial risks, and the FDA has yet to do the job we want it to do. That is such a great need that we need to take the legislative route that will not allow somatic cell nuclear transfer now for research purposes.

Dr. WELDON. Your position, though, is you support the use of Lupron in the setting where a woman wants to become pregnant, wants to go through the IVF process and has been properly counseled on the potential side effects of Lupron? You are opposed to the potential wide-scale large numbers of women who would be exposed to this drug in the setting of somatic cell nuclear transfer?

Ms. NORSIGIAN. "Support" is maybe too strong a term. I wish we had better safety data on this particular drug before it became in widespread use. It is in widespread use. The cat is out of the bag.

I do not agree with Dr. Zavos that cloning human beings is absolutely inevitable, it is just going to come, and we should just learn to accept it. This is a case where there might be better drugs. We might develop them.

I am not so sure that I am happy about the way Lupron has been used for off-label use. It has never been approved for this purpose in IVF clinics. I am not happy about this, but I am happy for the many women, some of whom are my good friends, were able to use IVF to become mothers. So for those women, and they are a minority, but for those women who were successful, even knowing there were more risks than they were told, they would have taken those risks to have a baby.

It is a very different risk-benefit ratio from a research setting where providing eggs for research cloning would have nothing to do with the opportunity of becoming a mother or treating a disease.

Dr. WELDON. Just for the record, and I know we have discussed this privately, you do come at this cloning issue from a pro-choice perspective? You support abortion rights, is that correct?

Ms. NORSIGIAN. Absolutely. I did not even think I had to say that because Our Bodies, Ourselves is so well-known. We have been strong reproductive rights advocates for many, many years. But we also believe in having a strong FDA and having a strong system of regulation. We are very concerned about the inability of IRBs to monitor research protocols adequately.

I also serve on the board of directors of Public Responsibility in Medicine and Research, which is doing a fair amount if not most of the training of IRB members in the country. So I am deeply concerned with research issues.

I support research, and I want to say that I come from that position, but that it is not to be construed as accepting any and all research simply because it can be done.

Dr. WELDON. I thank the gentlewoman.

If the chairman could just indulge me for a little longer, Ms. Howard—and by the way, I am very sympathetic to the problem that you are facing with your daughter. I have had the opportunity

to take care of some patients with Rett's disease, and I understand fully the challenge that you face.

Have you been led specifically to believe that there are researchers who have clinical applications of cloning technology specifically designed for the use in Rett syndrome, or are you just taking the position that you want to see all kinds of research go forward that might have a potential?

I am just curious. As a physician, I have never seen anything across my desk on a clinical application of cloning methods in Rett's, specifically.

Ms. HOWARD. Thanks for the question.

Let me say this, that after about a 20-year search, the Rett gene was finally found only 2 years ago, so there is a lot still unknown about Rett syndrome. Cystic fibrosis is a gene that I understand is a gene that was discovered in 1989, and therefore people in that field have had a much longer period to investigate how that gene works, unlike Rett syndrome, which actually was discovered after my daughter was born, in fact.

So my role as I see it in this debate is, since there is still so little known about how that gene works, what the remedies for Rett syndrome could ultimately be, I believe strongly that this avenue should be kept open. Because at the end of the day, it might best——

Dr. WELDON. But you have not seen any evidence——

Ms. HOWARD. I have not. I have not seen any evidence that any other pharmaceutical products could ultimately help, that any other—even knowing we are in the 21st century and medical science has advanced significantly, there is really nothing that can help Rett syndrome.

So I want this avenue kept open, since this may be ultimately the best avenue. I do not know that for certain.

Dr. WELDON. Just from a clinical perspective, I would argue that cloning is extremely unlikely to ever be beneficial to your daughter, but gene therapy would have the potential to help the victims of Rett syndrome. I don't want to burden the committee hearing with a lengthy scientific discussion of that.

Now, you are representing the Coalition for the Advancement of Medical Research, correct?

Ms. HOWARD. Yes.

Dr. WELDON. Their basic position is that they want to see this move forward just because it might have some potential, but they do not have any knowledge that it has any specific applications in any of the conditions they are concerned about, correct?

Ms. HOWARD. Correct. Let me speak to that.

First off, let me just say generally that I recognize that we are at a very new juncture in terms of science and that this is inevitably going to raise a lot of questions, all of which are good ones.

But, yes, indeed, the true application of therapeutic cloning has not fully been realized. But 40 Nobel Laureates believe it holds a lot of promise.

Let me also mention this point, that I know there is discussion in the Senate about potentially just putting a temporary ban on therapeutic cloning while we investigate further what its real promise is. But what you do then is take a significant amount of

momentum out of the focus on therapeutic cloning now, and even a 1-year ban or a 2-year ban could sap resources out of biomedical research companies, could make scientists go overseas.

So if one does want to realize the ultimate potential of therapeutic cloning, stopping it even for a year or two would set back significantly ever finding out the potential of therapeutic cloning.

I will not ever profess to have been or I do not think this is ultimately the cure. I am just looking for some potential to help my daughter and other people that are suffering.

Dr. WELDON. I could go on and on, but I see my time has well expired.

I just want to mention for the record, Mr. Chairman, the 40 Nobel Laureates who signed the letter, 31 of them signed a letter 1 year ago stating that they would oppose or they would only support embryo stem cell on excess embryos from fertility clinics, 31 of the 40, and that they would oppose creating embryos for this type of research, and 31 of these 40 in 12 months have changed their position and now support the creation of embryos for this kind of research, I think just essentially making the case that this is a tremendous slippery slope.

I yield back. Thank you, Mr. Chairman.

Mr. SOUDER. Mr. Cummings.

Mr. CUMMINGS. Thank you very much. I apologize for being out of the room. We have another hearing going on at the same time. I apologize.

Ms. Howard, what do you say to those who argue that cloning embryos is immoral?

Ms. HOWARD. First off, it is important to look at the difference between reproductive and therapeutic cloning. I think the differences between the two have been lost in the debate.

Also, as I understand it, some of this original debate arose out of knowing that there were embryos at fertility clinics that were not being used and, instead of just throwing them away in the trash bin, actually using them because they held some promise—again, promise. I understand that I am not saying that there is a solution, that therapeutic cloning is going to cure my daughter a year from now. I don't ever want to make that statement falsely.

Mr. CUMMINGS. But there is a possibility. You are looking at the possibility, I take it.

We have had extensive testimony on what you just talked about, the embryos that would normally be discarded. But go ahead.

Ms. HOWARD. OK. And then the idea, again, is to use an unfertilized egg and take the nucleus out and mix it with the person who has troubles, including my daughter—with their own DNA, mixing them together. I do think it is important to emphasize again that it is an unfertilized egg we are discussing.

Mr. CUMMINGS. Do you think there is a moral problem?

Let us deal with the therapeutic. You know, you have this group of people who are very, very emphatic about the fact that you should not mess with life. They do not care whether it is therapeutic or otherwise—or reproductive.

I was just wondering, before your daughter—or before you knew about your daughter's illness, did you have a position and has your position changed as a result of that?

Ms. HOWARD. My position has not changed at all. Even before Allison was born—and I think sometimes the point on pro-life is lost on people. I am pro quality of life for those who actually are alive now, and that is the extent to which I would extend my so-called pro-life position, is enhancing the quality of life of those who are suffering.

My daughter has the potential in the next year to 5 years of dying suddenly, and that is why I take this moral position to work with her and hope that there are treatments for her, including potentially this one, that could extend her life.

I don't think that fact should be lost on people, that this is not only about the life of the embryo, ultimately, but also the life of those who have made it through the gestation period and now have serious problems, as my daughter does.

Mr. CUMMINGS. Since we are seeing that you make the same argument that I have made, I can appreciate that. I mean, when we see people who stand the possibility of suffering for the rest of their lives or dying and if there is a possibility, I guess as a parent, I share with you, I guess I would try to go to the ends of the Earth to try to save my child. So I can understand that.

How do you respond to the notion that what is therapeutic cloning is basically offering some type of false hope? We have had some testimony about that today. There are some people who claim it is false hope. How do you feel about that?

Ms. HOWARD. In my testimony, I pointed out that there are lots of false hopes I could be chasing, not only therapeutic cloning, but there could be false hope that a pharmaceutical product is going to help my daughter.

After this juncture, after 20 or 30 years of miraculous advances in science in this country and overseas, there still is no cure for my daughter. So I am not walking around hopeful that there may be a cure next week or within 2 or 3 years.

Actually, even if it takes 20 or 30 years for this science to ultimately bloom and come to fruition, I, as a mom, would hope that the next generations of mothers who have Rett syndrome daughters could have a cure that I do not actually have for my daughter.

So if I am not here in this generation in the beginning of the 21st century able to help my daughter, I am hoping that science at least advances or I am pushing science along for the next 20 or 30 years so future generations do not have to cope with what I am coping with.

Mr. CUMMINGS. Dr. Kelly, if therapeutic cloning research produced, directly or indirectly, a cure for spinal cord injury, would you avail yourself of it?

Mr. KELLY. That is a really good question. That is a really good question. I appreciate your asking that.

As a matter of fact, I definitely would avail myself of it. At least I would—I thought I would several months ago, because I refused to look at the moral science of the question. I thought to myself, you know, let us not look at the moral science of it, because what happens if it turns out you need this to get cured? That is what led me to not look at the moral aspects of it.

Now I have come to the conclusion that, No. 1, it is not going to lead to a cure for spinal cord injuries, for reasons I have already

told the panel. No. 2, I have come to the conclusion that it is morally wrong, OK?

I have also looked at myself. I said, now, Jim, would you have the guts to stand up for your convictions, your moral convictions? If something came out next week for—and I don't believe it is going to happen, I don't think it is even possible it could happen, I don't think it is possible it could happen in 10 or 20 years—but if there was a miracle and somebody came out next week and the cure was with cloning, if that is what you are asking me, right——

Mr. CUMMINGS. Yes, sir.

Mr. KELLY [continuing]. I will tell you the truth, I don't think I would have my guts to turn my back on it, all right?

Now, having said that, having said that, you have to understand that I must really believe that it is not going to happen or else I would not be coming in front of you today and trying to talk whoever is listening to this panel, this testimony, talk you into backing Senator Brownback's bill and fully banning human cloning.

I would not be doing that, because I am fully admitting that I would avail myself of the cure if it was here. And I know it is im immoral. I am admitting it is immoral, and I am a weak person. I have a wife who would hate me, I know she would, because she does not have my moral views on this matter, and she would hate me if I told her, honey, you would have to stay with me the way I am, because I am not going to take the cure. I know that, if that is what it was. I will tell you, sir, I don't think I have the moral courage. But it is not going to happen.

Mr. CUMMINGS. Well, let me just leave you with this, then, with the Chair's indulgence. I think, when I look at science, when I look at something as simple as the computer, and the idea that maybe 20 or 30 years ago, 40 years ago, somebody could have easily said, one day we are going to be able to fax things across the wire and we are going to be able to have computers that talk to each other, I think or I am sure there were people who were naysayers and saying, it will never happen. Yet, it is happening, and things that I never imagined, never imagined, are happening.

I will never forget the first time I saw a fax coming over a fax machine, I could not believe it.

So I think that I often say it is the people who are the misfits that make a difference in our society, the ones that step out of the box. We are enjoying a lot of the benefits that come from people who have been misfits.

Mr. KELLY. Sir, can I say something about that?

Mr. CUMMINGS. Yes.

Mr. KELLY. You made the same comment as Dr. Usala, if I am not mistaken, about out-of-the-box thinking and misfits, right?

Supposedly, what is supposed to be so revolutionary about cloning, what it might be able to do, is offer embryo stem cells that have the patient's own DNA, right? OK. And what you are saying, if I understand correctly, is if you can use out-of-the box thinking, then maybe that might lead to a cure that nobody thinks is even possible. Maybe I don't think it is possible. My research is telling me it is not possible. Maybe I am wrong, OK?

I am glad you used the word "out-of-the-box." The reason why is what Dr. Usala does is he started out in his research 10 years ago

with the theory that he proved later on in clinical trials, you saw that, that the cells respond to the environment that is around it. But not only do the cells do that, but now they are finding out in cloning that the nucleus of the cells respond to the cytoplasm, which is the yoke of an egg, OK, or the yoke of a cell. They are finding that the nucleus responds to that.

So now they have come to the point, Dr. Wise Young, I mentioned, the Director of the Rutgers University Neuroscience Department, he wrote to me and he said that there is "a growing consensus in the field that the most desirable cells for transplantation are cells that are far enough along the way to differentiating into desirable cells, such as neurons, insulin-secreting cells, radial glial or olfactory ensheathing glial cells, that they have a high likelihood of producing such cells."

OK, that is not really what I wanted to say, here. What that is saying is that embryo stem cells—early stage embryonic stem cells which cloning can lead to are not even considered the most attractive cells for implantation anymore.

But that is not what I want to say. He wrote to me, and he said, "The other recent finding that has really turned a lot of heads in the regenerative field is the study showing that skin cells can be turned into lymphocytes by using a chemical to permeabilitize the skin cells and soak them in lymphocyte cytoplasm."

OK, now I know this is very confusing. What this is saying here is that they found out that if you take the yoke of an egg, what they are calling the cytoplasm, and if you inject that into a skin cell, what that does is it bathes the nucleus of that cell.

Instead of taking the nucleus out and putting in an embryo to make a clone in order to get stem cells, now they have found out that they can take the cytoplasm out of the embryo, the yoke out of it, or even the yoke out of another stem cell and put it into your skin cells, and that will bathe that nucleus in the skin cell, and that skin cell will turn into a stem cell or an embryo or whatever cytoplasm you put in it.

Now that is completely out of the box. Because, if you want to call an egg a box, you are taking the yoke out of the box and you are putting it in there. So what you are doing now is making—basically, what they are after with cloning, they are after embryonic stem cells with a patient's DNA. What he is telling us here is that you can make embryonic stem cells with the patient's DNA, and you don't have to make an embryo to do it. Now that is out-of-the-box thinking.

He also says that it is cheaper, it is safer, and it is more effective than going with the cloning process, and this man is in favor of cloning.

Mr. CUMMINGS. Thank you very much.

Mr. SOUDER. Thank you.

I appreciate your patience, Mrs. Davis, for letting us each go over on our time here.

I yield to Congresswoman Davis.

Mrs. JO ANN DAVIS OF VIRGINIA. Thank you, Mr. Chairman.

Ms. Howard, you said a moment ago, I believe, and you stressed it several times, that the cloned human embryo would be not fertilized. Is that correct?

Ms. HOWARD. Yes.

Mrs. JO ANN DAVIS OF VIRGINIA. President Clinton's National Bioethics Advisory Commission, in its 1997 Report on Cloning Human Beings, stated that the Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo with the apparent potential to be implanted in utero and developed to term.

If it is a nonfertilized egg, why would it be planted in utero and then come to full term?

Ms. HOWARD. I am not going to—I am not here to talk about eggs that would be implanted in utero. I am here to talk about growing cells in a petri dish for 3 or 4 days that could——

Mrs. JO ANN DAVIS OF VIRGINIA. I understand that, but you stated, and you emphasized it more than once, that it was a nonfertilized egg. I am trying to find out why you think that a cloned human embryo was a nonfertilized egg.

Ms. HOWARD. Go ahead.

Ms. NORSIGIAN. I was just mentioning to her that we were talking about asexual reproduction, but it is still potential reproduction. So you are right, it has the potential of being implanted and becoming maybe a malformed human being, but a human being.

So I think most people who look at this accept that somatic cell nuclear transfer introduces the possibility of having human reproductive cloning, and that is why we are having this discussion and why the Justice Department is looking at the question of enforcement.

I think it is also very important to get back to what you were saying, Mr. Cummings, about the question of, you know, research and the potential and do you say no.

There is a researcher at Johns Hopkins, Dr. Gerhart, who has demonstrated that he has been able to solve one of the problems with embryo stem cells. Two of the major problems are the tumorogenicity and the inability to control differentiation, and if he in an animal model lets the embryo grow to a fetus and it is at the 8- or 9-week-old stage and he harvests germ line cells—these are no longer embryo stem cells, but they are still stem cells—he harvests germ cells, he has been able to inject that into tissue and avoid the problem of creating tumors.

So that creates an example of the type of slippery slope we would be facing. If we knew we could have cures or we might potentially develop cures, do we then say, OK, we are not going to say 7 or 14 days is the limit, we are going to let ourselves grow embryos in an artificial setting to a later stage of development because we think we could have an effective cure?

It does create huge moral and ethical issues to simply say, because we can do it, maybe we should.

Ms. HOWARD. Let me speak——

Mrs. JO ANN DAVIS OF VIRGINIA. I would like to reclaim my time so I can ask all the questions I need to ask.

Ms. HOWARD. OK, but you did ask a question. Can I explain briefly how to——

Mrs. JO ANN DAVIS OF VIRGINIA. If the chairman will indulge me and let me go over my time, sure.

Ms. HOWARD. In SCNT, somatic cell nuclear transfer, i.e., therapeutic cloning, the nucleus of the donor's unfertilized egg is removed and replaced with the nucleus of a patient's own cells, like skin, heart, or nerve cells. These types of cells are called somatic cells. No sperm is used in this procedure. The cells are not transplanted into the womb. The unfertilized egg cells are stored in a petri dish to become a source of stem cells that can be used to treat life-threatening medical conditions.

What I think would be important to get you more background about——

Mrs. JO ANN DAVIS OF VIRGINIA. Is that a human cloned embryo?

Ms. HOWARD. This is an unfertilized egg. I am not sure—let me say this. I know that in both bills people have raised questions about the definition of what an embryo even is. I am not going to be here to tell you—to get into that. I will not have a definitional debate with you, but I think it is important for you to see the material that the coalition has put out about how they hope SCNT would be used.

Mrs. JO ANN DAVIS OF VIRGINIA. I am short on my time here.

As I understand it, the only difference in therapeutic cloning and reproductive cloning is simply the purpose, what they are used for. So I guess that is why I am having the confusion if it is nonfertilized.

I guess, Ms. Norsigian, I would ask you, do you think that approving and permitting therapeutic cloning would then lead to reproductive cloning when there is effectually no difference except for the purpose for which they are used?

Ms. NORSIGIAN. I think people who have—especially the statement that we heard read earlier, or parts of it that were read by the Chair, are very good comments about how it would be almost impossible to enforce a ban on human reproductive cloning if we allowed clonal embryos to be produced en masse, ostensibly for research purposes, but you would never be able to know that they would not be, and they could be fairly easily used in other ways, especially given the other bills that have absolutely no protections of the sort that might even reduce that likelihood.

So you are absolutely right, it is really the intent that matters here. But when you create a clonal embryo, it is an embryo that is capable of becoming a human being. We just would rely on people's good will not to do so, if there was a ban against human reproductive cloning.

Mrs. JO ANN DAVIS OF VIRGINIA. If you just stated that if you clone an embryo it has the potential to become a human being, then you disagree with the nonfertilized——

Ms. NORSIGIAN. Of course I disagree. If you have asexual reproduction, it is still reproduction. The fact that you are not using sperm is really not that relevant in terms of the issue of whether you can create a human being or not. It is very unusual, and there are people wondering, you know, this talk about the post-human future and all of that. But it is still the potential reproduction, even though it is not your classic fertilization the way we have always known it.

Mrs. JO ANN DAVIS OF VIRGINIA. Thank you, Mr. Chairman. I would yield to you, Doctor, but I don't have any time left.

Dr. WELDON. From a biological perspective, when you put a nucleus from a somatic cell into an egg and it begins to divide and form an embryo, you have a human embryo. It has the full potential, if it were introduced into a woman, to grow into a human baby. Just like Dolly the sheep was created, the same way, that is what they are talking about, in using humans.

What I think the gentlelady was trying to somehow imply is that it is somehow not human because you did not use a sperm to create it, that it is not an embryo somehow. The quote you have from the Bioethics Advisory Committee, President Clinton's Bioethics Advisory Committee, states very categorically that it is an embryo. That is because any biologist with his head screwed on right knows it is a human embryo. Despite some of the linguistic gymnastics that some people are trying to engage in on this issue, it is a human embryo.

Mrs. JO ANN DAVIS OF VIRGINIA. Thank you, Doctor, because it was very confusing to me.

Thank you, Mr. Chairman.

Mr. SOUDER. I want to thank this panel, as well as the first panel, for taking the time to come here to Washington. We may have additional written questions. I want to do a couple of things in summing up.

One is that I thought Mr. Kelly did a good job of pointing out the "box" question. In fact, cloning is inside the box. It is the currently PC term. It is the term that is the trendy thing to do. What we need are the creative proposals that we have heard at all the hearings that actually have produced results, and that research has basically been outside the box and shorter in duration than the types of research that have not been productive.

The question we need to be asking is, why is so much being driven toward nonproductive research and away from dollars that could be productive research? "outside of the box" is reversed on its head. There is a difference between a promise which is based on something and a possibility based on a hope that does not have any scientific evidence.

I think as we move forward in these hearings we continue to look for—and as we can see from today's hearing, we had—wide diversity. This was not an ethics of the debate hearing.

The second point, in one of these hearings we are going to get into the ethics more. I found Dr. Zavos' statement extremely troubling. That was what he said, we cannot be distracted by ethics. We are entering an era in the world where we had better be distracted by ethics, because these are very difficult questions. Individuals may disagree about when precisely life begins, how to define that life, how we should relate to each other, but just like here in the origins of life, we have to be concerned about ethics, and we are going to get into this in bioterrorism and when is a terrorist attack justified and not justified.

We need to have ethics as part of the public debate. It is scary to think it would not be part of the public debate.

Last, because I am sure anybody watching today is going to be very confused, because terminology in Washington changes based on kind of who wants to spin something for what time period, we

have seen a dramatic change in the argument toward research cloning from human cloning.

But somatic cell nuclear transfer, as has been stated here, is still a human embryo. It is a human embryo that is not necessarily being implanted. It is human cloning for research purposes, as opposed to human cloning for growing a future human being, but it is still human cloning, and it is just a different form. Changing a name to somatic cell nuclear transfer does not mean it is not human cloning, but it has a different purpose to the human cloning.

We are debating today about the different types of human cloning. We crossed two different types of human cloning, but we were still debating human cloning and not human cloning; and inside human cloning, two types, one just for research purposes, and one Dr. Zavos was arguing was for actually creating future, living human beings.

I want to once again thank all of the panelists who came forward today. If you have additional comments you want to insert for the record, or additional materials, you may.

I want to thank all the Members who participated and look forward to working with you in the future.

With that, our hearing stands adjourned.

[Whereupon, at 3:35 p.m., the subcommittee was adjourned.]

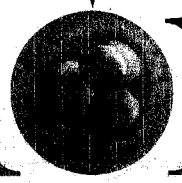
[Additional information submitted for the hearing record follows:]

BOSTON SUNDAY GLOBE APRIL 21, 2002

BIOETHICS

Cell division

With the president calling for an end to all cloning of human embryos and other countries backing a partial ban, one framework seeks regulation to clear the way for research while preventing the horrors envisioned by the Bush administration



A four-cell human embryo at 72 hours

By George J. Annas

Delegates from around the world met at the United Nations recently to begin preparing an international treaty to outlaw the reproductive cloning of humans. Representatives from countries as diverse as Brazil and Sweden, Uganda and China, Japan, Germany, and France all strongly support a treaty to ban reproductive cloning.

and most recently, rabbits and a kitten — to make a human child. Virtually every nation agrees that children should not be commodified like barnyard animals or pets, even like beloved cats or dogs.

The powerful global consensus that human reproductive cloning should be outlawed provides an unprecedented opportunity for the world to take united action on a bioethical issue that could profuses to support a ban.

The United States has, nonetheless, threatened to take its ball and go home if the world community does not give in to its demands to outlaw not just reproductive cloning but also research cloning. (Sometimes called "therapeutic cloning" — though no therapies have been produced — research cloning involves making human embryos by somatic cell nucle-

the same position taken by the House of Representatives last August, and repeated this month by President Bush, who has urged the Senate to join the House in outlawing both reproductive and research cloning.

The Senate will debate the ban soon. Observers think the outcome is too close

CLONING, Page E2

Cell division: Framework for compromise might be the answer

It is to call, but unless a compromise can be reached so that outlawing reproductive cloning is not held hostage to banning research cloning, the likely outcome is that no law will pass. Without congressional action banning reproductive cloning in the United States, it will likely be attempted by its radical proponents — Panos Zavos, a specialist in turkey sperm, and the Raelians, a Canada-based group that believes humans were created by extraterrestrials — long before any UN treaty comes into force. Zavos's partner, Italian physician Serverino Antinori, announced recently in Abu Dhabi that a patient of his is eight weeks pregnant with a human clone. Even though this is almost certainly untrue, Antinori and Zavos seem determined to try to produce the world's first human clone regardless of world opinion and the overwhelming scientific evidence of likely serious physical harm to the child. Can a compromise be found that can stop the renegades while permitting legitimate medical research?

The first step toward a solution is to understand the Bush administration's position. Leon Kass, its intellectual architect and the head of the president's newly formed Bioethics Council, has argued eloquently and passionately that if you oppose creating a child by cloning, you must also oppose creating human embryos for research by cloning. This is because, he says, if research cloning is permitted, it is inevitable that someone will try to implant one of the cloned embryos in a woman, and once this occurs, no government would ever force the woman to abort the clone. Moreover, he argues, research cloning would result in private industry stockpiling human embryos, and mining, exploiting, and selling them. Opponents of research cloning are already running radio ads warning of "embryo hatcheries" and "embryo farms." A ban on implanting these embryos, Kass says, would require the government to destroy cloned embryos rather than preserve and protect this form of nascent human life, action that would be repugnant to many.

Kass reiterated this position in January when he opened the first meeting of the Bioethics Council with a discussion of Nathaniel Hawthorne's "The Birthmark." In the story, a scientist, Alymer, marries a beautiful young woman, Georgiana, who has a small handlike birthmark on her face. Alymer becomes obsessed with removing it, and the potion he ultimately creates to successfully remove it also kills her. Imperfection, of course, is an inherent characteristic of humans, and attempting to make the perfect human is certainly dangerous, and ultimately impossible. Kass takes the story as a cautionary tale that science's attempt to perfect humans by, among other things, changing our basic sexual nature (as by making sexual reproduction optional) could have deadly consequences.

Congress has the authority to regulate all such research, not just publicly funded research, if it wants to.

I am sympathetic to Kass's slippery slope argument, and have even gone further than Kass by suggesting that by combining cloning technology with genetic engineering, we would inevitably put ourselves on the eugenics road not just to "designer babies" but to attempting to create perfect humans as well. If we fail, the consequences would be felt primarily by the children created in the failed experiments. But if we succeed, the consequences would be even deadlier, since the "improved" posthumans would inevitably come to view the "naturals" as inferior, as a subspecies of humans suitable for exploitation, slavery, or even extermination. Ultimately, it is this prospect of what can be termed "genetic genocide" that makes cloning combined with genetic engineering a potential weapon of mass destruction, and the biologist who would attempt it a potential bioterrorist.

So Kass (and Bush, and the United States at the United Nations) is right to caution us about the limits of our technology and the slippery slope. Alymer was wrong to see human perfection through scientific technique as a reasonable human goal, and "The Birthmark" rightly warns us about that nightmarish eugenic goal. But is Kass right to oppose research cloning aimed at finding cures for devastating human diseases and alleviating severe human suffering, historically both important and completely legitimate goals of medical research? I don't think so, at least not if we can take effective regulatory steps. And this points the way to a possible political compromise.

There are two basic ways the Senate could act to stop baby-making cloners without outlawing research on cloned embryos. The first is to put a moratorium on research cloning until the use of adult stem cells is fully explored, and/or until research using stem cells from "spare" or leftover embryos created at in vitro fertilization clinics is demonstrated to be of therapeutic value in tissue regeneration.

The second, and I think better and more permanent, solution is to create a regulatory framework that would make the administration's dreaded commercial stockpiles (and farms) of cloned embryos and the initiation of a pregnancy with one of them virtually impossible.

Regulation would be a challenge. Historically, embryo research has never been regulated, primarily because the US government has never funded it. Nonetheless, Congress has the authority to regulate all such research, not just publicly funded research, if it wants to. In particular, Congress could greatly improve the overall ethics of now wholly unregulated research with cloned human embryos, permitting the science to proceed, and at the same time virtually guarantee that no cloned human embryo lawfully made would be implanted — or even have to be ordered destroyed by the government.

To prevent the horrors envisioned by Kass . . . at least three prohibitions are required.

Here's how it would work. Ideally, Congress would create a federal oversight authority (similar to England's Human Fertilization and Embryology Authority) that would have exclusive authority to approve any proposed embryo research project, including those in the private sector. Approval would only be granted for those projects soundly designed to address a compelling medical need that could be successfully addressed no other way.

To prevent the horrors envisioned by Kass and the administration, specifically the stockpiling and commercial use of cloned research embryos and the implanting of a research embryo to start a pregnancy, at least three prohibitions are required:

- The freezing and storage of cloned embryos should be outlawed. Cloned embryos would be created solely for use in approved research projects, and there is no reason to "store" or "stockpile" them since the research embryos are destroyed in the research process. A strict limit of seven days should be placed on the length of time any cloned human embryo can be maintained.
- The purchase and sale of human eggs and human embryos should be outlawed. This would help to eliminate the increasing commercialization of embryo research and the commodification of both human eggs and embryos.
- All individuals, including physicians, scientists, and biotech companies who have not been approved to do research cloning must be prohibited from making or possessing cloned embryos. In addition, all in vitro fertilization clinics and physicians and embryologists associated with them would be specifically prohibited from doing research on cloned embryos — making it virtually impossible for a cloned embryo to ever be used to initiate a pregnancy.

Alymer's real crime was that he was unable to separate his love for his wife from his love of science, and in joining them, he killed her. Combining bans on both reproductive and research cloning in one bill is likely to kill the anticloning legislation as well. And since reasonable compromise is available, this lethal outcome is unnecessary.

We can sketch a parallel from another regulatory realm that helps demonstrate that the law can effectively ban one activity without banning two related activities. There is a reasonable argument that an effective ban on offensive biological weapons research requires a ban on defensive biological weapons research as well. Nonetheless, it would be self-defeating and irrational to refuse to support a ban on offensive weapons research solely because defensive research was not banned simultaneously. Defensive biowarfare research can be used to make an offensive weapon, of course, but this requires both a much greater volume of toxins as well as their introduction into a delivery system.

Likewise, cloned embryos could be used to make babies, but we are much more likely to prevent this eventuality with a ban on implanting human cloned embryos, such as that proposed by Senator Edward M. Kennedy, (coupled with regulation of embryo research) than with no regulation of cloning at all. It's time for Congress to pass a ban, and for the United States to support the treaty banning reproductive cloning. We can outlaw cloning to engineer children without outlawing cloning to engineer medicines.

"The Commission began its discussions fully recognizing that any efforts in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of any embryo, with the apparent potential to be implanted in utero and developed to term."

Cloning Human Beings: Report and Recommendations of the National Bioethics Advisory Commission, June 1997

"Because embryo cloning will compromise women's health, turn their eggs and wombs into commodities, compromise their reproductive autonomy and, with virtual certainty, lead to the production of 'experimental' human beings, we are convinced that the line must be drawn here."

Judy Norsigian
Co-Author Our Bodies, Ourselves for the New Century
Boston Women's Health Book Collective

Stuart Newman, Ph.D.
Council for Responsible Genetics
Professor Cell Biology at New York Medical College

CELLULAR CLONING:

TYPES	APPLICATION	DATE
Any Cells	Skin Grafts	1940's - Present
	Tissues	
	Monoclonal Antibodies	
	Recombinant Proteins	

NON-CELL CLONING :

TYPES	APPLICATIONS	DATE
DNA	Genetic Therapy	Late 1980's - Present
Proteins }	Recombinant Insulin: Diabetes	
RNA }	DNA Finger Printing	
	Diagnostic Tests	
	Forensics	
	Finger Printing	
	Parental Tests	
	Trace Genetic Diseases	

SOMATIC CELL NUCLEAR TRANSFER: CLONED EMBRYOS

TYPE	APPLICATIONS	DATE
Animal	Reproduction	1997
Human*	Research	2001

EMBRYO STEM CELL RESEARCH: NON-CLONED IVF EMBRYOS

TYPE	APPLICATIONS	DATE
Animals	Cardiac Cells	1998 - Present
Humans (IVF Embryos)		

ADULT STEM CELL RESEARCH: BODY CELLS

TYPE	APPLICATIONS	FEDERAL FUNDING
Human	Over 45 Clinical Trials	ALL
Animal	Diabetes	ALL

*H.R. 2505 only bans human somatic cell nuclear transfer, not other types of cellular cloning.

Adult Stem Cells

Bone Marrow

Marrow
Bone
Cartilage
Tendon
Muscle
Fat
Liver
Brain/Nerve
Blood cells
Heart
All Tissues

Fat Cells

Bone
Cartilage
Muscle

Peripheral Blood

Bone Marrow
Blood cells
Nerves

Skeletal Muscle

Skeletal muscle
Smooth muscle
Bone
Cartilage
Fat
Heart

Gastrointestinal

Esophagus
Stomach
Small Intestine
Large Intestine/Colon

Placenta

Bone
Cartilage
Muscle
Nerve
Bone Marrow
Tendon
Blood vessel

Brain

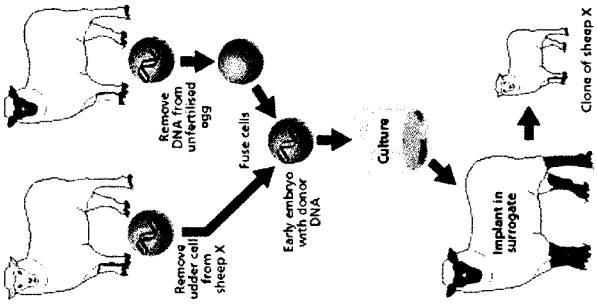
Brain
Nerves
Blood cells
Muscle
All Tissues

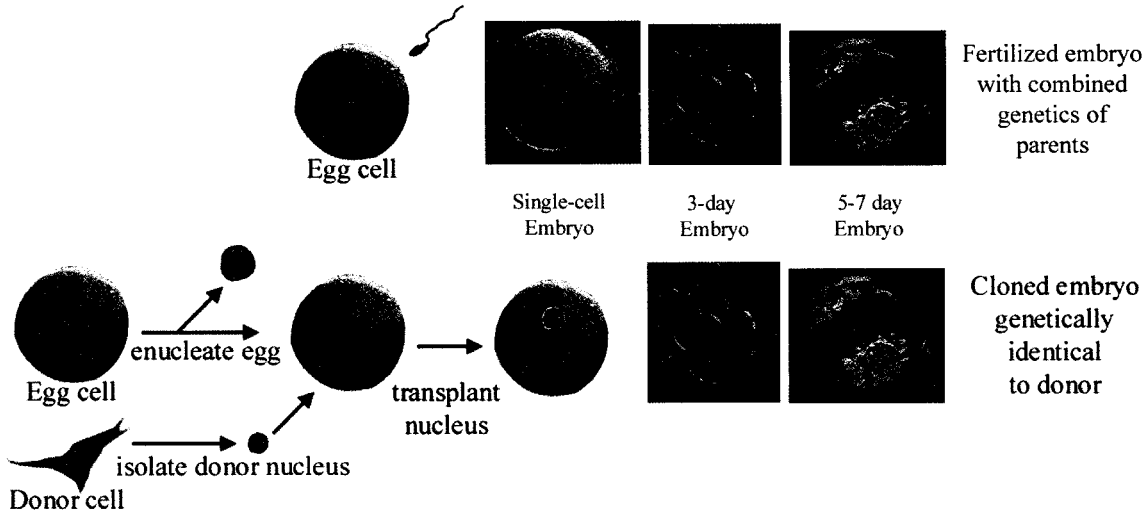
Skin (epidermis)
Cornea
Retina
Pancreas
Liver
Heart
Lung
Spermatogonia

CORD BLOOD

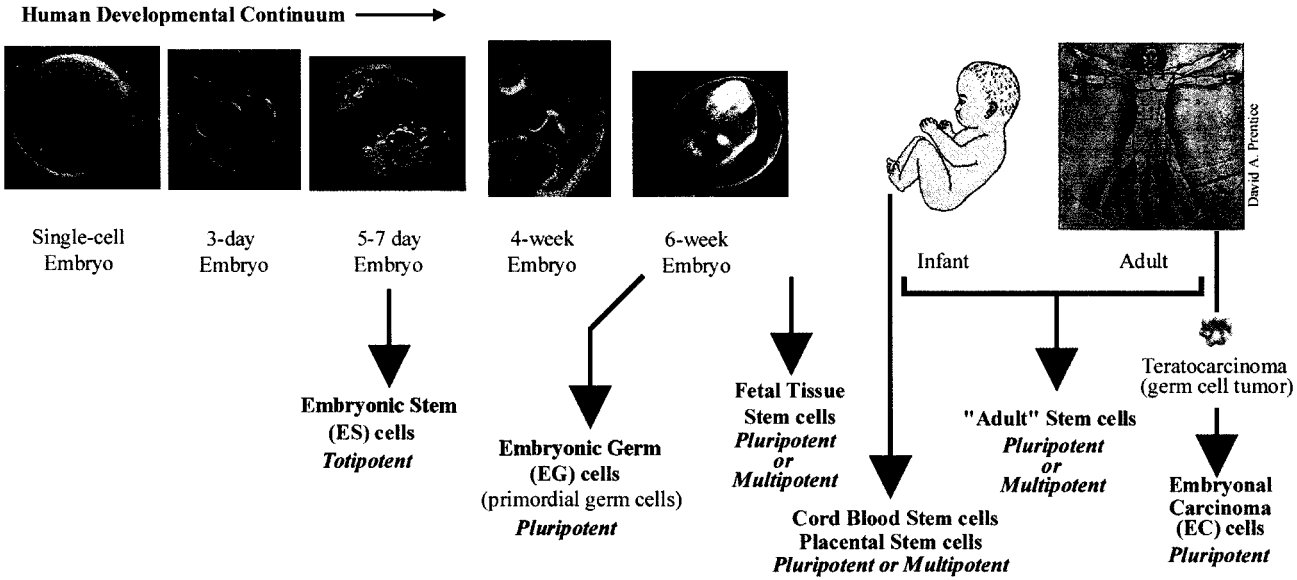
Various Tissues

David A. Prentice


Remove udder cell from sheep X
Remove DNA from unfertilised egg
Fuse cells
Early embryo with donor DNA
Culture
Implant in surrogate
Clone of sheep X


Egg cell
Single-cell Embryo
3-day Embryo
5-7 day Embryo
Fertilized embryo with combined genetics of parents
Egg cell
enucleate egg
Donor cell
isolate donor nucleus
transplant nucleus
Cloned embryo genetically identical to donor

Stem Cells


Human Developmental Continuum
Single-cell Embryo
3-day Embryo
5-7 day Embryo
4-week Embryo
6-week Embryo
Infant
Adult
David A. Prentice
Embryonic Stem (ES) cells
Totipotent
Embryonic Germ (EG) cells
(primordial germ cells)
Pluripotent
Fetal Tissue Stem cells
Pluripotent or Multipotent
Cord Blood Stem cells
Placental Stem cells
Pluripotent or Multipotent
"Adult" Stem cells
Pluripotent or Multipotent
Teratocarcinoma
(germ cell tumor)
Embryonal Carcinoma (EC) cells
Pluripotent

Statement of Stuart A. Newman, Ph.D.

Committee on Government Reform
Subcommittee on Criminal Justice, Drug Policy & Human Resources
U.S. House of Representatives

Hearing on Human Cloning

May 15, 2002

The U.S. Senate will soon be considering several bills to ban human cloning, including one that also calls for a ban on cloning for nonreproductive purposes, such as research and possible therapies. Advocates of research with clonal embryos say that they may facilitate the production of embryo stem cells that are genetically matched to prospective patients. But what is not generally appreciated is how simply following the logic of scientific and medical reasoning could pave the way for a "brave new world" in which cloning technology may eventually be extended to include even fully-developed clonal humans.

More than two decades of work on mouse embryo stem cells has yielded just a handful of published studies showing modest therapeutic results—in all cases less than what has been achieved with grafts of non-embryonic cells, including "adult" stem cells. Despite great efforts, embryo stem cells never become just one cell type or coherent tissue, but differentiate into disorganized mixtures of cell types. Most importantly, they are genetically unstable. If placed in adult mice they cause tumors. There is every reason to believe that human embryo stem cells, including those from cloned embryos, would cause cancer in human patients.

These problems may be overcome by additional research. But this may take years, and technologies, like water, tend to follow the path of least resistance. Embryo stem

cells are derived from embryos that are less than two weeks old—often described by advocates of experimental cloning as "a clump of cells in the bottom of a Petri dish." But scientists at Johns Hopkins University have isolated a different kind of human stem cell. These "embryo germ cells" are derived from 8-9 week embryos, and like embryo stem cells can differentiate into all cell types. Most importantly, when transplanted into experimental animals they do not cause cancer.

On purely scientific grounds, embryo germ cells show greater promise than embryo stem cells. If they were derived from *clonal* embryos they would be ideal candidates for the proposed regenerative therapies. Now, if the supporters of embryo cloning were perfectly frank they would also be advocating research into sustaining clonal embryos for 8 to 9 weeks so that genetically matched embryo germ cells could be harvested. These embryos would, of course, no longer be clumps of cells in a Petri dish, and some Congressional supporters of embryo cloning might object. Some may reason that it is better to do these things incrementally: once we have clonal embryos for a while and have gotten used to the idea, who would turn a deaf ear to calls by patients and their loved ones for these superior therapeutics?

And once stem cell harvesting from two-month clonal embryos was in place, who could resist the pleas to extend the time-frame so that liver and bone marrow could be obtained from six-month clonal fetuses to cure sufferers of life-threatening blood disorders such as beta-thalassemia, or so that brain lining cells could be harvested from near-term fetuses to treat Parkinson's sufferers?

All of this makes perfectly good scientific and medical sense. The only thing that stands in its way is a sense of propriety concerning the uses to which developing human

embryos and fetuses may be put. Some may draw the line at the tiny clump of cells; others at the two-month embryo; still others somewhat short of full-term. A prominent British biologist has advocated producing headless human clones for spare body parts. Few engaged in this debate would go along with the more extreme possibilities, but what about future generations growing up in a world in which producing clonal embryos for spare parts is medicine as usual?

A recent study from the laboratory of Dr. Rudolf Jaenisch at MIT suggests how, if embryo cloning were permitted to proceed, there would be medical incentives to bring full-born clones to term. This group started with a strain of mice lacking a gene needed for immune function. They used nuclear transfer to make embryo stem cells from one of these mouse embryos. They corrected the gene deficiency in some of the stem cells. They then used the corrected ES cells to generate mice that were genetically identical to the nuclear donor, but with a repaired gene. (The established method of "tetraploid complementation" allows the production of embryos derived solely from ES cells). They furthermore used these cloned/germline-modified mice as bone marrow donors for the diseased mice. Large sectors of the public have now accommodated to the idea that you can have a child (even with the help of preimplantation diagnosis) to provide tissues for another, sick child. This paper shows that you can make the second child by cloning the first, with genetic corrections. This provides a motivation for full-term cloning that would not be viewed as sinister; indeed, it would be welcomed by many. It also shows that existing technology can bring it off.

Once the cloning of human embryos is underway the spread of the technology will make it all but impossible to stop short of any of these applications. The Food and Drug

Administration has claimed jurisdiction over full-term cloning. But cloning is neither a food nor a drug, and most commentators agree that FDA prohibitions on cloning would not hold up in court. After the FDA sent a warning last year to two groups who claimed to be at the point of cloning humans, the bioethicist and lawyer R. Alta Charo asked in a Washington Post story (May 23, 2001), "Can the government really stop me from cloning myself? Right now, the law is clear as mud." When asked by the Post's reporter how the Supreme Court would be likely to decide a challenge to a human cloning ban, she replied: "If they were interested in protecting a broad notion of genetic connection to the next generation, then cloning might be included as a fundamental right."

Even without clonal human embryos scientists will still be in a position to study embryo stem cells, as well as adult stem cells. If embryo stem cells prove to more realistic as therapeutics than they now seem, researchers will undoubtedly find ways to genetically modify them so that they will not be immunologically rejected by patients. Not going down the road of producing clonal human embryos will leave open the major routes of stem cell research but spare us as a society from winding up in a place where virtually none of us wants to be.

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The Ethical and Scientific Dilemmas of Cloning

Ethical Dilemmas

(1) Allowing research cloning in effect legalizes human cloning.

A prohibition on cloning that is limited only to preventing the implantation of a cloned embryo in effect legalizes cloning. This is because cloning actually occurs with the creation of an identical-- or nearly identical-- genetic copy of a DNA molecule, cell, or individual plant, animal or human. Any cloning that creates a human embryo is human reproductive cloning, regardless of if the manufacturer intends to allow the clone to undergo the birthing process.

Recent scientific developments involve a cloning technique called "somatic cell nuclear transfer." The product of somatic cell nuclear transfer is an embryo. In short, this embryo is created by replacing the nucleus of a female egg cell with genetic material from a "somatic" cell (which is a cell from the body other than a sperm or egg cell). There is no involvement of sperm. The resulting embryo is a clone that is nearly genetically identical to the donor of the somatic cell.

There is no difference between a cloned human embryo created for reproductive or research purposes. Whether or not the newly created embryo is implanted with the intent of reproduction or destroyed for the purpose of research is irrelevant to the fact that a form of human has been created.

(2) Research cloning creates human life for the specific intention of killing it.

A ban that permits embryonic clones to be created but forbids them to be implanted in utero legally requires the destruction of human life and criminalizes efforts to preserve and protect it once created.

(3) Once created, cloned embryos could be used for reproduction.

Under a partial ban that permitted the creation of cloned embryos for research, human embryos would be widely cloned in laboratories and assisted-reproduction facilities. Once cloned embryos are available, it would be virtually impossible to control what was done with them.

Stockpiles of embryonic clones could be produced, bought and sold without anyone knowing it. Implantation of cloned embryos-- an easy procedure-- would take place out of sight, and even elaborate and intrusive regulations and policing could not detect or prevent the initiation of a clonal pregnancy. Scientists agree that once begun, a clonal pregnancy would be virtually impossible to detect or differentiate from a routine pregnancy. And if detected, governments would be unlikely to compel the pregnancy to be aborted or severely penalize the pregnant woman for allowing the implantation or for failure to abort the pregnancy. Numerous efforts in the U.S. and elsewhere are already ongoing to produce reproductive human clones.

A ban only on "reproductive" cloning would therefore be a false ban, creating the illusion that such cloning had been prohibited.

(4) Cloning exploits women and jeopardizes their health.

Cloning is entirely dependent upon the availability of eggs that can only be derived from women. Therefore, millions of women would be needed to undergo substantial health risks in order to harvest enough eggs for experimentation. If the 16 million diabetics in the U.S. could be treated via human cloning, a minimum of 800 million eggs would be needed.

Little data exists on the overall safety of the super-ovulating drugs that women would have to take in order to provide the massive amounts of eggs necessary for embryo cloning. These drugs are known to cause severe pelvic pain, nausea, liver dysfunction, reduced blood flow to critical organs, pulmonary complications, clotting and even death. And the impact on a donor's future fertility is unknown.

It is likely that women with limited financial resources will be the primary providers of human eggs.

(5) Allowing the cloning of embryos will open the door to other objectionable forms of experimentation.

Producing cloned human embryos will inevitably lead to calls to extend the lifespan of clonal embryos to permit the harvesting of more advanced cells and tissues—including organs from full term clones-- for research and potential therapies. If the harvesting of stem cells from days old embryos is permitted, what is to stop the removal of organs from weeks old embryos? Or months old fetuses?

(6) Without a ban, human embryos will be massed produced and cloned embryo farms will be developed.

A California biotech company is devising a computer chip that could automatically create hundreds of cloned embryos at a time. If developed, the chip would make cloning cheap and easy to mass-produce cloned embryos. Cloned embryo farms would likely arise to ensure easy access to specimens for scientists, researchers and others seeking clones.

(7) The high cost would make cloning too expensive to be a medically available therapy.

Even if cloning's problems are overcome and therapies are developed, the high cost would make therapeutic cloning far too expensive to use on an individual patient basis. Few companies and even some of those who support cloning research acknowledge cloning is unlikely to produce affordable medicines and has limited commercial promise. Lutz Giebel, CEO of CyThera, a cell therapy company in San Diego acknowledged that even if therapies were developed from cloning, "no one can afford the treatment."

Cloning of cats and dogs—which is much more simple than cloning humans-- is expected to cost somewhere in the low five figures. This price reflects merely the cost of the creation of the clone and not the development and application of a therapy.

Collecting just ten eggs—a small fraction of the total amount needed for the procedure-- costs $22,000, and this is merely the beginning of the cloning process. It has taken hundreds of eggs to produce just one successful cloned embryonic stem cell line in animal models, and as of yet, no human cloned embryonic stem cell lines have ever been produced.

Cloning would also be highly inefficient for other reasons as well. Each patient's cells, for example, would have to be put through Food and Drug Administration-mandated safety testing individually.

(8) Cloning would turn procreation into manufacture and make human life a commodity.

Human cloning would allow for the mass production of a class of human lives for the explicit purpose of exploitation. The factory manufacturing of cloned human embryos would result in the patenting of human lives by the Biotech Industry. The U.S. Patent and Trademark Office has already allowed a number of patents involving human embryonic stem cell lines.

(9) Once human cloning begins, there will be little oversight of the process or the outcomes.

At least 5 organizations have announced that they have either created human clones or are in the process of doing so. With no regulations to monitor or prohibit these endeavors, countless efforts could ensure to create human clones with unknown consequences. The five groups that have announced their efforts are:

Advanced Cell Technology in Massachusetts reported last November that they had cloned several human embryos, which died before they matured enough to use for research purposes. The company is paying women $4,000 to supply the eggs needed to continue their efforts.

Dr. Severino Anitonori, an Italian fertility doctor, recently revealed his plans top create cloned children for a dozen couples this summer. Dr. Anitonori claimed on April 3 that one of his patients was eight weeks pregnant with a cloned fetus. Dr. Anitonori more recently stated that three cloned human pregnancies are underway—"two in the former Soviet states and one in an Islamic country."

Dr. Panayiotis Zavos, a physician based in Lexington, Kentucky and formerly associated with Dr. Anitonori, is also working to create human clones. Dr. Zavos hopes to implant his first cloned embryos at two secret locations by August. He has described 2002 as the "year of the clone." Dr. Zavos said "The status is looking good, and we're ready to execute. We have selected the final 10 to 12 couples, and it's a matter of time now."

The Raelians, a religious cult, also claim to have cloned human embryos and plan to produce cloned babies. Scientists from Clonaid, which is

linked to the Raelians, announced in April that they have implanted the first cloned human embryos in the hope of bringing the first human clone into the world. "We have developed human embryos," claims Clonaid's scientific director Brigitte Boisselier. "When they are well developed, we implant them." She did not say how many clonal pregnancies were planned or were in progress.

Scientists at the Roslin Institute in the United Kingdom who cloned Dolly the sheep announced April 9 that they are prepared to clone human embryos for research.

Scientific Dilemmas

(1) Clones have been universally flawed and significant risks are associated with cloning.

There has been no animal research to date to support the claim that cloned embryonic stem cells are therapeutically efficacious. In fact, clones have been universally genetically unstable and suffer severe abnormalities. Cloning has also been linked to cancer, genetic mutations and even immune response rejection. A recently published review of all the world's cloned animals found that every one of them is genetically and physically defective.

Dolly the cloned sheep developed arthritis at an early age. And a high percentage of cloned monkey embryos that look healthy are really a "gallery of horrors" within according to a researcher at Advanced Cell Technology, which supports human embryo cloning. The success rate with other animal—such as mice and cows—has not been very high either. At best, around one half of cloned animal embryos develop to the point where they can be implanted, and only a tenth of these survive to birth. Often more than a hundred nuclear transfers must be carried out to create a single clone. Such low success rates calls into question the long-term viability of cells created from cloning. And of those that do survive to birth, many suffer from premature death. According to findings in the journal Nature Genetics, few cloned mice survive longer than two years.

Because of the instability of clones, the possibility exists that therapeutic experiments based upon cloning could actually worsen a medical condition or create new problems—such as cancer-- for a patient.

The Food and Drug Administration has stated that "with regard to the safety issues, there are far too many unanswered scientific questions to adequately assess the risk of human cloning at this time. Based on the

experience with animal models, the risks of human cloning are considerable. Failure rates for cloning animals are high and numerous abnormalities in the offspring and safety risks to the mother have been observed. There is general scientific agreement on these facts. Further, many noted scientists have pointed out that problems with human cloning may result in genetically-related disorders and diseases that may not appear for decades."

(2) Cloning siphons off limited resources from far more promising avenues of research.

To allow "therapeutic" human cloning would take limited resources away from far more promising and less problematic research alternatives such as adult stem-cell research. Scientists recently announced that they were able to transform ordinary human skin cells in a way that would offer patients a "grow-your-own transplants" option that would not require the creation or destruction of a cloned human embryo. Adult stem cell research has already yielded treatments for many conditions and new breakthroughs in this field are announced on almost a weekly basis. Many experts believe these and other alternatives will prove to be more efficient and cost-effective and less controversial. In addition, cloning would siphon funds away from the highly touted, yet still unproven, embryonic stem cell research.

(3) Clones do not provide an exact genetic match.

Since the donor egg also contains non-nuclear DNA in subcellular structures called mitochondria, the clone's cells contain a very small amount of mitochondrial DNA from the donor egg cell. Thus, the clone is not exactly genetically identical to the somatic cell donor and may face the same rejection problems that cloning advocates are seeking to avoid. Studies in mice and rats have shown that these mitochondrial proteins can provoke an immune rejection response.

(4) There has been no proven demonstration of the therapeutic effectiveness of cloning.

Cloning has not been shown to be effective in directly treating any injury or disease in experimental animal studies that form the essential basis for human clinical trials. The practical applicability or even development of therapeutic cloning remains highly speculative.

The odds favoring success of utilizing cloning for treatments "are vanishingly small" and the cost are daunting according to the chief executive of Geron Corp., a cell therapy company which opposes a ban of cloning research.

(5) Cloning 'therapies' would be ineffective for treating genetic diseases and disorders.

Cloning therapy in theory would utilize a patient's own cloned cells to correct a medical condition. Because the cells being used are identical to the source patient, any genetic defect that afflicts the patient would be contained within the cloned cells. Therefore, it would be very unlikely that cloning could ever be successfully utilized to treat genetic disorders such as Juvenile diabetes or Alzheimer's.

Cloning Claims and Facts

"Prohibiting 'reproductive cloning' but allowing 'therapeutic' cloning will prevent human cloning."

A prohibition on cloning that is limited only to preventing the implantation of a cloned human embryo in effect legalizes cloning. This is because cloning actually occurs with the creation of an identical-- or nearly identical-- genetic copy of a human. Any cloning that creates a human embryo is human reproductive cloning. Whether or not the newly created embryo is implanted with the intent of reproduction or destroyed for the purpose of research is irrelevant to the fact that a form of human life has been created.

Under a law permitting the creation of cloned embryos for research, cloned human embryos would be massed-produced in laboratories and possibly in assisted-reproduction facilities. A ban on clonal implantation may be a deterrent, however any penalties imposed on those who initiate a clonal pregnancy would take place after the fact. Actually preventing clonal implantation would require stopping the procedure from the start, with the creation of the cloned embryo. Once cloned embryos are available, it would be virtually impossible to control what was done with them. Stockpiles of embryonic clones could be produced, bought and sold without anyone knowing it. Implantation of cloned embryos-- an easy procedure-- would take place out of sight, and once cloned embryos are available in the lab even elaborate and intrusive regulations and policing would not detect or prevent the initiation of a clonal pregnancy.

Scientists agree that once begun, a clonal pregnancy would be virtually impossible to detect or differentiate from a routine pregnancy. And if detected, governments would be unlikely to compel the pregnancy to be aborted or severely penalize the pregnant woman for allowing the implantation or for failure to abort the pregnancy. Numerous efforts in the U.S. and elsewhere are already ongoing to produce cloned human babies.

A prohibition on the implanting of cloned embryos would, therefore, be a false ban, creating the illusion that human cloning could not occur. Such a law would not stop the creation of cloned humans because reproductive cloning necessarily occurs with the same procedures as research cloning, the creation of a cloned human embryo. Allowing for the creation of cloned human embryos would enhance the possibilities for cloned babies to be born by allowing for the development of both the technology to produce clones and a countless supply of cloned embryos that would be difficult to monitor.

"Using cloned human embryos for research will lead to the development of medical treatments and cures for millions of patients."

This is entirely speculative. No treatments or cures for any medical condition in animals or humans have been developed as a result of cloning. Researchers do not know how to

—or even if they can—control the transformation of stem cells from cloned human embryos into neurons, pancreatic cells, or any other specialized cells.

Even supporters of cloning research acknowledge that cloning is unlikely to produce cures. A complete ban on human cloning would have "a limited impact on corporate product development," admits Lutz Giebel, CEO of CyThera, a cell therapy company in San Diego. And even if therapies were developed, "no one can afford the treatment," according to Giebel.

Research has found that virtually every animal clone created to date is genetically and physically defective. There is no way to know how such genetic abnormalities would affect the psychology of human clones. These abnormalities are thought to be due to faulty reprogramming of clones' genetic material (DNA). This may lead to abnormal gene expression of any of the 30,000 genes residing in the organism. Methods used in routine prenatal screening to detect chromosomal or genetic problems in a fetus cannot detect these reprogramming errors. Further, it is unexpected that any methods to access whether the genome of a cloned embryo has been correctly programmed will be available in the foreseeable future.

Due to their recognized inherent genetic instability, clonal stem cells may never be able to be utilized for medical therapies. If there are undetectable genetic abnormalities in a developing human clone, then there may also be problems with the tissues and cells derived from the cloned embryo. Using cloned cell may, in fact, create new problems for patients, including the possibility of cancer or other unforeseen and previously inexperienced conditions and syndromes.

Human cloning for research would take limited resources away from far more promising and less problematic research alternatives such as adult stem-cell research. Scientists recently announced that they were able to transform ordinary human skin cells in a way that would offer patients a "grow-your-own transplants" option that would not require the creation or destruction of a cloned human embryo. Adult stem cell research has already yielded treatments for many conditions and new breakthroughs in this field are announced on almost a weekly basis. Many experts believe these and other alternatives will prove to be more efficient and cost-effective and less controversial. In addition, cloning would siphon funds away from the highly touted, yet still unproven, embryonic stem cell research.

Even if research cloning's problems are overcome and therapies are developed, the high cost would make therapeutic cloning far too expensive to use on an individual patient basis. Cloning cats and dogs—which is much less complex than cloning humans-- is expected to cost somewhere in the low five figures. This price reflects merely the cost of the creation of the clone and not the development and application of a therapy.

"Therapeutic cloning avoids the rejection often associated with cell, tissue or organ donation."

This is also speculative, and very possibly unlikely due to the process by which clones are created. Since the donor egg also contains non-nuclear DNA in subcellular structures called mitochondria, the clone's cells contain a very small amount of mitochondrial DNA from the donor egg cell. Thus, the clone and the stem cells derived from it would not be genetically identical to the somatic cell donor and may face rejection problems that cloning advocates are seeking to avoid.

The use of patients' own adult stem cells is already being used to treat many medical conditions without rejection. And a newer experiment recently reported transforms a patient's skin cells into other cell types offer also alleviates rejection. Neither of these requires the destruction of the creation or destruction of cloned human embryos. Further, embryo stem cell researchers believe that there are ways of dealing with immune rejection without research cloning.

"The result of somatic cell nuclear transfer, or cloning, is not a human embryo."

Some supporters of research using cloned human embryos claim that an embryo created without sperm or that exists outside of the womb is not a real human embryo. This is scientifically and biologically inaccurate. The product of cloning—also called "somatic cell nuclear transfer" (SCNT) or "nuclear transplantation"-- is an embryo. The significant difference between a cloned embryo and a natural embryo is that unlike natural fertilization a cloned embryo is created when the nucleus of a cell other than sperm is introduced into an egg. However, there is no noticeable difference between a cloned embryo and a naturally created embryo, and if implanted into the womb, both will grow and develop into a fetus, a child and ultimately an adult human. One would have unique genetic make-up created from two parents, whereas the cloned person would have the same genetic male-up as the individual who served as the genetic source.

Some may claim that "Life does not begin in a petri dish," but the scientific fact is that the lives of hundreds of thousands of born children have indeed begun in the laboratory, and the life of every cloned sheep, cow, and cat began in a petri dish.

The scientific community, and even proponents of research cloning, has widely acknowledged and accepted that the result of somatic cell nuclear transfer or nuclear transplantation or whatever term one uses for cloning is indeed an embryo:

President Clinton's National Bioethics Advisory Commission, in its 1997 report *Cloning Human Beings*, explicitly stated: "The Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo, with the apparent potential to be implanted in utero and developed to term."

The National Institutes of Health Human Embryo Research Panel also assumed in its September 27, 1994 Final Report, that cloning results in embryos. In listing research

proposals that "should not be funded for the foreseeable future" because of "serious ethical concerns," the NIH panel included cloning: "Such research includes: . . . Studies designed to transplant embryonic or adult nuclei into an enucleated egg, including nuclear cloning, in order to duplicate a genome or to increase the number of embryos with the same genotype, with transfer."

A group of scientists, ethicists, and biotechnology executives advocating "therapeutic cloning" and use of human embryos for research -- Arthur Caplan of the University of Pennsylvania, Lee Silver of Princeton University, Ronald Green of Dartmouth University, and Michael West, Robert Lanza, and Jose Cibelli of Advanced Cell Technology -- confirmed in the December 27, 2000 issue of the *Journal of the American Medical Association* that a human embryo is created and destroyed through "therapeutic cloning": "CRNT [cell replacement through nuclear transfer, another term for "therapeutic cloning"] requires the deliberate creation and disaggregation of a human embryo. ... because therapeutic cloning requires the creation and disaggregation ex utero of blastocyst stage embryos, this technique raises complex ethical questions."

On September 7, 2000, the European Parliament adopted a resolution on human cloning. The Parliament's press release defined and commented on "therapeutic cloning": ". . . 'Therapeutic cloning,' which involves the creation of human embryos purely for research purposes, poses an ethical dilemma and crosses a boundary in research norms."

Lee M. Silver, professor of molecular biology and evolutionary biology at Princeton University, argues in his 1997 book, *Remaking Eden: Cloning and Beyond in a Brave New World*: "Yet there is nothing synthetic about the cells used in cloning . . . . The newly created embryo can only develop inside the womb of a woman in the same way that all embryos and fetuses develop. Cloned children will be full-fledged human beings, indistinguishable in biological terms from all other members of the species."

The President and CEO of the biotechnology firm that recently announced its intentions to clone human embryos for research purposes, Michael D. West, Ph.D. of Advanced Cell Technology, testified before a Senate Appropriations Subcommittee on December 2, 1998: "In this . . . procedure, body cells from a patient would be fused with an egg cell that has had its nucleus (including the nuclear DNA) removed. This would theoretically allow the production of a blastocyst-staged embryo genetically identical to the patient... ."

Dr. Ian Wilmut of PPL Technologies, leader of the team that cloned Dolly the sheep, describes in the Spring 1988 issue of *Cambridge Quarterly of Healthcare Ethics* how embryos are used in the process now referred to as "therapeutic cloning": "One potential use for this technique would be to take cells -- skin cells, for example -- from a human patient who had a genetic disease . . . . You take this and get them back to the beginning of their life by nuclear transfer into an oocyte to produce a new embryo. From that new embryo, you would be able to obtain relatively simple, undifferentiated cells, which would retain the ability to colonize the tissues of the patient."

As documented in the *American Medical News*, February 23, 1998, University of Colorado human embryologist Jonathan Van Blerkom expressed disbelief that some deny that human cloning produces an embryo, commenting: "If it's not an embryo, what is it?"

Dr. John Gearhart of Johns Hopkins University, one of the discoverers of human embryonic stem cells, told the President's Council on Bioethics on April 25, 2002, that he the product of cloning is and should be called an "embryo." He said: "I know that you are grappling with this [question of whether a cloned embryo created in the lab is the same thing as an embryo produced by egg and sperm, and whether we should call it an "embryo"], but anything that you construct at this point in time that has the properties of those structures to me is an embryo, and we should not be changing vocabulary at this point in time. It doesn't change some of the ethical issues involved."

In its February 23, 2002 editorial, the magazine "New Scientist" deplored "shifty" tactics by cloning supporters to attempt to change the terminology for cloning, concluding, "Here at New Scientist we will continue to call a clone a clone."

"Prohibiting research on cloned human embryos would hinder medical research and chase researchers overseas."

Presently no ban on experimentation using cloned human embryos exists in the United States, yet little research is being done in this area. Only one U.S. company—Advanced Cell Technology of Massachusetts—is known to be conducting such research. Several others have announced their intentions to create a clones, but not for research purposes. Therefore, a ban on creating clones would have little, if any, impact on therapeutic research endeavors underway if the U.S. It would however discourage rogue scientists from creating human clones for the intent of reproduction. Because other countries proceed with human cloning does not justify the United States proceeding as well.

"Supporting cloning for research is pro-life."

Most of those who support cloning only advocate the creation of clones for destruction and research. They believe that if cures are found from the destruction of human clones, lives could be potentially saved or improved. This they claim is a "pro-life" position. Yet they propose that any attempts to preserve the life they have created be harshly penalized. This is not a pro-life position. There is no proof that cloning will save lives, but only that it will create life for the specific purpose of destroying it.

"Therapeutic cloning can provide cures to those afflicted by diabetes, Parkinson's, Alzheimer's and other genetic disorders."

Cloning therapy in theory would utilize a patient's own cloned cells to correct a medical condition. Because the cells being used are identical to the source patient, any genetic

defect that afflicts the patient would be contained within the cloned cells. Therefore, it would be very unlikely that cloning could ever be successfully utilized to treat any genetic disorders.

"Cloning will produce a limitless supply of embryonic stem cells."

Scientists have yet to produced stem cells from human cloning. To date, the most successful human embryo clone has reached only six cells before it stopped dividing, thus yielding no embryonic stem cells or other transplantable tissue.

"Human cloning is a reproductive right and is a legitimate cure for infertile couples."

The courts have not found an absolute right to reproduction or a right to reproduce however one chooses. Incest, for example, is illegal and should remain so even though it is a means to reproduce.

Efforts to create human beings by cloning mark a new and decisive step toward turning human reproduction into a manufacturing process in which "designer children" are produced in laboratories to preordained specifications and, potentially, in multiple copies.

Because it is an asexual form of reproduction, cloning confounds the meaning of "father" and "mother" and confuses the identity and kinship relations of any cloned child.

Because cloning requires no personal involvement by the person whose genetic material is used, cloning could easily be used to reproduce living or deceased persons without their consent.

The severe genetic abnormalities to the cloned offspring and the significant health risks to both the mother and the women who are used to provide the eggs necessary for cloning also make 'reproductive' cloning highly unethical.

"A ban on 'reproductive cloning' that allows cloning for research, or 'therapeutic cloning,' will provide effective safeguards to prevent the creation and birth of cloned human children."

The task of enforcing a general ban on human cloning for any purpose, like that proposed in the "Human Cloning Prohibition Act of 2001" (H.R. 2505) passed by the U.S. House of Representatives (or S. 1899 currently pending in the Senate), does not seem to pose insuperable challenges. The legislation clearly defines the exact activity to be banned, which is the use of the procedure known as somatic cell nuclear transfer (the procedure that produced "Dolly" the sheep) to produce human embryos. The activity involves certain visible steps, and can be distinguished from the usual process of in vitro

fertilization (IVF) with the naked eye. The cloning procedure uses complete nuclei extracted from body cells, not sperm, and requires additional steps (e.g., extraction of the egg's existing nucleus, chemical or electrical stimulation of the egg after transfer of the nuclear material) to produce an embryo. The eggs used in the procedure would have to be donated by women who will not be using them for their own reproductive goals, and any pursuit of clinical research based on cloning would require obtaining a great many eggs from these women. These visible activities and interactions are not different in kind from those which law enforcement is ordinarily called upon to address. Those participating in these activities could be questioned and, with sufficient evidence, apprehended and prosecuted as the legislation provides.

Enforcing the policy of S. 2439 is a challenge that raises a different set of questions. This legislation is designed to "protect" the activities described above when they are conducted for the purpose of research. The Act seeks only to forbid "implanting or attempting to implant the product of nuclear transplantation into a uterus or the functional equivalent of a uterus." Several difficulties arise at this point:

1) The prohibited activity – transfer of an embryo to a uterus – is an activity that is otherwise permitted now in all states and is performed thousands of times a year in fertility clinics. This legislation does not seem intended to establish a broad prohibition on such activity. However, the act of transferring a cloned embryo to a uterus is presumably exactly the same regardless of whether the embryo involved was originally produced by cloning or fertilization. There is no visible difference between the prohibited activity and permitted activity. Law enforcement would have to choose between allowing some of the former, and imposing a new degree of careful scrutiny on the latter. This would be a formidable task in light of the number of embryo transfers performed in fertility clinics across the country every year.

2) At the point when embryo transfer occurs, at the blastocyst stage (about 5-6 days after the embryo is produced), there does not seem to be any reliable means for determining the difference between a fertilized embryo and a cloned embryo. Biologically these embryos are, for all intents and purposes, indistinguishable. While animal trials indicate that cloned embryos may undergo a heightened risk of metabolic and other problems, these are not detectable prenatally through any existing genetic or other test. Moreover, the embryos maintained in the laboratory long enough to be considered for either research or implantation would presumably be those which show few or no visible signs of such problems. Therefore it is not clear how, upon hearing that someone may be engaging in the activity prohibited under the Act, law enforcement personnel could determine that it was taking place even if they were present and observing the activity firsthand. Moreover, if a researcher mixed cloned and fertilized embryos in culture and then implanted only some of these embryos, there would be no way of proving that the implanted embryos were the ones which arose from cloning. Even after the fact, it is not clear how one could determine that the fetus in utero was originally produced by cloning, unless one could demand a prenatal genetic profile and show that this profile is genetically virtually identical to a particular pre-existing individual, at which time a cloned human has already been produced.

3) Permitting, by law, the development of technology to create cloned human embryos for research will allow for the development of the same technology needed to create cloned human embryos for the intent of reproduction. Only by prohibiting the development of these technologies for any reason will prevent the capability to produce clones and deter the creation of cloned humans.

In general, it is difficult to construct a scenario in which law enforcement could be aware of the prohibited activity in time to prevent it, unless the participants publicly announced it in advance. Both before and after implantation, the evidentiary challenge of proving that a particular pregnancy arose from cloning would be formidable. And even if that challenge could be met, it is not clear what if any steps could be taken by law enforcement to effectuate the Act's goal of preventing the birth of cloned infants. Once a pregnancy were established, no governmental authority could compel an abortion. Pursuing a federal prosecution of a woman for becoming pregnant or for giving birth is a task that few would welcome – and in any case, the birth would still take place.

It is imperative then in order to prevent this scenario from occurring, federal law enforcement would have to impose new and unprecedented scrutiny upon all fertility clinics and/or research facilities that produce extracorporeal human embryos for any purpose, by any means (whether cloning or fertilization). At this point the resources and the authority to impose such scrutiny do not seem to exist, and would likely be siphoned away from other urgent needs such as detecting and combating bioterrorism. While S. 2439 seeks to apply current standards for federally funded human subjects research (45 CFR Part 46) to privately funded research involving nuclear transplantation, neither these standards nor any other federal regulations establish requirements for research involving cloning, in vitro fertilization or extracorporeal embryos. Therefore the cloning ban as envisioned by S. 2439 is by and large unenforceable and will do little to deter or prevent clonal pregnancy or cloned offspring and may even contribute to haste that such events may occur.

Cloning Terms and Definitions

Clone—A clone is, quite simply, a copy of something else. In this debate, the term clone is used to describe a genetic copy of another being, such a human or animal.

Embryo—The first stage of development of a living being. For humans, the embryo stage occurs from the moment of conception through the eighth week of development following implantation. An embryo can be created by the union of an egg and a sperm either naturally or in a laboratory or via cloning when an egg is "fertilized" by replacing its DNA with someone's DNA.

Nuclear Transplantation—Another term for cloning.

Reproductive cloning—Term used by cloning proponents to describe cloning in which the intent is to implant a clone and bring it to birth. All cloning is in of itself 'reproductive' cloning.

Somatic cell nuclear transfer—Another term for cloning.

Stem cells— Stem cells are the fundamental building blocks for all the tissues in the body. The three types of stem cells being explored are adult stem cells, embryonic stem cells and cloned embryonic stem cells. Only adult stem cells have been successfully used for therapeutic purposes. Likewise, adult stem cells are the only type that can be derived without killing the human source of such cells.

Therapeutic cloning—Term used by proponents of human cloning to describe cloning in which the intent is to use cloned human embryos for research, which always requires the destruction of the clone.

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INDEPENDENT

April 5, 2001

Bernard A. Schwetz, D.V.M., Ph.D.
Acting Principal Deputy Commissioner
Food and Drug Administration
Rockville, MD 20857

Dear Dr. Schwetz,

As you know, the Food and Drug Administration (FDA) has outlined its authority over clinical research using cloning technology under the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act.

I applaud the testimony of Dr. Kathryn C. Zoon, Director of FDA's Center for Biologics Evaluation and Research (CBER) at the March 28 Committee on Energy and Commerce hearing in which she stated "FDA views the use of cloning technology to clone a human being as a cause for public health concern" and that "FDA would not permit the use of cloning technology to clone a human being at this time." Dr. Zoon further stated that 'the Administration is unequivocally opposed to the cloning of human beings."

In the FDA's October 26, 1998 Dear Colleague letter regarding the agency's opposition to human cloning and again in Dr. Zoon's testimony, however, the actual definition of "human being" is left unanswered. International scientific consensus recognizes that human embryos are biologically human beings and acknowledges the physical continuity of human growth and development from the one-cell stage forward. Specifically, both the Human Embryo Research Panel and the National Bioethics Advisory Commission have described the human embryo as a living organism and a "developing form of human life." While I also understand that the term "human being" would encompass an embryo as well as all other stages of human development, some do not recognize this truth.

I would like to know:

(1) If the FDA considers an embryo to be a human being;
(2) What the FDA's definition of "human being" is; and

(3) If the FDA published or otherwise announced a definition of "human being?"

In the conclusion of Dr. Zoon's testimony, she stated that "because of the unresolved safety questions pertaining to the use of cloning technology to clone a human being, FDA would not permit any such investigation to proceed at this time." Could you elaborate as to what safety questions would have to be resolved in order for the FDA to approve human cloning investigations or research to begin?

Because the FDA has outlined its authority under law to regulate cloning, and clinical research can not legally be conducted without an investigational new drug application (IND) in effect, what penalties would be levied by the agency against an individual or entity found to be either attempting human cloning or found to have cloned a human being without FDA approval?

Thank you for your prompt attention to this important subject.

Sincerely,

Mark Souder

Mark E. Souder
Chairman
Subcommittee on Criminal Justice,
Drug Policy and Human Resources

CC: The Honorable Tommy G. Thompson
Secretary
Department of Health and Human Services

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUN - 1 2001

The Honorable Mark E. Souder
Chairman
Subcommittee on Criminal Justice, Drug Policy,
and Human Resources
Committee on Government Reform
House of Representatives
Washington, D.C. 20515-6148

Dear Chairman Souder:

Thank you for your letter dated April 5, 2001, regarding human cloning technology. You asked for the Food and Drug Administration's (FDA or the Agency) definition of "human being" and opinion as to what safety questions would have to be resolved in order for FDA to permit human cloning research to begin.

First, it is important to bear in mind that the Administration is unequivocally opposed to the use of cloning technology to clone a human being. FDA has not published or otherwise announced a definition of "human being." Because human cloning is intended to make a copy of a person using the genetic material from a single somatic cell, FDA does not believe it is necessary to define the term human being to establish whether or not human cloning has taken place. Also, we do not believe that the definition of such term is necessary or that it is a prerequisite for FDA to establish or exercise its jurisdiction over the use of cloning technology to clone a human being.

In evaluating the products and procedures regulated by FDA, the fundamental consideration in evaluating cloning or any other regulated activity is whether the products and processes are safe and effective *for their intended use*. In accord with the laws the Agency is charged with administering, FDA would consider whether the products used for this purpose are safe and effective, and would not allow clinical trials to proceed unless and until the Agency received sufficient evidence from the sponsor that the trial could proceed safely.

As part of this process, FDA would consider the safety of the surrogate mother and the safety of any child born from the procedure. The definition of human being is not necessary in reaching these conclusions of "safety and effectiveness for their intended use."

With regard to the safety issues, there are far too many unanswered scientific questions to adequately assess the risk of human cloning at this time. Based on the experience with animal models, the risks of human cloning are considerable. Failure rates for cloning animals are high and numerous abnormalities in the offspring and safety risks to the mother have been observed. There is general scientific agreement on these facts. Further, many noted scientists have pointed out that problems with human cloning may result in genetically-related disorders and diseases that may not appear for decades.

Finally, it is important to note that FDA's role in assessing the use of cloning technology to clone a human being is a scientific one. As recognized by the National Bioethics Advisory Commission, there are additional unresolved issues including the broader social and ethical implications of the use of cloning technology to clone a human being. Because of the profound moral and ethical issues, as previously noted, the Administration is unequivocally opposed to the cloning of human beings.

As you note in your letter, FDA's position is that it has jurisdiction to regulate human cloning and that failure to adhere to FDA regulations would expose individuals to penalties under the Public Health Service (PHS) Act and the Federal Food, Drug, and Cosmetic (FD&C) Act.

FDA may seek to restrain and enjoin individuals who fail to adhere to laws administered by FDA, including the FD&C and the PHS Acts. The maximum penalty that could be imposed on an individual for a criminal violation of the PHS Act or a misdemeanor violation of the FD&C Act is one year imprisonment and/or a fine of up to $100,000 (for a misdemeanor not resulting in death) or an alternative fine of twice the amount of gross pecuniary gain or loss. The maximum penalty that could be imposed on an individual for such a felony violation of the FD&C Act "with the intent to defraud and mislead" is three years imprisonment and/or a fine of up to $250,000, or the alternative fine described above.

It is possible that fraudulent conduct involving cloning could also violate provisions of the Federal criminal code (Title 18) such as the conspiracy, mail fraud, wire fraud, or false statement laws. The maximum penalty for such crimes is five years imprisonment and/or the fines set forth above.

Thank you for contacting us regarding this important issue. If you have further questions, please let us know.

Sincerely,

Melinda K. Plaisier
Associate Commissioner
for Legislation

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INDEPENDENT

April 17, 2002

Honorable Tommy G. Thompson
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Thompson,

In March 2001, Kathryn C. Zoon, Ph.D., Director of the Food and Drug Administration's Center for Biologics Evaluation and Research (CBER), submitted testimony to the House Energy and Commerce Committee in which she declared that "the use of cloning technology to clone a human being would be subject to both the biologics provisions of the Public Health Service (PHS) Act and the drug and device provisions of the Federal Food, Drug, and Cosmetic (FD&C) Act."

In that same testimony, Dr. Zoon made clear the consequences of that regulatory authority, "Before such research could begin, the researcher must submit an IND request to FDA, which FDA would review to determine if such research could proceed."

Dr. Zoon also explained how FDA would respond to such a request. "FDA believes that there are major unresolved safety questions on the use of cloning technology to clone a human being and therefore would not permit any such investigation to proceed at this time."

Additionally, in a letter to this Subcommittee dated June 1, 2001, Melinda K. Plaisier, FDA Associate Commissioner for Legislation, outlined extensive penalties, including the violation of federal criminal code, which would result from not complying with FDA regulations in regard to conducting unapproved human cloning.

Since these statements by the FDA were made, Advanced Cell Technology, Inc. (ACT) of Massachusetts has made it publicly known that it is creating cloned human embryos for research purposes. According to an article printed in the January 13, 2002

edition of The Boston Globe, ACT has created a number of cloned human embryos, all of whom have thus far died, and that "the US Food and Drug Administration has quietly encouraged the firm's cloning work." The Globe reports that "In August, with ACT's headline-grabbing human cloning announcement imminent, the company briefed enthusiastic FDA officials on its ambitious plans, according to company officials present at the private meeting. At that same meeting, FDA officials discussed eventually conducting clinical trials on medical treatments derived from human embryo clones. And they compelled ACT officials to sign an affidavit promising not to clone embryos for the purpose of creating new human beings, explaining that such a document would provide cover for their work, according to [ACT's medical director, Dr. Robert] Lanza."

Following the August meeting with the FDA, ACT announced plans to clone human embryos in November and has been attempting to do so since.

In light of these developments, could you provide the following information:

(1) Did ACT formally seek approval from FDA before pursuing its cloning activities? If so, please provide ACT's application(s).

(2) Is the Boston Globe account of ACT's meeting with the FDA factually correct? If not, please provide the FDA's version of the meeting(s) with ACT.

(3) ACT is clearly violating the FDA's stated policy on human cloning. FDA has outlined the penalties for doing so. Does the FDA intend to pursue sanctions or other remedial measures against ACT?

(4) Please provide a list of the names and titles of FDA officials and staff that attended any meetings with ACT regarding ACT's cloning efforts, and/or were on any conference calls with ACT regarding this topic.

(5) In addition to ACT, have any other scientists or research organizations contacted or been in touch with the FDA to discuss their potential or on-going experiments involving cloned human embryos?

(6) Please provide a copy of the affidavit signed by ACT and any other affidavits or compliance agreements between FDA and ACT regarding cloning and any affidavits or compliance agreements between ACT and any other agencies under HHS regarding cloning.

(7) Please provide a copy of any minutes (including informal notes) from any ACT "briefings" to or meetings with FDA officials and staff regarding cloning of human embryos.

(8) Please provide any electronic communication (including e-mails) from FDA staff to ACT officials regarding human cloning.

(9) Does the FDA recognize that cloned human embryos are in fact cloned human beings in their earliest stage of development?

I look forward to a prompt response and in learning how the FDA intends to exercise its regulatory authority with respect to ACT's past and continuing human cloning activities.

Sincerely,

Mark E. Souder,
Chairman
Subcommittee on Criminal Justice,
Drug Policy and Human Resources

Enclosures: Boston Globe article
FDA correspondence

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The Boston Globe

January 13, 2002, Sunday ,THIRD EDITION
Correction Appended

SECTION: METRO/REGION; Pg. A1

LENGTH: 1951 words

HEADLINE: FIRM FACES UNCERTAIN FUTURE WHILE TOILING WITH EMBRYOS

BYLINE: By Raja Mishra, Globe Staff

BODY:
WORCESTER - The first security card opens the door. A second opens the freezer housing human eggs. Only after clearing those checkpoints can scientists at Advanced Cell Technology here begin their work. Out comes the egg's DNA, in goes another adult's DNA. Chemicals are injected. A human embryonic **clone** is born.

They have done this dozens of times in the last two months. Talk radio blares in the background. A video camera hovers. To date, every one of the cloned embryos has died before it could produce the stem cells the scientists sought. But ACT vows to continue until one embryo yields the prized cells.

On the outside, this small biotech firm is one of the most controversial companies in America. It has been a target of President Bush, who seeks to outlaw all human cloning. The US Senate, in coming weeks, will consider criminalizing the firm's work. But inside ACT's tidy lab there is no hesitation. Scientists here display a quiet resolve to **clone and clone** again until the firm makes its point: Human embryonic cloning can revolutionize medicine.

"I've been in some controversial places. But this is by far the most extreme," said ACT's medical director, Dr. Robert Lanza.

These are heady, complicated times for the privately held Worcester company. Its work, more than any other lab or company, has forced the public to weigh ethics against medical progress.

And its relationship with the US government grows increasingly contradictory.

In coming weeks, the US Senate plans to debate a human cloning ban, a bill that in effect targets ACT alone. No other US company is known to be trying to **clone** a human embryo. Bush champions the ban, even singling out ACT for condemnation.

But at the same time, one wing of his administration - the US Food and Drug Administration - has quietly encouraged the firm's cloning work.

In August, with ACT's headline-grabbing human cloning announcement imminent, the company briefed enthusiastic FDA officials on its ambitious plans, according to company officials present at the private

meeting.

At that same meeting, FDA officials discussed eventually conducting clinical trials on medical treatments derived from human embryo **clones.** And they compelled ACT officials to sign an affidavit promising not to **clone** embryos for the purpose of creating new human beings, explaining that such a document would provide cover for their work, according to Lanza.

"It was a very amicable affair," he said. "They were thankful that we took the time to come down to the FDA to brief them about our activities. They said the meeting helped them tremendously, and that they hoped we would think of them as a resource."

The FDA has declined comment on its dealings with ACT, but a spokeswoman cited recent federal mandates giving the agency authority over all human cloning-derived medical applications.

Lanza, 45, runs ACT's cloning effort, housed in a cramped office suite in Worcester's booming biotech corridor. Born in Boston and raised in Stoughton, he published his first scientific paper while attending Stoughton High School and was accepted to the University of Pennsylvania's medical school before finishing 12th grade.

The author of numerous texts on organ transplants, Lanza grew frustrated as patient after patient rejected transplanted organs. And then a sheep **clone** was born.

"Dolly happened and that was it," said Lanza. "That was the answer."

In 1998, he sought out ACT, which was at the fore of animal cloning science. He met a receptive CEO in Michael West, an ambitious scientist with a taste for pushing boundaries.

Now the company views cloned human embryos as a treasure chest of treatments: Individual patients would **clone** themselves; the embryos would grow for a few days, yielding stem cells, and the primordial cells would be coaxed into brain, heart, muscle or whatever tissue the patient required. Rejection would not be a problem because the tissue would genetically match the patient.

The first hurdle in advancing this approach was human cloning itself. No one had done it. In the late summer and fall of last year, ACT made 19 attempts to **clone** human embryos, succeeding 11 times. Most of the embryos died within hours. But three lasted for two days, developing four to six cells. If they had lived about a week, long enough to grow into 60 to 100 cells, stem cells could be harvested.

But the process requires a delicate act of nurturing that ACT has yet to master.

"If ACT succeeds, I happen to think that's going to be very important," said Dr. George Daley, a prominent embryonic stem cell researcher at the Massachusetts Institute of Technology-affiliated Whitehead Institute. "But it's a very labor-intensive process. It's a real challenge."

To accomplish even the first step - creating a successful cloned embryo - requires a deft combination of knowledge and technique. ACT hired the steadiest hands in the field from around the world, people known for their ability to pierce and poke at delicate microscopic cells, to suck and insert DNA without damaging them. Still, months were spent producing the first **clone.**

The next step - growing them - is perhaps more complex. ACT's embryos sit in petri dishes, far from the nurturing environment of the womb. They appear silver under the microscope, dwarfed by the hair-thin

pipettes used to feed them. The embryos require a precise and elusive mix of nutrients to develop properly. And they need just the right amount of oxygen. ACT scientists, peering for hours through microscopes, adjust these with each experiment, seeking the magic combination. But to date, the embryos have withered and died in their dishes.

As ACT continues its laboratory trial and error, involving the death of microscopic human embryos at each turn, some cloning opponents said the firm's work confirms their worst fears, that the destruction of large numbers of human embryos would become a routine feature of medical research.

"This is like the '30s, when the Nazis had no moral qualms about conducting experiments on and destroying people they considered subhuman," said Ray Neary, former president of Massachusetts Citizens for Life, who organized a protest at ACT last month.

Lanza, a Roman Catholic who supports abortion rights, appears squarely focused on how to move forward. The combined progress of his lab and that of other stem cell researchers could quickly produce treatments ready for testing in patients, he said.

"I could be in clinical trials next year, if I had the OK," said Lanza.

To that end, ACT officials this summer contacted the FDA. In August, they flew down to meet with Kathryn Zoon, director of the FDA's Center for Biologics Evaluation and Research, and her staff, which has jurisdiction over all human embryonic cloning applications. Lanza and West presented their ambitious plans, including their then-unrevealed effort to **clone** the first human embryo.

FDA officials outlined potential governmental hurdles, ACT scientists said. The FDA officials, along with getting ACT to promise not to allow any cloned embryos to become fully formed humans, also offered encouragement.

"They were wonderful. We have an excellent relationship," said Lanza.

ACT's stunning November announcement that it had created the first human embryo **clones** reignited calls in Congress to ban all forms of cloning. The US House passed such a ban earlier this year. The Senate plans to take up the matter in either February or March. Massachusetts Senator Edward M. Kennedy plans to lead a push to modify the bill to allow work on cloned embryos while preserving the ban on cloning humans, according to his aides.

But Bush supports the House's approach. If the Senate approves, ACT would be legislated out of business. With this looming, the company has found it hard to raise the money to push its science forward, said Lanza.

Nonetheless, ACT has conducted several notable experiments in cow cloning, still unpublished, the company said. Heart tissue was grown with stem cells from a cloned cow embryo, then successfully transplanted. Using the same process, a functioning miniature cow kidney was created and transplanted. And a similar process yielded high-potency cow immune cells, according to ACT.

Lanza said these experiments are "proof of principle" that ACT's vision can be realized.

A security guard has recently been stationed at the firm's Worcester offices and many of its 50 employees are wary of all the attention. But Lanza said he was surprised at the timidity of the blacklash. The protests have been quiet and small. And he counts only two threatening letters.

Far more profuse, he says, are the pleas for help. During a recent interview he held up a letter from a quadriplegic man who lives in the Tamil Nadu state of India, complaining of a "vegetable existence" and urging Lanza to "continue to carry on your research with compassion."

"This is not some academic debate," said Lanza. "This is reality. This is why we push forward."
SIDEBAR: THE PROCESS PLEASE REFER TO MICROFILM FOR CHART DATA.

CORRECTION-DATE: January 13, 2002, Sunday

CORRECTION:
Because of a reporting error, a Page 1 story last Sunday on Advanced Cell Technology of Worcester misstated the number of times that the company failed in human embryonic cloning attempts. ACT has acknowledged only eight failures to date. The story also incorrectly said that the US Food and Drug Administration asked ACT to sign a letter promising not to use cloning for reproductive purposes. The letter was conceived and drafted by ACT, not the FDA.

GRAPHIC: PHOTO CHART, Medical director Robert Lanza doing research on cow cells at Advanced Cell Technology. / GLOBE STAFF PHOTO / JANET KNOTT

LOAD-DATE: February 5, 2002

Adult Stem Cell's Offer Ethical and More Promising Alternative to Cloning

Unlike cloning and embryonic stem cell research, adult stem cell treatments do not require the destruction of a form of living human life.

Adult stem cells are already being used to treat and cure a host of diseases. No one has *ever* been cured or even treated with the use of either cloning or embryonic stem cells and their potential uses continue to be largely speculative.

Cloning advocates believe potential cloning therapies would be unique because they may avoid immune rejection commonly associated with other transplantation techniques. Adult stem cells are not rejected by a patient's immune system.

Embryonic stem cell research advocates believe that these cells are capable of being transferred into any cell in the body. Adult stem cells have been shown to turn into nearly every cell type.

Cloning requires the creation of human embryos that must then be destroyed. Cloning human embryos has proven to be highly problematic and nearly all clones contain genetic abnormalities. Adult stem cells are widely available throughout the human body, even in fat, and can be harvested from numerous sources from umbilical cords to human cadavers.

Limited resources should be directed into research that holds the most promise and least ethical and moral dilemmas, which adult stem cell research has proven to be.

washingtonpost.com

Study Finds Potential in Adult Cells

Discovery Will Likely Fuel Ethical Debate

By Justin Gillis
Washington Post Staff Writer
Friday, June 21, 2002; Page A01

Researchers have isolated a type of cell from bone marrow that seems capable of transforming itself into most or all of the specialized cells in the body, a dramatic new finding likely to fuel the debate over the ethics of stem-cell research.

The finding was reported by researchers at the University of Minnesota and published online yesterday by the journal Nature. It heightens the prospect that therapies scientists are trying to create -- cures for diabetes, Parkinson's disease, hemophilia and many others -- can be made entirely with adult cells, alleviating moral concerns over using discarded embryos and fetuses as sources of tissue.

There has been conflicting evidence about whether cells found in adults might be as useful as those derived from embryos. But the work by Catherine Verfaillie, known as a fastidious and cautious researcher, was widely acknowledged as the most definitive evidence to date that adult cells may be almost as versatile as embryonic cells.

Austin Smith, a prominent researcher in Scotland who has criticized some prior studies using such cells, called the Verfaillie paper "extraordinary."

The work is still at an early stage, however, and Verfaillie asked that it not be used as a political weapon to fight simultaneous work on embryonic and fetal cells.

"I think it is going to be important to be in a position to really compare and contrast the cells," she said, with the ultimate goal of determining "which cells are going to work for which therapy."

As if to underscore that point, Nature simultaneously published work at the National Institutes of Health showing that embryo-derived cells can vastly improve symptoms similar to those associated with Parkinson's disease in mice. That work, led by Ron McKay, is one of the most convincing demonstrations to date that such embryonic cells may be useful in medical care.

The cells in McKay's experiments, derived from mouse embryos, took up residence at the right spot in the brains of adult mice and produced dopamine -- a critical substance that is in short supply in Parkinson's disease -- in exactly the way that would be needed to relieve the symptoms of the ailment. It is far from proof of a cure, but "it's absolutely definitive evidence that these cells can work in the brain," McKay said.

The more unexpected finding was that of Verfaillie, director of the University of Minnesota's Stem Cell Institute. With the paper, she joined the company of biologists who are overturning the dogma that animal development proceeds in one irreversible direction, from the unspecialized cell formed when sperm and egg fuse to the highly specialized cells of an adult body.

Hints of her work had been emerging for two years in papers and scientific conferences, and scientists had been eagerly awaiting it. Many other reports, some of them controversial, already emerged in recent years of various adult cell types being able to perform unexpected feats of transformation. But Verfaillie has discovered what appears to be the most flexible adult-derived cell yet.

She calls the cells in question "multipotent adult progenitor cells." She and her colleagues have isolated them from mice, rats and people, though they are only able to do so in 70 percent to 80 percent of the people they test, for unknown reasons.

In animal experiments, the cells proved to lack certain characteristics of embryonic stem cells, which are capable of making every tissue in an animal's body. But they shared many other characteristics and proved to be able to transform into cells of the liver, lung, gut, blood, brain and other organs. They have proven particularly amenable to transformation into liver cells.

Many of the types of experiments Verfaillie reported, which involved injecting the adult cells into developing mouse embryos, cannot ethically be done in humans. But further animal experimentation may clear the way to use the cells in treating human disease. Several scientists cautioned that this will take years, at best.

Verfaillie's results suggest the tantalizing possibility that every adult may carry around the raw material of his or her own repair kit -- one that nature is somehow failing to use in many diseases but that scientists might be able to exploit to make new tissues and revivify failing organs.

Cells derived from a person's bone marrow would be unlikely to be rejected by the immune system, a potential problem with treatments based on embryonic- or fetal-derived cells.

Verfaillie said the cells might even be useful for correcting genetic diseases. They could be taken out of the body, a repaired gene could be inserted, doctors could grow many copies and then the cells would be inserted into a deficient organ such as the liver, along with proper manipulations to get them to turn into functional liver cells.

The Verfaillie work "is a nice research paper," said John Gearhart, a biologist at Johns Hopkins University in Baltimore and one of the two American scientists known for isolating human embryonic and fetal stem cells. "I think it's good, solid work. We'll see where it goes."

Verfaillie's work was particularly welcomed yesterday by opponents of embryonic stem cell research. They have long contended that adult-derived cells offer just as much promise and don't pose the same moral concerns as embryonic cells.

The Senate is embroiled in arguments over a related issue. Sen. Sam Brownback (R-Kan.) wants a federal ban on the transfer of nuclei from adult cells into hollowed-out human eggs.

The intent of the scientists who want to perform that procedure, a type of cloning, would be to derive healthy replacement cells that are a perfect genetic match for a human patient. But because the procedure would create a microscopic embryo that would be capable, briefly, of turning into a human clone if implanted into a woman's uterus, some groups oppose it, saying destruction of the microscopic embryo would be tantamount to murder.

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'Supercell' Controversy Sets Off a Scientists' Civil War

By Antonio Regalado
The Wall Street Journal
PAGE B1

AT A PRESS CONFERENCE yesterday at the University of Minnesota, two teams of scientists came together to present evidence showing the great therapeutic promise of stem cells—both those from adults and from embryos. But the friendly session masked underlying rancor. In fact, political wrangling over stem cells has ignited a civil war among biologists, with proponents of cloning and embryo research waging a crusade that has discredited alternatives carrying fewer ethical burdens.

At the center of the debate is research showing that existing cells in the body can act like stem cells extracted from embryos-- that is, they are "supercells" that can turn into nearly all the other cells in the body. A leading researcher in this area, Catherine Verfaillie, is publishing today in the journal Nature her findings that bone-marrow cells can be turned into nerve, liver and other types of cells.

Reports showing how adult stem cells share many of the properties of those from embryos constitute a powerful argument for those in favor of banning cloning. When the New Scientist magazine first reported Dr. Verfaillie's findings in January, Republican Sen. Sam Brownback of Kansas, a staunch opponent of cloning, quickly saw its value as ammunition. "I am heartened to know that scientific research has proven, once again, that destructive human embryo research and human cloning are unnecessary," he said in a news release.

At the same time, however, U.S. scientific leaders were mobilizing to cast doubt on research pointing to a supercell. Rushing out papers showing the benefits of cloning research, they castigated the alternative research as unproven and sloppy science.

Those attacks have left a residue of battered egos and hard feelings. "The doubters have a campaign to let their doubts be known," says Diane Krause, a researcher at Yale University in New Haven, Conn., whose results are among those being questioned. "But I believe my data."

How technological alternatives to cloning fizzled in biology's biggest debate in decades is a testament to strong scientific opposition to any law that would criminalize basic research. Sen. Brownback and Democratic Sen. Mary Landrieu of Louisiana were pushing White House-backed legislation that would ban human-embryo cloning in all forms, whether for research or to create a baby. A rival bill, supported by the Democratic leadership and some influential Republicans, would bar only reproductive cloning. Last week, a vote on the cloning measures was again put off.

The stem-cell field is so hot and the political stakes so high that vying for grants, corporate funding and scientific reputations has at times turned ferocious between the two camps. "It would be a tragedy for science to become an intellectual monoculture and to suppress this variety of views," says William B. Hurlbut, a professor at Stanford University. "The whole spirit of science is open inquiry."

In her paper, Dr. Verfaillie and her team at the University of Minnesota were able to isolate cells from mouse or human bone marrow that multiply rapidly and form many other types of tissue. Dr. Verfaillie says the all-purpose cells appear when bone marrow is grown in a lab dish for several months under special conditions.

It is possible that the cells are an artifact of the lab manipulations, and Dr. Verfaillie concedes that she has fallen short of proving that the cells -- which she calls multipotent adult progenitors -- exist as such in the adult body. But she says she has been able to grow the cells from the bone marrow of more than 70 human volunteers so far, as well as scores of mice and rats.

Still, Dr. Verfaillie says, "we had a hard time getting it into Nature" because the paper has had to clear unusually high hurdles. Yet she concedes there was good reason for

the extra scrutiny. "It's against the rules of embryology. It's not supposed to be this way," she says.

Stanford biologist Irving Weissman, a staunch pro-cloning scientist and a reviewer of Dr. Verfaille's paper for Nature, called her to sound her out on her views, eventually asking her to draft a letter rebutting Sen. Brownback's conclusions.

At a Senate hearing in early February, Sen. Brownback met with a swift rebuke from Dr. Weissman, who read from Dr. Verfaillie's letter. All research must move forward, Dr. Verfaillie had written, since her own results were still uncertain. "It is far too early to say whether they will stack up," she wrote.

One of the most senior figures in the adult stem-cell field, Dr. Weissman has emerged as a devastating critic of some of the newer results. "I do not rejoice in contradicting so publicly someone of your reputation," he wrote in an e-mail to Sen. Brownback after the February hearing.

Some mainstream scientists agree that cloning embryos may not be a good idea, but few say so publicly. "Because you have such highly visible scientists speaking out in favor of therapeutic cloning, people are afraid there may be retribution for piping up" with different views, says John Wong, chief executive officer of MorphoGen Pharmaceuticals Inc. of San Diego. The company is working with a muscle cell that it believes can also become many other cell types.

As part of their effort to bolster therapeutic cloning and overshadow alternative research such as that of Dr. Verfaillie, scientists were trying to quickly make a scientific case for cloning. At the Massachusetts Institute of Technology, Prof. Rudolf Jaenisch concedes he had politics in mind when he rushed into print a paper showing that therapeutic cloning could work, at least in mice, to treat a genetic blood disorder.

Along with data in support of therapeutic cloning, embryonic stem-cell researchers also released two papers in Nature casting doubt on reports that adult cells could change type. The authors suggested that all such results,

including Dr. Verfaillie's, could be the result of scientific errors.

By late March, adult stem-cell researchers were at the receiving end of what became a concerted effort to throw into question their most spectacular results. Dr. Weissman and other opinion leaders led the effort at a conference in Keystone, Colo., where 700 stem-cell researchers had converged for a week of technical talks and skiing.

"I have never been at a meeting that was so nasty," says one scientist whose results came under frequent attack. Yet in some cases, the criticisms were warranted. Scientific teams had been unable to reproduce a report that nerves could become blood cells. And other researchers had abandoned their hypothesis that muscle could become blood.

Scientists such as Dr. Weissman were also fighting to uphold scientific standards in the quickly growing field, as well as the decades-old scientific dogma that cells committed to become blood or bone can't switch. "It is not yet time to abandon traditional notions," wrote Princeton molecular biologist Ihor Lemishka following the meeting.

In a separate report today in Nature, Ron McKay of the National Institutes of Health describes how he used mouse embryos to generate nerves that cured other rodents of a Parkinson's-like condition. He had been unable to do that with adult stem cells. "Stem cells are not all equivalent," said Dr. McKay at yesterday's press conference in Minnesota, urging support for all avenues of research.

The Mercury, Hobart
June 29, 2002, Saturday
SECTION: WORLD; Pg. 20

'Bubble boy' disease cured

Using an experimental technique that altered genes in bone marrow stem cells, doctors cured two children who were born with the "bubble boy" disease that leaves patients defenseless against infection. The children were born with a form of severe combined immunodeficiency disorder caused by a gene flaw. The flaw blocks production of an enzyme called ADA, which is essential to make disease-fighting immune cells.

Doctors in Italy and Israel cured the children with injections of bone marrow stem cells that had been altered to contain the missing enzyme gene. In a matter of months, the researchers reported in this week's edition of the journal Science, both children had healthy immune systems.

W. French Anderson, a University of Southern California researcher and a pioneer in the field, said the research is an important advance for the entire concept of gene therapy because the patients have developed normally functioning immune systems.

Severe combined immunodeficiency disorder (SCID) is rare, striking only about 50 children a year. It was always fatal, causing uncontrollable infections, until doctors began isolating patients in sterile environments-- the most famous was an American known as "David, the bubble boy".

In the study, the Italian and Israeli researchers treated two children, a seven-month-old and 2½-year-old, who were born without functioning normal ADA enzyme genes. The researchers corrected the flaw by changing the genes in the stem cells of the bone marrow that make blood cells.

To do this, the doctors removed stem cells from the bone marrow of each patient and then used a virus to insert in these cells the normal gene for ADA. The stem cells where then re-injected and naturally migrated to the bone marrow.

The bone marrow in both children quickly began producing normal disease-fighting blood cells. Within months, their immune systems were able to overcome some common childhood infections which previously they could not combat with treatment.

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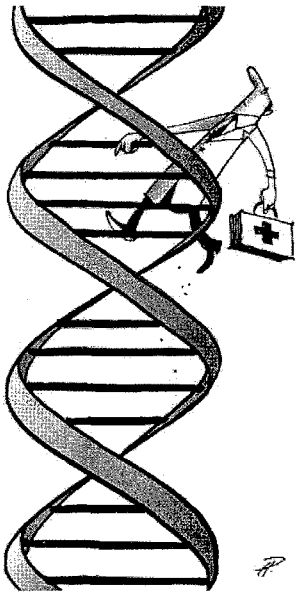
Adult stem cell research holds more scientific promise for cures

Should embryonic cloning research be banned?

By James Kelly / Special to The Detroit News



"For the last seven years, I have not been able to eat, wash, go to the bathroom or get dressed by myself. Some people are able to accept living with a severe disability. I am not one of them."

Thus spoke actor Christopher Reeve at a recent Senate hearing. I couldn't agree more. I also have a cervical spinal cord injury and share some of Reeve's symptoms. I also want to find a cure for spinal cord injuries, as do many of the 300,000 Americans who have this condition.

Unfortunately, my agreement ends there. Reeve claims embryonic stem cells taken from cloned human embryos are needed to cure spinal cord injuries and other illnesses. He made misleading claims to support this contention:

* "In my own case, I require remyelination of nerves (their recoating with insulation). ... At the moment, only embryonic stem cells have the potential to do that, and experiments are being done now in larger animals demonstrating that."

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But the research clearly shows otherwise. For example, Japanese researchers have recoated rats' spinal cords using adult bone marrow stem cells. Neural stem cells (from adults) have been successfully used to recoat tissue in the central nervous system in animal models in France,

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England, Japan, and at the University of Wisconsin. Adult cells found in the nose have been widely reported to cause nervous system recoating upon transplantation.

After years of successful animal tests, researchers and doctors at Yale are already treating two human patients suffering multiple sclerosis by using coating cells taken from their own peripheral nerves.

* "Efforts to repair central nervous system disorders may need to recapitulate the process of fetal development. And that can only be accomplished by human (embryonic stem) cells."

The first statement may be correct -- although many studies using adult stem cells, or no stem cells, have led to functional improvements after spinal cord injuries in both animals and humans. But Dr. Maureen Condic's peer-reviewed work at the University of Utah has shown that adult neurons can be induced into an embryonic regenerative state without using embryonic or fetal tissue. And Dr. Anton Usala, a noted diabetes researcher, has shown in a human pilot study that certain adult tissues will regenerate using an embryonic process without embryonic or fetal tissue when exposed to an artificial embryonic-like extracellular scaffolding.

* "Why do we need therapeutic cloning? As a layman, several important reasons come to mind: One, implantation of human embryonic stem cells is not safe unless they contain the patient's own DNA. ... So without the ability to use my own DNA, without that somatic cell transfer, I'm out of luck."

Several well-designed studies have clearly shown that our bodies contain easily accessible adult stem cells capable of maturing into virtually every crucial cell type, including neurons and a vital central nervous system cell type. And when taken from the patient, these cells all contain the patient's DNA.

So exactly what do we need cloning and embryonic stem cells for?

America's disabled and the public are being flagrantly misled concerning the immediate and long-range therapeutic potential of cloning. I have no doubt that Reeve wants to get out of his wheelchair as badly as I want to walk away from mine, but regarding this issue he is sadly misinformed.

The tragedy is that valuable public and private research funds may end up being diverted to basic embryonic stem cell and cloning research with little clinical potential, to the detriment of proven and further developed avenues that could help both of us during our lifetimes. If that happens, Reeve will have more to answer for than the destruction of some embryos.

Yes

James Kelly is a liaison between academic and corporate researchers and the Mike Utley Foundation, an Orondo, Wash. group dedicated to finding cures for spinal cord injuries like the one that paralyzed former Detroit Lion Mike Utley.

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Scientist believe emerging medical breakthrough would use adult stem cells—rather than stem cells created from destructive embryonic or cloning research-- to treat patients with AIDS and cancer:

XINHUA NEWS AGENCY
June 17, 2002, Monday

Australian Scientists Claim World-First Find

DATELINE: CANBERRA, June 17

Australian scientists claimed a world-first in detecting stem cells that could restore the body's immune system in HIV and cancer patients.

The Australian Associated Press reported Richard Boyd and Jason Gill, of the Monash University Medical School in Melbourne, said Monday they had used the stem cells to grow a complete and functional thymus organ in mice. The next step was to identify the human equivalent in stem cells and recreate a human thymus in a mouse. Boyd said he hoped the research would eventually be used to repair or renew the thymus of people with damaged immune systems including those who had undergone chemotherapy and radiation treatment, and HIV sufferers.

"We have the possibility of rebuilding someone's thymus after it has been destroyed or using gene therapy to correct gene mutations that lead to thymus problems," he was quoted by the Australian Associated Press as saying.

The Australian
June 18, 2002, Tuesday
SECTION: LOCAL; Pg. 5

Stem-cell research to treat HIV, cancer

BYLINE: Helen Tobler * Medical reporter

SCIENTISTS have succeeded in rebuilding an organ crucial to the human immune system entirely from stem cells, opening the way for the treatment of HIV and cancer.

Stem cells in the thymus -- the organ that is crucial to the normal functioning of the immune system -- have been identified by a team at Monash University in Melbourne. T-cells, the cells that fight infection, are only created in the thymus. In an article, published today in the international journal Nature Immunology, research scientists Richard Boyd and Jason Gill reveal they were able to rejuvenate a damaged thymus and then regenerate the immune system in mice.

Associate professor Richard Boyd, who led the research, said the discovery had opened an opportunity to rebuild a patient's thymus after it had been destroyed. But the real significance of the research was the ability to create T-cells, Dr Boyd said.

The research, which took 15 years and was funded by the federal Government, could lead to treatments for conditions in which the T-cells have been severely depleted, such as AIDS, and after radiation therapy or chemotherapy.

"It will also be useful in controlling organ transplantation and correcting auto-immune diseases. We know these diseases are caused by abnormal T-cells," Dr Boyd said.

In auto-immune diseases, such as diabetes, multiple sclerosis and lupus, a malfunctioning thymus is symptomatic.

Dr Gill said the studies on mice enabled them to generate a fully functional organ from stem cells.

"It's the first time people have generated a fully functional organ that has been shown to conduct every function exactly the same from very few starting stem cells.

"We haven't effectively shown that the cells we're looking at are able to give rise to themselves, which is an issue we bring up in the paper. But we've clearly shown that these cells are able to give rise to all the other cells within the thymus, and that these cells are able to attract other various cells in, and make a fully functioning organ."

The thymus normally was fully functional before puberty and replenished the blood with T-cells, Dr Gill said.

"But after puberty, when the sex steroids come out, the thymus drastically decreases its function. Normally it's not a big issue but when you have to replenish the immune system, say in diseased states, it can be a problem.

"So we're looking at therapies to be able to activate these stem cells and give rise to a fully functional thymus in the adult situation."

If the epithelial cells -- cells in the thymus that are essential to the immune response -- can be stimulated to produce a thymus, this will regenerate the T-cell pool.

Dr Gill said human trials were still some way off.

TwinCities.com

Posted on Wed, May. 15, 2002 PIONEER PRESS

Adult stem cells viable

BY TOM MAJESKI
St. Paul Pioneer Press

University of Minnesota researchers have coaxed adult bone marrow stem cells into becoming functioning liver cells, the latest in their efforts to demonstrate the versatility of these miniature building blocks and their potential to someday replace more controversial embryonic stem cells in research and treatment.

The first-of-its-kind discovery opens the door to a number of potential uses, including treating genetic and other liver diseases, creating bio-artificial livers that could be used as bridges to transplants and enabling pharmaceutical companies to screen new drugs for liver toxicity and efficiency prior to testing them on humans.

Dr. Catherine Verfaillie, director of the university's Stem Cell Institute and author of the latest study, said the plasticity of adult bone marrow stem cells is real. The development was published in today's edition of the Journal of Clinical Investigations.

"We were able to show that the same cells that were made to produce blood vessels also can produce liver cells," said Verfaillie, who has gained a national reputation for her cutting-edge research. "So a single cell can do both things, if you give it the right growth factors and nutrients."

Results of the study are likely to add fuel to the debate over the need to continue research on embryonic stem cells, which are both highly versatile and controversial because embryos created in vitro die when stem cells are extracted.

Despite her promising discoveries, Verfaillie said it is still too early to say which cell is best, so studies on both the embryonic and adult versions should continue. Because of the uncertainty, the Stem Cell Institute has hired a scientist from the University of Wisconsin- Madison, which has an active embryonic stem cell research program, to conduct similar research here. The researcher, who is originally from the Twin Cities, will begin his new job in July, Verfaillie said. She said she could not release his name at this time.

In previous studies, Verfaillie and her colleagues showed that adult bone marrow stem cells can be coaxed to grow into blood vessels as well as repair stroke-damaged brains in laboratory rats.

In the current study, the researchers used the same stem cells they had used to produce blood vessels to

make the functioning liver cells.

"We showed that they turned on all the genes and proteins that you expect them to turn on," Verfaillie said of the new liver cells. "If you looked at the final product, you found that they had the form of liver cells and all the proteins you would expect in liver cells. We tested seven different functions and they did them all."

Among other things, the new liver cells secreted three key elements: albumin, the most abundant protein made by the liver; urea, produced only by liver and kidney cells; and cytochrome P450, the major detoxifying enzyme.

Verfaillie said the cells also were able to store sugar, which is a major function of the liver, and even began making tiny bile ducts.

The next step will be to inject the cells into mice and rats, then larger animals, to see if they work as well in bodies as they do in test tubes and petri dishes. It will take several years to complete these studies, Verfaillie said, so human trials are far into the future.

But if test results confirm the laboratory findings, the new liver cells could be used to treat a number of genetic liver diseases, including the high cholesterol that tends to run in some families. They also could be used to treat victims of deadly mushroom poisoning and create bio-artificial livers that would be safer than the current version, which use cells from pig livers.

Pharmaceutical companies also could use the cells to more efficiently test new drugs for toxicity. Companies now test drugs on cadaver livers that are not suitable for transplant.

"Drugs are processed by the liver, so it's important to know what impact they have on liver cells," Verfaillie said.

Meantime, Verfaillie and her colleagues will continue to expand the diversity of adult marrow stem cells with two more studies. One paper already has been accepted for publication. Another is in the final stages of acceptance, she said.

Tom Majeski, who covers medical news, can be reached at tmajeski@pioneerpress.com or (651) 228-5583.

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May 6, 2002 Monday, SPORTS FINAL EDITION

SECTION: Commentary; Pg. 15; ZONE: CN

LENGTH: 736 words

HEADLINE: A way around human cloning;
Liberals turn a blind eye to promising alternatives like skin cell research

BYLINE: Dennis Byrne. Dennis Byrne is a Chicago-area writer and public affairs consultant.

BODY:
Sometimes, all the bad things happening smother the good news. But here is stunningly happy news that should have made every front page: Scientists can take a part of you and turn it into a cure. Specifically, scientists have converted an adult skin cell into a cell that can treat a particular disease. This has great promise for treating diseases like diabetes, immune deficiencies, Parkinson's, Alzheimer's and spinal cord injuries.

Scientists from the biotech start-up Nucleotech LLC reported last week in the journal Nature Biotechnology that they reconfigured skin cells to behave as if they were immune system cells, raising hopes of grow-your-own transplants. They created these designer cells by punching holes in mature skin cells and bathing them in extracts of the immune cells, in effect washing out the cell's regulatory factors with new ones. The usual cautions apply: This is only experimental. It could be some time before it has a practical application. Still, this is joyful news. Well, not everywhere. In fact, in some circles, it's almost as if it never happened, and never could happen. The reason appears to be that it has run into a public relations juggernaut that claims that the best, if not the only, route to this kind of medical treatment is human cloning. With near-religious fervor, the argument is made that the best source of master cells for making designer cells is the undifferentiated stem cells taken from cloned embryos.

That's the debate in the U.S. Senate as it gets close to voting on legislation that would entirely ban human cloning, or, alternatively, allow it for only "therapeutic" reasons. Hollywood personalities, politicians from the right and the left and even the fictional "Harry and Louise" couple used in ads to defeat the Clinton health-care package are on the side of human cloning. They claim the compassionate high ground, insisting that cloning is the faster way to cures. So, they argue, we all must support legislation that would allow scientists to **clone** human embryonic cells for the purpose of killing them for research, but not for the purpose of growing them into human beings.

What they fail to mention is the fact that the science is far from settled on the best source of stem cells. What they fail to acknowledge is the principle that if there are two ways to get to the same goal, and one is less morally objectionable than the other, then in conscience we should take the less morally objectionable path. Especially when the alternative route is more direct and, as scientists say of admired discoveries, "elegantly simple." Most Americans agree. In a poll conducted by The Polling Co. for Stop Human Cloning, a grass-roots advocacy group, Americans rejected human cloning of embryos, 59 percent to 26 percent, even if it is for the purpose for curing cancer and other major diseases. No problem, the pro-cloning groups said, we'll just rename it. Henceforth creating embryos shall be called "somatic cell

nuclear transfer. It's only cloning if the embryo is grown into a real human." Never mind that the embryos to be used for "therapeutic" purposes are created the same way and are identical to those that would be grown into adults.

Rep. Dave Weldon (R-Fla.), a physician who treats patients with many of these diseases, called this distinction between **clones** used for research and **clones** meant to grow into real humans "pretty close to hogwash." Yet some senators introduced a bill last week that would permit such a distinction, thereby allowing research cloning. Thankfully, the House last year decisively rejected all cloning, 249-to-178, and President Bush recently repeated his opposition.

Why oppose it? I won't get into all the arguments here about when human life begins. But if you can accept the idea that an embryo is at least nascent human life, then you ought to be worried about creating what Ken Connor, president of the Family Research Council, called "an underclass of sub-humans . . . whose parts can be cannibalized and scavenged for the benefit of others." If you are not troubled by the idea that human life should be created for the sole purpose of serving others (this used to be called slavery in America and the Nazis used to do experiments on mentally and physically disabled people deemed to have no other value), then we don't have much to discuss.

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GRAPHIC: GRAPHICGRAPHIC: Illustration by Jon Krause.

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EurekAlert!

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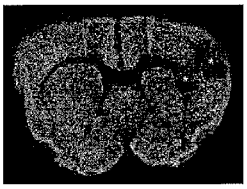
Medical College of Georgia

Stem cells help brain repair, make new neurons and blood vessels after stroke

(Left to Right) Dr. William D. Hill, Dr. David Hess and research assistant Angeline-Martin Studdard look at image of a brain that has been damaged by stroke.

In the first hours and days following a stroke, stem cells leave the bone marrow to help the injured brain repair damaged neurons and make new neurons and blood vessels, according to researchers at the Medical College of Georgia.
The research, reported in the May issue of Stroke, used a mouse model in which the animal's marrow was replaced with that of a transgenic mouse with cells that make a jellyfish protein that fluoresces green so they could trace the cells and the natural repair process that apparently occurs after stroke.
The researchers are now looking for the right factors to enhance the normal repair mechanism, improve stroke recovery and, since the patient's own cells would be used, avoid issues such as the compatibility of donated stem cells and the ethical controversy surrounding embryonic stem cells.
They also want to identify which bone marrow stem cell types are targeted for this repair and how they are called to the site of injury, suspecting that inflammation may be part of this 'homing" process.



The image shows a slice of a mouse brain that has been damaged by stroke on the right side; green stains show where the cells bodies are located. Regions on the right, highlighted by asterisks, show where neurons died.

"We tried to determine whether cells that reside in your bone marrow and circulate throughout the blood could turn into any of the major brain cells types," said Dr. David Hess, neurologist, stroke specialist, chairman of the MCG Department of Neurology and lead author on the study.
They found in the animal model, evidence that bone marrow cells naturally migrate to injured regions of the brain after stroke to help repair damaged tissue; they also become endothelial cells that form new blood vessels and what appear to be new neurons.
"Such repairs occurred naturally in response to stroke and the bone marrow is involved in those repair mechanisms," said Dr. William D. Hill, neuroscientist in the MCG Department of Cellular Biology and Anatomy and second author on the research paper. "We think that when you have a stroke, you have this central core area that is highly affected. Then you have this area like a shell surrounding the core, called the penumbra, like a shadow, that has a gradient of damage as you move from the core of the stroke to the unaffected tissue. This is the area that is going to be the most sensitive to being repaired. So maybe if we can enhance that repair, we could preserve a region that would normally die but is an area we can target to recover."
Enhancement could come through the use of growth factors that affect subsets of bone marrow cells; possibly some already on the market, for example to help leukemia patients rebuild bone marrow after chemotherapy, might be useful.

"If this works out, you will be able to give individuals shots following stroke to boost their bone marrow to proliferate these stem cells to do specific tasks, target specific groups of these stem cells important to blood vessel repair and the genesis of new neurons," Dr. Hill said. The work has implications for all sorts of brain injuries early and late in life such as cerebral palsy, Parkinson's and Alzheimer's disease.

This repair process mimics embryological development when stem cells from the bone marrow help form blood vessels in the brain.

"There are some data that older people don't have as many circulating stem cells as younger, healthier people do," Dr. Hess said, so enhancing the cell number involved in repair should enhance the natural process.

Enhancing the natural process could avoid more aggressive measures such as transplanting cell-laden bone marrow. "Why would we transplant bone marrow cells into people when their bone marrow already has these cells?" Dr. Hess said. "It makes much more sense to actually maximize what they already put out. Also, rather than taking bone marrow out and injecting it into the brain, why not make use, again, of this natural process that summons the cells to the location of the brain injury?"

This image shows new blood vessel formation; the new cells derived from the bone marrow are in green and the endothelial or lining cells have a red marker.

This image shows how how bone-marrow derived cells can be turned into new neurons. The new cells have a red dot labeling them and green is the neuronal marker.

Finding what summons the cells to the injury site is key, and the researchers are looking at specific molecules up-regulated in inflammation that they suspect are also involved in homing. "Certain factors released and expressed on the surface of damaged endothelial cells may act as flags to wave down passing white blood cells or stem cells to attach there," Dr. Hill said.

Also key is identifying which specific stem cells are summoned and are needed to make new blood vessels, support cells and neurons. This may permit selective recruitment and proliferation of just the cells needed for repair, Dr. Hill said.

There are two known broad classes of these cells, hematopoetic and mesenchymal, but there may be many unknown cell types, including a separate group involved in making endothelial cells, Dr. Hess said.

Just last week, through a collaborative study with the Medical University of South Carolina, they received the first mouse that, through a process called clonal analysis, will enable them to tag a single cell, then watch for its descendents' roles in the normal repair process.

They also are collaborating with fellow MCG researcher Nevin Lambert to do a functional analysis of the new neurons produced by the stem cells to ensure that they not only look like but function as neurons.

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The published research was funded by the American Heart Association and has been presented at recent meetings of the association and the Society of Neuroscience. The scientists have received funding from the National Institutes of Health for follow-up studies.

EXPAND STORY

Method May Transform Cells Without Cloning

The New York Times via Dow Jones

Publication Date: Wednesday May 1, 2002 National Desk; Section A; Page 20, Column 3 c. 2002 New York Times Company By ANDREW POLLACK

A team of scientists from Norway and the United States say they are developing a technique that transforms one type of cell from the body into another type without using cloning or embryonic stem cells.

The scientists say they have made human skin cells in a test tube behave as if they were immune system cells, by bathing the skin cells in extracts of the immune cells. In more preliminary work, they have been able to get skin cells to behave as if they were nerve cells.

"We can take a skin cell from your body and turn it directly into a cell type that you need to treat a particular disease," said Dr. Philippe Collas, the leader of the team, whose work is being published today in the journal Nature Biotechnology.

"The message here is we are developing an entirely new approach to tissue replacement therapy that avoids many of the issues" related to cloning, Dr. Collas said.

But Dr. Collas, a researcher at the University of Oslo Medical School and chief scientific officer of Nucleotech, a biotechnology company in Westport, Conn., conceded that the skin cells were not completely transformed into other types of cells. Other experts said it remained to be seen how complete and long-lasting a transformation could be achieved.

"It's an interesting step," said Dr. M. Azim Surani, a professor of developmental biology at Cambridge University. "It still would need quite a bit of work to be able to use it in a practical sense."

Still, if such a technique could be perfected, it could have a big impact, not only in medicine but perhaps in the political and ethical debate over cloning.

Many scientists hope to use embryonic stem cells to generate tissues like new brain cells to treat Parkinson's disease or cardiac muscle to repair damaged hearts. One way to generate the embryos needed for stem cells is by so-called therapeutic cloning, in which a cell from a patient, like a skin cell, is fused with a woman's egg that has had its nucleus removed. But use of embryonic stem cells and therapeutic cloning are controversial because they require the destruction of the early stage human embryos, which some people see as nascent life.

The technique being developed by Dr. Collas would allow skin cells from a patient to be turned directly into other types of cells without having to revert first to an embryonic state and without needing women's eggs.

Dr. Jose Cibelli, vice president for research at Advanced Cell Technology, a rival, said Dr. Collas's technique could be a breakthrough that would be easier than therapeutic cloning. But Dr. Cibelli said tissues made by therapeutic cloning might have a longer life than cells made directly from skin cells, because reverting to the embryonic state appeared to rejuvenate cells.

The Senate is now debating whether to ban all cloning, including therapeutic cloning. Mary Cannon, executive director of Stop Human Cloning, an advocacy group, said the new work showed that tissues could be generated from adult cells without the need to destroy embryos.

But Michael Werner, vice president for bioethics at the Biotechnology Industry Organization, a trade group that opposes a ban, said the new work was not advanced enough to make it a sure substitute for therapeutic cloning.

Dr. Collas's work is based on the fact that all the body's cells have the same genes, but different genes are active in different types of cells.

Dr. Collas's team took skin cells known as fibroblasts and poked microscopic holes in their membranes using chemicals. The skin cells were then immersed for an hour or two in a soup made of extracts of immune cells known as T cells. The skin cells were then removed and the pores were sealed with calcium.

It appears that some T-cell proteins that turn on particular genes migrated from the soup into the skin cells. Certain genes that are active in T cells became active in the skin cells, while some genes normally active in skin cells became inactive, he said. The skin cells also produced certain surface molecules, known as receptors, that are characteristic of immune cells. The effect lasted several weeks.

Still, it is unclear whether skin cells that display the behavior of T cells or nerve cells would actually function that way in the body or would be useful for therapy.

(END)

05:30 EDT May 1, 2002

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Scientists Reprogram Cells Without Cloning

Last Updated: April 30, 2002 04:57 PM ET

Print This Article

By Maggie Fox, Health and Science Correspondent

WASHINGTON (Reuters) - Scientists said on Tuesday they had transformed ordinary human skin cells into immune cells in an experiment that, if it can be repeated, might bypass the need for either stem cells or highly controversial cloning technology for many medical therapies.

The team at biotech start-up Nucleotech LLC hope to be able to offer patients grow-your-own transplants that could theoretically be used to treat diseases such as immune deficiencies and juvenile diabetes.

Many teams are working on the idea, but nearly all had assumed the need for stem cells, the body's master cells, which are elusive and difficult to grow in the lab. They can be found in blood and tissue, or can be taken from embryos -- usually obtained from fertility clinics.

Such stem cells could also theoretically be made using cloning technology -- something highly controversial and the subject of competing legislation in the U.S. Congress. President Bush supports a complete ban on the use of cloning technology involving humans.

A coalition of senators introduced a new bill on Tuesday that would specifically allow the use of cloning technology in medical research but ban it for the purposes of making a baby.

James Robl, Philippe Collas and colleagues at Nucleotech and the University of Oslo believe they have found a way around the controversy.

By punching holes in mature skin cells and soaking them in a solution made from immune system cells, they said, they turned them into what look like T-cells -- key immune system cells.

"They start acting like T-cells," Collas told Reuters.

Robl, a leading stem-cell researcher who left the academic world to work for biotechnology companies, wants to use the approach to transform medicine.

"It would be a one-day procedure, in principle," he said. "The patient would come in and give a skin biopsy to the lab to reprogram and the day after you could put the cells back into the patient."

Researchers working with stem cells have had a similar idea for treating diabetes by making pancreatic cells, for treating Parkinson's or Alzheimer's by making new brain cells and for treating spinal cord injuries by making new nerve cells.

IMMEDIATE APPLICATIONS IN CANCER

Making T-cells could have immediate applications in treating cancer, said Collas, who led the study. A patient's skin cells could be transformed into T-cells that would recognize and attack the patient's

own tumor.

The company was also looking at making pancreatic islet cells -- the cells that make insulin and which are destroyed in juvenile or type-I diabetes, Robl added.

Writing in the journal Nature Biotechnology, the team said they made the skin cells permeable by punching tiny pores in the cell walls. They then grew them in a solution containing extracts from T-cells.

The new cells stopped expressing the genes that skin cells express -- meaning they stopped functioning like skin cells, and instead turned on genes usually active only in immune cells, such as IL2, IL7, CD3, CD4 and RANTES.

"In effect you are washing regulatory factors out from inside the cell and replacing them," Robl said.

Instead of harnessing an early stem cell whose genes have not yet been all turned on, the team completely changed the cell's environment and thus changed the cell's function.

Although Robl hopes the technology will rival stem-cell and cloning approaches, both he and Collas oppose restriction of any kind on such research.

Dr. Irving Weissman of Stanford University, a supporter of cloning and stem-cell research, said he had not seen the study but added, "I would be highly skeptical."

Others agreed with Robl that all techniques need to be explored. "There is so much that we don't know," Donald Coffey, a specialist in cancer and molecular biology at Johns Hopkins University in Baltimore, said in an interview. "I say let all flowers bloom."

In a commentary in Nature Biotechnology, Azim Surani and Patrick Western of Cambridge University in Britain said it looked to them as if the cells had only been partially reprogrammed but said Collas had come up with a "potentially powerful system" for studying cell biology.

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EXPAND STORY

The Nation

Stem Cell Therapy May Help Multiple Sclerosis

Los Angeles Times via Dow Jones

Publication Date: Wednesday April 17, 2002 Page A-19 Los Angeles Times (Home Edition) Copyright 2002 Los Angeles Times By LIZ KAY TIMES STAFF WRITER

Stem cell transplants, first developed to treat blood cancers, may halt the progression of multiple sclerosis, researchers reported Tuesday.

Most scientists believe multiple sclerosis is an autoimmune disorder. A victim's immune system attacks nerve fibers in the brain and spinal cord, destroying an insulating layer called myelin.

People with the disease suffer pain, have difficulty controlling their muscles and experience cognitive problems.

But a study from the University of Washington Medical Center in Seattle suggests that obliterating a person's immune cells and then growing a new set by using the patient's own stem cells might prevent the disease from getting worse.

Dr. George Kraft, director of the university's Multiple Sclerosis Research and Training Center, presented results of the study Tuesday at the American Academy of Neurology meeting in Denver.

Scientists have known since the 1950s that suppressing the immune system reduces the progression of MS. But "if that were the end of things, the patient would die" because the absence of a working immune system would leave the way open to deadly infections, Kraft said. The technique has "always been in the back of our minds, but you couldn't get up to a therapeutic level because of the toxicity."

To avoid that problem, the researchers use stem cells. Nearly all cells in the body have a specific function--blood cells cannot become muscle cells, nerve cells cannot become skin cells and so on. By contrast, the cells of an embryo are unspecialized: They can develop into many different types of tissue. Stem cells, which in adults are mostly found in bone marrow, retain that flexibility.

In the research, doctors gave the patients an injection of growth factor to send stem cells from the bone marrow to the bloodstream. The doctors then harvested the stem cells by drawing the patient's blood and filtering it, keeping the stem cells and discarding immune cells that might perpetuate the disease.

"We're trying to prevent the reintroduction of the disease," said Richard Nash, a transplant physician at the Fred Hutchinson Cancer Research Center in Seattle. He helped develop the procedure used in the research.

Once the stem cells were harvested, researchers used radiation, chemotherapy and antibodies to wipe out the patient's immune system.

Finally, the stem cells were reintroduced to the patient's bloodstream, where they turned into new immune system cells. The level of immune cells recovers within nine days, Nash said.

The researchers, working with transplant physicians in different centers, followed 26 patients for an

average of 15 months after the procedure, called autologous stem cell transplantation. In more than 75% of the patients, their disability stopped getting worse after the treatment, Kraft said.

There is, however, no guarantee that the immune cells won't begin attacking nerve fibers again in the future, he noted.

Researchers are not sure what triggers the immune response that causes MS, said Dr. Michael Racke, associate professor of immunology and neurology at the University of Texas Southwestern Medical Center in Dallas.

Genetic and environmental factors likely contribute. If one person in a set of identical twins gets MS, for example, the other, who has the same genetic material, has only a 25% chance of developing the disease, he explained. That is a much higher rate than a person in the general population but still not a sure thing.

The hope with stem cell transplants is that "I then become my own twin," with a reduced chance of getting MS again, Racke said.

The procedure has risks. Some patients--about 5% to 10% in these studies--have died of infection due to immune system suppression.

Kraft limited his study to patients severely affected by MS who had not responded to other available treatments. Patients in earlier stages of the disease, who might be progressing more rapidly, will be included in future studies. A National Institutes of Health study, for example, will compare transplants with Novantrone, an FDA-approved drug to prevent relapses, said Richard Burt, director of immunotherapy at Northwestern Memorial Hospital in Chicago.

(END)

04:16 EDT April 17, 2002

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Neural Stem Cells Develop into Functional Neurons

4/15/2002 -- Researchers have found that neural stem cells isolated from the brains of adult rats can mature into functional neurons. Stem cells, which are found in tissues throughout the body, are immature progenitor cells that give rise to more specialized cells that form tissues and organs.

The scientists emphasized that although their studies show that adult stem cells have the capacity to develop into functioning brain cells, their findings do not mean that clinical application of adult neural stem cells is imminent. The studies were published April 15, 2002, in an advance online article in Nature Neuroscience by Howard Hughes Medical Institute (HHMI) investigator Charles F. Stevens and colleagues Hong-jun Song, an HHMI research associate, and Fred H. Gage at The Salk Institute.

According to Stevens, previous experiments showed that adult neural stem cells bear certain molecular markers that suggested that they could become neurons. "It's absolutely clear that embryonic stem cells can make perfectly good neurons, otherwise there would be no development of the brain," said Stevens. "But nobody had demonstrated before that adult stem cells can generate fully functional neurons, beyond just having particular protein markers."

To see whether adult neural stem cells possessed the ability to develop into functional neurons, Gage and his colleagues first isolated stem cells from the hippocampal region of the rat brain and then tagged the cells with fluorescent molecules that made it possible for the researchers to track the stem cells as they developed. The scientists "co-cultured" these tagged cells along with normal adult neurons on a carpet of supporting cells called astrocytes, which are known to produce chemical signals that trigger neuronal growth.

"The normal neurons were necessary to show that our stem-cell-generated neurons were genuine, in the sense that they could incorporate into the neural circuitry that attempts to become established in cell culture," explained Stevens.

In their initial studies, the scientists found that the fluorescently tagged stem cells developed normal neuronal structures, including the long, cable-like axons and branching dendrites that form connections with other neurons. The researchers observed that the axons and dendrites produced protein markers that were characteristic of normal neurons.

By recording electrical signals from the cultured cells when they were stimulated, the scientists observed that functioning connections, called synapses, were established between the stem-cell-derived neurons and normal adult neurons. Synapses are the junctions between neurons where nerve impulses are transmitted. Electron microscope studies of the synapses revealed that they appeared normal.

The researchers also showed that the stem-cell-derived neurons produced neurotransmitters, chemical signals by which neurons communicate to each other across synapses.

"However, we did find that the stem-cell-derived neurons did not make as many synapses as normal neurons," said Stevens. "It might be that adult stem cells by themselves don't give rise to cells with sufficient synapses; that we didn't give them

the right environment for synaptic production, or that these particular cultured cells might have contained mutations that reduced synapse production."

To test whether astrocytes played a role in triggering the maturation of adult neural stem cells, the scientists cultured the cells with both neonatal and adult astrocytes. The studies showed that both types of astrocytes produced factors that supported stem cell maturation.

According to Stevens, the observation that adult neural stem cells can mature into functional neurons could have clinical implications. "There has been considerable debate about whether adult neural stem cells, as well as embryonic stem cells, could be used to regenerate damaged brain tissue," he said. "These findings give some indication that if we ever reach the point where stem cell therapy is feasible to treat such disease, there's some hope that adult stem cells might work."

But Stevens emphasized that extensive comparative studies of both embryonic and adult neural stem cells will be needed before their relative advantages and disadvantages can be determined.

"It is absolutely vital to continue research using embryonic neural stem cells," he said. "It may be that, for reasons we don't yet understand, adult stem cells will never be useful in therapy and that we will always need embryonic cells. Or, it may be the other way around. We just don't know."

Source: HHMI

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Reuter's Medical News for the Professional

Australian Researchers Use Stem Cells to Repair Heart Damage in Elderly Man

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Introduction

SYDNEY, Australia (Reuters) Apr 10 - Australian surgeons have carried out the world's first trial using adult stem cells to repair heart damage in a 74-year-old man, researchers said on Wednesday.

Surgeons at Newcastle's John Hunter Hospital north of Sydney extracted stem cells from patient Jim Nichol's bone marrow then injected them back into his heart wall to stimulate blood vessel growth in areas which lacked sufficient blood supply.

Nichol was discharged from the hospital on Tuesday and his condition will be monitored over the next 6 months by researchers who undertook the trial as part of an international experiment also being carried out in Hong Kong and China.

Autologous stem cell transplantation could offer hope to about 30% of patients in the final stages of coronary heart disease and those unable to undergo bypass surgery or angioplasty.

"This is a trial which is seeking to examine the efficacy of the patient's own adult bone marrow derived stem cells to increase the blood vessel growth in the heart," cardiologist Suku Thambar told reporters.

Dr. Thambar said it was too early to determine whether embryonic stems cells would be more effective in helping repair heart damage. "There are some theoretical reasons why embryonic stem cells may be more suitable for this, but that has to be borne out in clinical trials," he told Australian radio.

Australia's states and territories last week endorsed a national plan to allow human embryos to be used for stem cell research.

washingtonpost.com

Stem Cell Transplant Works in Calif. Case

Parkinson's Traits Largely Disappear

By Rick Weiss
Washington Post Staff Writer
Tuesday, April 9, 2002; Page A08

The hand tremors and other symptoms of Parkinson's disease that had started to interfere with a California man's life have largely disappeared since doctors retrieved stem cells from his brain, grew them into neurons and then transplanted those cells back into his brain, doctors reported yesterday.

The brain cell transplant was the first in humans involving "adult neural stem cells," a recently discovered type of cell that can morph into every kind of brain cell.

If studies confirm the procedure's usefulness in other patients, the approach could evolve into a biological therapy for the disease in which patients would essentially grow their own cures from a few starter cells taken from their own brains.

But doctors and neuroscientists warned against reading too much into the initial results. They noted that Parkinson's is a notoriously variable disease that ebbs and flows unpredictably, and improvement in a single patient does not prove the therapy works. Indeed, some studies have found that simply traumatizing the brain with surgery can trigger neuronal sprouting and clinical improvement, without adding any new cells or drugs. And mysteriously, the man's improvement has persisted even though the cells that were transplanted have apparently stopped making the brain chemical they were intended to produce.

"It's very exciting and promising as research," said Alex Valadka, a neurosurgeon at Baylor College of Medicine in Houston who heard the results presented yesterday in Chicago at an American Association of Neurological Surgeons meeting. "However, it's always a good idea to temper your enthusiasm with a little bit of caution. This is, after all, reported in only one patient."

Several scientists noted that the report seemed to be getting far more attention than a single-patient study would normally garner, apparently because of the intense political debate over the science and ethics of embryonic stem cell research. As part of their push for a greater focus on adult stem cells, opponents of embryo cell studies bolstered the researchers' own publicity effort by highlighting the report in repeated e-mails to media outlets.

"It's wonderful for this one guy, but that's all we know," warned Ronald McKay, a neuroscientist and stem cell expert at the National Institutes of Health.

The work was led by Michel Levesque, a neurosurgeon with Cedars-Sinai Medical Center in Los Angeles and Celmed BioSciences. He removed 50 to 100 cells from the brain of a San Clemente engineer with Parkinson's, then cultivated them in dishes for months. In March 1999 he injected about six million of the cultured brain cells into the patient's brain. About 35 percent of them were neurons, and a small fraction of those were the type that secrete dopamine, the brain chemical lacking in Parkinson's patients.

Using a brain-scanning technology, the team tallied an initial increase in dopamine levels of 58 percent and the patient improved. After a year those levels returned to what they'd been before surgery, but an 83

percent reduction in symptoms, such as tremor, has inexplicably persisted, Levesque said.

"It's not just psychological. His motor improvement is real. And the improvement is beyond the level for placebo effects," he said, referring to studies that have shown a 20 percent to 25 percent improvement in some patients who receive no treatment.

Levesque and others said the improvement may be due to other cells in the transplanted mixture -- ones that secrete not dopamine but a brain chemical known as GABA. More than half of the cells transplanted into the patient were GABA-secreting neurons, and some recent studies have suggested that GABA can suppress tremors and other symptoms of Parkinson's.

The patient, 59-year-old Dennis Turner, yesterday praised the procedure. "Two years ago I couldn't put my contact lenses in without a big problem. Now it's no problem. And I don't have to take any anti-rejection medication because the cells are myself."

Levesque is seeking permission to try the method in more patients later this year. But he also expressed his support for research on human embryonic stem cells, which he said may prove to have advantages over adult cells for some applications.

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Adult Stem Cells Used to Repair Damage from Parkinson's Disease

Researchers studying technique for possible treatment of other nervous system conditions

MONTREAL, Quebec, April 8 /CNW/ - Scientists from Celmed BioSciences, a subsidiary of Theratechnologies, reported today at the annual meeting of the American Association of Neurological Surgeons (AANS) in Chicago that adult neural stem cells taken from a patient's own central nervous system have been successfully used to treat Parkinson's disease. Their research suggests this method of using adult stem cells may possibly be useful in treating a variety of other neurological conditions.

The research was conducted by Celmed's researchers, Dr. Michel F. Lévesque, Vice President, Medical Affairs, also neurosurgeon at the prestigious Cedars-Sinai Medical Center, in Los Angeles, California, and Dr. Toomas Neuman, Program Director, Neurodifferentiation, at Celmed BioSciences USA.

Dr. Lévesque and Dr. Neuman isolated adult neural stem cells from a patient, induced them to differentiate into the desired nervous system cells, and implanted them back into the patient's brain. One year after the procedure, the patient's symptoms were reduced by more than 80%. Dr. Lévesque has been authorized by the FDA to conduct a Phase II clinical trial for Parkinson's disease, using cell therapy derived from autologous neural stem cells, once certain animal studies are completed and approved. This will be the first study of its kind in the world evaluating the benefits of autologous cell therapy for this disease.

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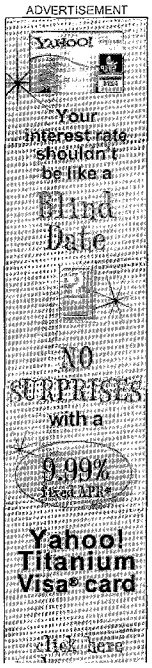

The research demonstrates that adult stem cells can be coaxed to become the crucial cells that produce dopamine and that those cells can function after implant. Dopamine is an essential brain chemical, which is deficient in people who suffer from Parkinson's disease.

In their study, Dr. Lévesque and Dr. Neuman demonstrated that the implantation of dopamine-secreting cells increases the available supply of dopamine to the brain. However, they also found evidence that symptoms of Parkinson's disease appear to be reduced even if the uptake of dopamine is not increased.

The patient's clinical symptoms continued to improve after the procedure, but PET-scan studies of the patient's brain taken one year after the procedure suggest that the benefit results from factors other than the dopamine- secreting cells. PET-scans taken at three months showed increased dopamine uptake. At one year, the dopamine uptake returned to the same level it was right before the implantation.

"We need to investigate whether there are other mechanisms involved in Parkinson's disease that could lead to alternative treatment strategies," said Dr. Lévesque, who believes that other nervous system cells that were generated from the patient's stem cells and implanted along with the dopamine-secreting cells may be responsible.

In addition to its use for Parkinson's disease, the technique is under study for juvenile diabetes, stroke, brain tumors, spinal cord injury, and other conditions. The use of an individual's own stem cells offers advantages over other sources because it reduces the infection and rejection dangers and because it avoids the limitations and ethical concerns of using stem cells from other sources.

The patient in the current study, a nuclear reactor engineer and fighter jet pilot, was diagnosed with Parkinson's disease when he was 49. He had to stop piloting airplanes at 52 because of progressive rigidity and tremor, especially of his right hand. Traditional drug therapy did not stop the symptoms from getting worse.

After stem cells were harvested from the patient's cortex using a routine brain biopsy procedure, they were cultured and expanded to reach several million cells. About 20% of differentiated neurons became mature dopamine- secreting cells. In March 1999, the cells were delivered by microinjection at six locations in the left putamen.

To measure the technique's effects, post-operative clinical assessments, including measures of the patient's motor scores, were performed a three, six, nine and twelve months by neurologists who were unaware of the transplantation. Three months after the procedure (while still on oral medication), his motor scores improved by 37% and there was a 55.6% increase in dopamine uptake. One year after the procedure, the patient's overall Unified Parkinson's Disease Rating Scale (UPDRS) improved by 83% while not taking medication.

Dr. Michel Lévesque, is Vice President, Medical Affairs at Celmed BioSciences; a neurosurgeon on the medical staff at Cedars-Sinai Medical Center, Los Angeles, California; an Associate Clinical Professor, Division of Neurosurgery, and member of the Brain Research Institute at the UCLA School of Medicine. He has authored over 75 articles in professional journals, contributed chapters to many leading neurosurgery treatises and over 150 scientific abstracts.

Dr. Toomas Neuman, is Program Director, Neurodifferentiation at Celmed BioSciences. He is the author of approximately 50 scientific papers and has collaborated on several inventions relating to DNA synthesis and integration in neurons that resulted in patent applications.

CELMED BIOSCIENCES

Celmed BioSciences is a new subsidiary created by Theratechnologies in June 2001 in order to maximize the significant potential offered by its cell therapy activities. With facilities in Canada and the US, Celmed is dedicated to the treatment of neurological, hematological and immunological disorders using adult stem cell technologies. By integrating personalized medicine and basic molecular biology tools revealing each individual genomics and proteomics profile, Celmed dedicates its efforts to develop new biological selective therapies.

Celmed BioSciences' website is located at www.celmedbio.com.

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Theratechnologies' website is located at www.theratech.com . The Company is listed on the Toronto Stock Exchange under the symbol TH.

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April 2, 2002

Canadian team 'supercharges' adult stem cells
Offers hope for blood treatments, embryo controversy

Margaret Munro
National Post

VANCOUVER - A Canadian team's stem cell "breakthrough" could one day lead to powerful new treatments for leukemia and other blood diseases and eliminate the need for bone marrow transplants.

The researchers discovered how to "supercharge" adult stem cells taken from the blood and mass-produce them in the lab. The discovery is being announced today by the B.C. Cancer Agency.

As evidence of the enormous potential of the discovery, the agency points to an experiment involving mice at the Terry Fox Lab in Vancouver. The mice had their blood systems destroyed by radiation and then rebuilt using blood stem cells grown in the lab.

"They're now perfectly healthy," said Dr. Keith Humphries, the UBC professor who heads the team at the cancer agency.

"They're now perfectly healthy," said Dr. Keith Humphries, the University of British Columbia professor who heads the team at the cancer agency.

Blood stem cells, also known as hematopoietic stem cells, give rise to all the cells in the blood system. Because these stem cells are so rare, it is difficult to obtain enough from natural sources, such as umbilical cord blood or bone marrow, to treat people whose blood has been ravaged by diseases such as cancer or radiation.

Researchers have long dreamed of growing blood stem cells in the lab to treat disease and mass-produce blood products. But the cells have proven next to impossible to grow outside the body.

Dr. Humphries and his colleagues at the University of British Columbia got over the hurdle by "supercharging" the cells with a gene called HOXB4. They inserted a copy of the gene in adult blood stem cells and were amazed to see the cells grow and multiply at unprecedented rates.

"We're getting 40- to 100-fold increases," said Dr. Humphries, whose Vancouver group collaborated with Dr. Guy Sauvageau at the Université de Montréal to engineer the gene into the cells. The scientists detail the work in the April 5 edition of the journal Cell.

While the HOXB4-enhanced cells multiply at extraordinary rates in the lab, Dr. Humphries said they behave normally when injected into mice. The cells turn into normal blood cells and go about their business.

"There is no evidence the daughter cells are abnormal in any way," he said. The experimental mice "rescued" by the cells in the last two years have led long, normal lives.

The HOXB4 gene appears to be involved solely in the multiplication of stem cells, Dr. Humphries said. It seems to turn off once the cells differentiate into white or red blood cells.

While most of the researchers' work was done on mouse blood stem cells, they have also shown HOXB4 can stimulate production of human blood stem cells, said Dr Humphries, who credits his graduate student Jennifer Antonchuk with much of the work.

Dr. Humphries, who was a member of the advisory committee that helped draft the Canadian guidelines for research on stem cells released last month, said the findings help affirm the promise of adult stem cells, which are much less controversial than the variety created by killing days-old embryos. The embryonic stem cells can morph into any type of cell found in the body, while adult stem cells are less malleable.

Dr. Humphries and his colleagues say the research on HOXB4 stem cells shows great promise, but they caution that they are not about to start injecting the genetically "supercharged" blood stem cells into people.

Scientists must first understand the biochemical process HOXB4 uses to get the cells to grow; then they must learn how to control the potent "genetic throttle."

Ideally, he said, they would like to be able to simply "tickle" the human blood stem cells using growth factors the HOXB4 gene produces. This would circumvent the need to insert genetically altered cells into the body.

HOXB4 is from a family of intriguing genes that help control how stem cells multiply and develop, Dr. Humphries said. By tweaking some of the genes from the family, researchers have been able to grow flies with four wings instead of two, and legs on their heads instead of antennae. Some of the genes are also known to behave abnormally in blood cancers, which is what attracted Dr. Humphries to the genes.

HOXB4 appears to be a harmless gene, he said, but added that one needs to be very sure before starting any experiments on people.

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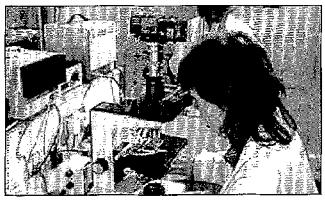
Scientists develop 'cloning alternative'



Adult stem cells could be used to grow human tissue

An American scientist may have discovered a cell in adults that can turn into every single tissue in the body.

Until now, it was thought that only embryonic stem cells could do this.

Anti-abortion groups, who object to embryology research on ethical grounds, have welcomed the news which is reported in New Scientist magazine.

Work is in its early stages but efforts are now being made to turn the adult cells into tissues such as muscle, cartilage and brain cells, which can be transplanted back into the patient.

> **An option such as this which doesn't involve the deliberate production and destruction of life is much better**
>
> **Tom Horwood, Catholic Church**

The research has not been published in a scientific journal. However, it has been carried out by a highly respected team and received favourable reviews from those familiar with the work.

Ihor Lemischka of the US's Princeton University said: "The work is very exciting. They can differentiate into pretty much

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everything that an embryonic stem cell can differentiate into."

The cells were found in the bone marrow of adults by Catherine Verfaillie at the University of Minnesota.

Scientific potential

The cells, named multipotent adult progenitor cells (MAPCs), are said to have the same potential as embryonic stem cells (ESCs).

Irving Weissman of the US's Stanford University said: "It's very dramatic the kinds of observations Verfaillie is reporting. The findings, if reproducible, are remarkable."

Religious groups and "pro-family" organisations in the UK are among those who regularly raise concerns about the ethics of using embryo clones.

Tom Horwood from the Catholic Church said: "Over the last couple of years, researchers on both sides of the Atlantic have been looking at adult stem cells, so that's very much to be welcomed.

"An option such as this which doesn't involve the deliberate production and destruction of life is much better. What it needs is more support and finance."

The adult stem cells seem to grow indefinitely in culture, like ESCs.

Ethical debate

Some cell lines have been growing for almost two years and have kept their characteristics, with no signs of ageing, researchers claim.

The discovery of such "versatile adult stem cells" is likely to fan the debate about whether embryonic stem cell research is justified.

Anti-abortion groups argue the ethical concern is that the procedure involves creating an embryo for the sole purpose of providing a treatment for a disease.

They claim the adult stem cell development demonstrates the alternatives to therapeutic cloning. They believe these alternatives have been constantly underplayed by the scientific community.

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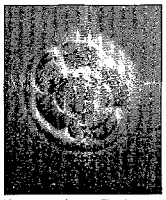
But scientists say that at this early stage of research, it is prudent to keep all options open. One expert is sceptical about the findings, questioning the nature of stem cells.


Human embryo: Cloning raises ethical concerns

Verfaillie's team thinks MAPCs are rare cells present in the bone marrow that can be fished out through a series of enriching steps. But others think the selection process actually creates the MAPCs.

Neil Theise of New York University Medical School said: "I don't think there is a cell that is lurking there that can do this. I think Catherine has found a way to produce a cell that can behave this way."

Stem cell researchers say it is too early to tell whether the ultimate stem cell has been discovered and most believe research with embryonic stem cells must continue.

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Human cloning may be impossible and therapeutic stem cell cloning may be unnecessary - new research

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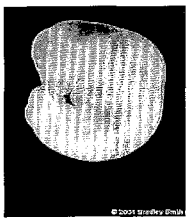

As the debate on cloning of both humans and stem cells continues on both side of the Atlantic, latest research indicates that a cloned human may be impossible.

An embryology conference in Washington DC, USA, heard that the particular nature of primate embryos could mean that attempts to clone them cannot be successful. Attempts to clone monkeys, primates with similar genetic makeup, have not been able to go beyond the early embryo stages, possibly due to the damage caused when the nucleus is removed from the egg.

Although this technique was successful in the cloning of Dolly the Sheep by the Roslin institute in Edinburgh, Scotland, research has found that the cells in primate clones do not form distinct nuclei that contain all the chromosomes. The finding, by Advanced Cell Technology, adds further doubt to the potential for human clones, something which was already questioned following the high failure rate found in attempts already made with other animals, such as sheep.

For scientists more concerned with stem cell development, therapeutic cloning of cells appeared less necessary following a find of a new type of 'perfect' cell. The need to find a cell which would not be rejected by the human immune system had initially led to attempts to clone human stem cells. Researchers at McGill university in Montreal, Canada, have found a cell found in bone marrow (mesenchymal stem cells) which is safe, even to the point of being transferred between species. Scientists have found no signs of rejection as the cells do not carry markers and have been successfully transferred from pigs to rats.

For further information on science and society, please consult the following web address:
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The Times (London)
July 18, 2002, Thursday
SECTION: Home news; 13

Stem cells may hold cure for diabetes

BYLINE: Mark Henderson, Science Correspondent

INSULIN-PRODUCING cells that could reverse diabetes have been successfully grown from adult stem cells for the first time in an experiment that paves the way for new treatments of the disease.

Scientists at Massachusetts General Hospital in Boston have found that a naturally occurring hormone can coax stem cells found in the pancreas to mature into pancreatic beta cells that secrete insulin. This means new beta cells can be made from a patient's own pancreatic stem cells, which could be used to treat diabetes.

Diabetes, which can lead to heart and circulatory disease, kidney failure and blindness, is caused by a shortage of insulin, a hormone that regulates blood sugar levels, or by the body's failure to respond to it.

In type 1 diabetes, the body's immune system mistakenly destroys beta cells in the insulin-making parts of the pancreas, called the islets of Langerhans. Sufferers, who are mainly children and young adults, lack insulin and must inject it daily.

Type 2 diabetes, which is more common, arises when the body becomes resistant to insulin, often as a result of obesity. In both forms, beta cells in the islets die off, creating further insulin shortages.

In the study, published today in the journal Endocrinology, experts sought to coax islet stem cells - precursors of insulin-producing cells - to mature. They found the glucagon-like peptide-1 hormone, or GLP-1, spurred the reaction.

Pain & Central Nervous System Week
July 8, 2002
SECTION: EXPANDED REPORTING; Pg. 19

STEM CELLS: Adult fat stem cells transformed to resemble nerve cells

Like biochemical alchemists, investigators from Duke University Medical Center and Artecel Sciences, Inc., have transformed adult stem cells taken from fat into cells that appear to be nerve cells.

During the past several years, Duke researchers and scientists from Artecel demonstrated the ability to reprogram adult stem cells taken from human liposuction procedures into fat, cartilage, and bone cells. All of these cells arise from mesenchymal or connective tissue, parentage. However, the latest experiments have demonstrated that researchers can transform these stem cells from fat into a totally different lineage, that of neuronal cells. Although it is unclear at this point whether or not the new cells will function like native nerve cells, the researchers are optimistic that if future experiments are as successful as the ones to date, these new cells have the potential to treat central nervous system diseases and disorders.

"**These experiments are proof of principle that it is possible to change one lineage of adult stem cells into another using fat**," said Duke's Henry Rice, MD, pediatric surgeon and senior author of the paper published in the journal Biochemical and Biophysical Research Communications. "If future studies in animal models are successful, we'll have gone a long way toward demonstrating the power of these cells to treat human diseases."

The research was supported by the American College of Surgeons and Artecel Sciences in Durham. Rice is a consultant for Artecel Sciences.

The team conducted parallel experiments in mice and human cells. In both cases, mouse adipose (fat) cells and fat cells taken from human liposuction procedures were treated with chemicals and growth factors and allowed to grow in the laboratory.

"Within hours the treated cells in both models began to look like neuronal cells and began to produce measurable amounts of proteins normally expressed by nerve cells," Rice said.

"This is a promising first step in the use of an abundant source of adult stem cells in the setting of central nervous system repair," said Jeffrey Gimble, MD, chief scientific officer at Artecel and coauthor of the BBRC paper. "While it is known that you can create neuronal cells from adult stem cells taken from bone marrow, we feel that **our approach with fat offers a limitless supply of readily obtainable adult stem cells**."

Until recently, it was believed that organisms were born with the full complement of neuronal cells, and that new neurons could not be formed. According to the scientists, their latest research, as well as the experiments performed by others on bone marrow stem cells, opens up new possibilities for the treatment of nervous system disorders or injuries.

"We are trying to think about human disease in a new way," Gimble said. "Everyone is used to the concept of surgical, medical, or pharmacological approaches to the treatment of disease - we're looking at one of the next steps in biotechnology, which is using cellular therapies."

The researchers are quick to point out that there are still many hurdles to be overcome before the use of these cells can occur in a clinical setting.

First, the cells were grown in tissue culture and survived after neuronal differentiation for several days. The researchers are confident that as they refine their techniques and evaluate different growth factors, they can extend the lifespan of these cells.

Second, while the new nerve cells have a form and function that resemble native nerve cells, it is not known if they will function in the same way as native nerve cells. The next series of experiments in the mouse model will test how the new cells react in a living system and if they will function like nerve cells, the researchers said.

The researchers believe the first animal models will focus on acute injuries such as stroke, in which blocked blood flow to the brain causes brain cell death, and spinal cord injuries.

EXPAND STORY

Drugs to Spur New Cells, And Without the Politics

The New York Times via Dow Jones

Publication Date: Thursday December 13, 2001 Business/Financial Desk; Section C; Page 1, Column 3
c. 2001 New York Times Company By ANDREW POLLACK

IRVINE, Calif. -- As debate again heats up over cloning and stem cell research, several biotechnology companies are trying to develop a far less controversial approach to cell regeneration.

The companies are actively working on drugs that stimulate the brain and other organs to grow new cells and repair themselves.

Drugs do not face the same problems with rejection by a recipient's immune system that cells and tissues often do. And in most cases, giving drugs would not require the surgery that might be needed to implant new cells grown from stem cells.

"It's certainly a lot easier to swallow a pill or take a spoonful of liquid than to have a hole drilled in your head and have embryonic stem cells put in," said Alvin J. Glasky, chief executive of NeoTherapeutics, a small biotechnology company based here that is working on a berry-favored medicine to stimulate the brain to grow new cells.

In addition, big pharmaceutical companies, which have been largely uninvolved in stem cell research, might be more interested in developing drugs to promote new cell growth. While cell therapies often require the use of a patient's own cells -- a customized approach that is a departure for big drug companies -- drugs that promote new cell growth could be mass-produced.

"We can look forward to the time when any cell in the body can be regulated with natural factors to grow or be inhibited from growing," said William A. Haseltine, chief executive of Human Genome Sciences. The company, based in Rockville, Md., is using a process of gene-hunting to find proteins that act as growth factors and is already testing in patients a protein that stimulates the healing of wounds.

"That is the medicine that will be the new medicine for the next 20 years," he said. "Stem cells and their uses will be very limited because we don't know much about them."

The drug approach to new cell growth has already produced some successes. The biotechnology industry's most lucrative drug, for example, is Amgen's Epogen, which fights anemia through a human protein that stimulates the body to produce red blood cells. A protein developed by Curis Inc. of Cambridge, Mass., stimulates bone growth and is used as an alternative to a bone graft to treat fractures that do not heal.

Still, using growth factors is not as easy as it sounds. Human Genome Sciences' wound-healing protein just failed to work in two clinical trials. And Regeneron Pharmaceuticals of Tarrytown, N.Y., has tested various nerve growth factors to treat illnesses like Lou Gehrig's disease and Parkinson's disease. The company's trials, some done in partnership with Amgen, have all failed. "We are experts in all this, and we've only been increasingly humbled by how difficult it is to create structure," said George D. Yancopoulos, Regeneron's chief scientific officer.

The interest in stimulating the body to heal itself has been spurred by discoveries in recent years that

organs like the brain and heart, which were thought not to have the ability to regenerate, appear to do so in certain circumstances. Various organs have been found to harbor small quantities of stem cells that can turn into specific types of cells to repair damage.

But many scientists and biotechnology executives say they doubt that the drug strategy will work. The fact that people do not recover on their own from brain injuries or heart attacks probably indicates that the body cannot produce enough stem cells to make a difference.

"Certainly being able to deliver the required number of cells directly from laboratory-isolated stem cells seems more straightforward technically," said Karl Johe, chief scientist at NeuralStem Biopharmaceuticals, a company working on cell therapies for brain disease.

Some scientists say drugs will work better for some diseases, cells for others. Pancreatic cells are already restoring the ability of some diabetics to produce insulin.

Growth factors can also stimulate the wrong cells, causing unintended effects. In Regeneron's tests, nerve growth factors in some cases made people sensitive to pain or changed their behavior, Dr. Yancopoulos said. Yet some of those unintended effects may help salvage Regeneron's business. One nerve growth factor, instead of alleviating a disease, made people feel full, and is now being tested as an obesity drug.

Both Genentech and Chiron failed in clinical trials using growth factors to stimulate the body to grow new blood vessels and bypass clogged arteries.

But despite the setbacks with growth factors, work is continuing. James H. Fallon, professor of anatomy and neurobiology at the University of California at Irvine, reported that a protein called transforming growth factor alpha stimulated the stem cells in the brains of rats to proliferate and migrate to the site of injuries similar to those caused by Parkinson's disease. The stem cells turned into neurons and repaired some of the damage. The work was partly sponsored by Stem Cell Pharmaceuticals, a private company in Seattle that wants to harness the growth factor as a drug.

Dr. Piero Anversa and colleagues at New York Medical College in Valhalla, N.Y., used drugs to treat mice with heart attacks. The two drugs -- stem cell factor and granulocyte colony stimulating factor -- stimulated the bone marrow to produce numerous stem cells, which entered the bloodstream, migrated to the damaged heart, and turned into new heart muscle. Only 4 of 27 mice given the drugs died from their heart attacks, compared with 43 of 52 that had not been given the drugs.

In some cases, drugs will not be any easier for patients than cell implants. The brain, for instance, is protected by a barrier that keeps out large proteins, so growth factors must be injected directly into the brain, just as for a cell implant.

Several companies are trying to develop so-called small-molecule drugs that can be taken orally and can pass through the blood brain barrier, but this has not proved easy. Amgen and Guilford Pharmaceuticals announced in July that such a drug was not effective in a clinical trial in treating Parkinson's disease.

NeoTherapeutics now seems to be the front-runner in the oral drug approach. Its drug, Neotrofin, appears to be able to stimulate the production of certain nerve growth factors and stem cells in animals. The drug is being tested on Alzheimer's disease patients in a late-stage clinical trial and, if all goes well, it could reach the market by 2004. NeoTherapeutics has also begun testing the drug on patients with Parkinson's disease and spinal cord injuries.

Many investors and other scientists are skeptical, saying that Dr. Glasky has a reputation for making premature claims of success. For instance, he said in an interview that Neotrofin might work for every neurological disease, potentially becoming the biggest-selling drug ever.

Neotrofin failed in the first big clinical trial, though the company says it now realizes it used too small a dose. Its shares closed yesterday at $3.80, down from a high around $24 early in 2000.

"It's like the boy who cried wolf," said Harry M. Tracy, publisher of NeuroInvestment, a newsletter that follows companies developing treatments for neurological diseases. "People are very wary of taking him seriously." Still, he thinks there is a chance that the company will succeed. Results of the Alzheimer's clinical trial are expected early next year. Whether the drug works or not, he said, "they are going to know that a whole lot sooner than they'll know that about embryonic stem cells."

Photos: Alvin J. Glasky at a NeoTherapeutics lab in Irvine, Calif. His company's new oral drug is in late-stage trials. (Lee Celano for The New York Times)(pg. C1); James H. Fallon, a neurobiologist at the University of California at Irvine, discussing laboratory tests as a colleague prepares an injection. (Lee Celano for The New York Times)(pg. C7)

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The Leader-Post (Regina)
July 9, 2002 Tuesday Final Edition
SECTION: News; Pg. B3

Umbilical cords may be used for research

SOURCE: Canadian Press

MONTREAL (CP) -- Stem cells from umbilical cords could become an alternative to ethically controversial embryonic cells in the treatment of several diseases, delegates to an international blood conference said Monday.

Research indicates the umbilical-cord blood cells, harvested from newborns at birth, can boost the immune systems of adults whose natural defenses have been destroyed by chemotherapy. Doctors say the umbilical blood is a potential alternative to bone-marrow transplants and doesn't carry the controversy of using stem cells from fetuses. A stem cell is a cell from which specialized cells develop.

"Normally, (umbilical-cord) cells are thrown in the garbage, but now we can save lives (with them)," Montreal blood specialist Dr. Denis-Claude Roy said at the conference.

"The use of cord blood would allow us to solve some of the problems that are associated with the use of embryonic stem cells, and that definitely is a very important answer to the ethical problem."

Many leukemia patients cannot find suitable bone-marrow donors and several thousand North Americans die each year while awaiting a bone-marrow match. The stem cells drawn from umbilical-cord blood have so far been reserved mostly for treating children because experts believed there was too little tissue to rebuild an adult's immune system.

But new U.S. research shows that umbilical-cord cells proliferate rapidly enough to be used to treat adults.

The Guardian (London)
July 9, 2002
SECTION: Guardian Home Pages, Pg. 1

Baby cord cells offer leukemia breakthrough

BYLINE: James Meek Science correspondent

A male nurse with leukemia has been brought back from the brink of death by blood from a newborn baby's umbilical cord which, in virtually all British births, is thrown away as useless.

The extraordinary recovery of Stephen Knox, 31, the first time an adult in Britain has been treated this way, is certain to lead to calls for more publicly funded cord blood banks to be set up. At present there are only two. The usual last-ditch treatment for leukemia sufferers is a transplant of bone marrow, which makes blood cells. This involves destroying the patient's existing bone marrow and replacing it with marrow from a family member or compatible donor. Hundreds of patients still die because they cannot find a match.

It has been known for some time that blood from newborn babies' umbilical cords, normally discarded at birth, contains stem cells which could be an alternative to bone marrow.

A handful of British children have been treated in this way but it had been thought that adults could not. Even if matching cells could be found from one cord, they would not be enough to repopulate the entire marrow.

Then Professor Stephen Proctor, a consultant and leukemia researcher at Newcastle University, heard by chance of operations in Canada where doctors had mixed matching and non-matching batches of cord cells together with remarkable success. On February 22, at Newcastle's Royal Victoria Infirmary, Prof Proctor's team injected a mixture of stem cells from the umbilical cords of seven babies into Mr Cox, from Middleton-St-George, near Darlington, Co Durham.

Mr Cox had been given a few months to live after chemotherapy had failed.

One of the cords was a perfect match: the other six were not. But instead of the body rejecting the unmatched cells, they appeared to act as boosters for the tiny number of matched ones, and Mr Cox began to recover.

The amount of blood which can be taken from an umbilical cord is about enough to fill a wine glass. But of that, only a tiny fraction - a few hundred out of billions of cells - will be the kind of stem cells needed to replace some six pounds of destroyed bone marrow.

To the astonishment of Prof Proctor, Mr Cox's white blood cell level was up to adequate levels by five weeks.

"I wouldn't have believed that was possible," Prof Proctor said. "Stephen is progressing much better than we thought he would and the transplant has worked much better and more quickly than we expected. It's a really exciting development and opens up huge possibilities. It has been carried out 23 times in the UK on children but never with an adult."

The two publicly funded cord blood banks in Britain - one in Newcastle, the other in London - have too little money to collect and store the amount of blood that would be needed for a comprehensive nationwide transplant program.

Private cord blood banks are available but expensive. The parents of the first so-called "designer" baby to be born in Britain, genetically pre-selected to be a tissue match for her brother, who had suffered from leukemia, stored her cord blood when she was born in case their son had a relapse.

The Australian
July 12, 2002, Friday
SECTION: LOCAL; Pg. 3

Nose-cell bid to restore spine

BYLINE: Stefanie Balogh

Adult stem cells have been harvested from a paraplegic patient's nose and injected into his spinal cord in the first stage of a pioneering clinical trial in Brisbane that could lead to a breakthrough treatment for paralysis. The team from Princess Alexandra Hospital and Queensland's Griffith University used olfactory ensheathing cells that connect the lining of the nose with the brain and provide the sense of smell. The researchers have already done tests on rats and Alan Mackay-Sim from Griffith has detailed the early stages of tests on humans in New Scientist magazine. The Princess Alexandra Hospital, which refused to discuss the operation yesterday, will detail the research today.

The trial has re-ignited debate over the use of adult stem cells. Tasmanian Liberal senator Guy Barnett said the Brisbane trial "bolsters the case for our opposition to embryonic stem cells." He said it also highlighted that adult stem cells "fulfilled the same objectives" as embryonic stem cells. But Joanna Knott, a director of the Australasian Spinal Research Trust, said there was a need for both types of research, adding the benefit of using embryonic stem cells was their flexibility. "Obviously we're still at the trial stage but I have had credible scientists saying to me that they believe major breakthroughs will be possible in the next two to three years if funding is available. So, it's a very exciting time," she said. Researchers have recruited three people paralysed from the waist down and plan to gather five more. Half of them will receive a spinal injection of the cells from the nose, according to New Scientist.

Researchers hope the transplanted cells will allow the spinal nerves to grow and bridge the damaged area. Gary Evans, head of the Princess Alexandra Hospital Foundation, said it had provided $200,000 for the first stage of the trial and that "this is the first time this final step has been made." He confirmed that the eight-hour operation on an anonymous male paraplegic was performed last month at the hospital and said it would be about three months before any results were available.

Giles Plant, who co-ordinates the spinal cord research laboratory at the University of Western Australia, said the Brisbane trial was "certainly not the first because they've done it in Lisbon and then they've also done some work in China".

However, Dr Plant, who does similar research with olfactory cells on spinal injuries but not yet on humans, described it as "a step forward". "We'll just have to wait and see how it goes," he said. "It certainly doesn't stop this important work carrying on everywhere else in terms of finding out exactly how these cells behave." He also said it did not "knock on the head any embryonic stem-cell work".

"It may be that a lot of the adult cells cannot work in the same way. I think that we just don't know enough and I think it is worth keeping all options open," he said. Leading adult stem-cell researcher Perry Bartlett of Victoria's Walter and Eliza Hall Institute described the Brisbane trial as a "brave venture" and said it was examining that "they don't do any damage to the human recipient, they are not really looking for gross improvements".

"It will be interesting to see what happens but one should keep in mind that the animal models haven't shown overall that these cells are capable of reconnecting or promoting reconnection fibres, nevertheless, it may be another mechanism by which they work."

The Mercury, Hobart
July 17, 2002, Wednesday
SECTION: INDEPTH; Pg. 19

Nosing towards a 'miracle'

BYLINE: ANNA PATTY

It would seem to be one of the most unlikely territories for a medical breakthrough but the human nose may harbor the key to repairing gravely damaged spinal cords.

Cells taken from inside the nose are offering medical scientists the latest hope of a means of producing tissue regrowth over damaged spinal cords.

Not to be confused with stem cells, which have yet to assume their final identity, the nose cells are fully developed and know exactly what they are.

Their special talent is in being able to regrow after they die. They are continually regenerated throughout their life and form the nasal tissue connecting the lining of the nose to the brain, controlling the sense of smell.

Because they are taken from and injected back into the same patient, there is no risk of rejection associated with the use of embryonic stem cells.

At Griffith University in Queensland, Drs Francois Feron and Alan Mackay-Sim have pioneered a method of harvesting and cultivating these special nerve cells.

Known as olfactory ensheathing cells, they are distinct from any other cells in the central nervous system and can quite happily exist both inside and outside the nervous system.

The spinal injuries unit director at Princess Alexandra Hospital, Tim Geraghty, and a team of specialists have injected these cells into a paraplegic patient, the first of eight people taking part in a three-year clinical trial.

The team involved in the eight-hour operation last month included spinal specialist Paul Licina, the head of neurosurgery Adrian Nowitski and ear, nose and throat specialist Chris Perry.

"What makes what we've done different from anyone else in the world," said Dr Geraghty, "is that we've been able to get these cells out of the nose with a simple nasal biopsy, grow and purify them outside the body in a laboratory and then put them back into the spinal cord."

While this method has shown some promise in rats whose spinal cords had been severed -- they were able to move their legs weeks after transplanted nasal cells helped regenerate the damaged area -- the same degree of success is not foreseen in human patients.

"We are certainly not expecting people to get up and be able to walk after this kind of surgery," said Geraghty.

"We are hopeful there will be some nerve regeneration so that people would get back some feeling or control over their bladder or bowel function.

"These cells have been able to produce some regeneration of the nerves in rats but we don't know whether they are going to work in humans and that is the point of the trial.

"Also, to make sure we are not causing any harm to the patient by doing this."

Geraghty said a principal aim of the trial was to determine how the cells worked and whether they could effectively be manipulated to do the job wanted.

"I think it is unrealistic to be too hopeful," he said. "We are not expecting that people will be able to walk.

"This is really the first stage of what will be an ongoing process, looking at the way these cells work and whether we can get them to do what we want them to."

He was unsure how long it might take to see a result -- but it was likely to be "months, rather than weeks".

He said: "The trial is set up to run for three years because we think we need that long to fully assess the patients involved and to make sure we are not doing any harm and to see if we are getting any positive results.

"There have not been any safety concerns that have arisen so far but we need longer to assess that."

The Princess Alexandra Hospital team is still in the process of recruiting eight patients, half of whom will not receive the nasal cells.

"We've taken a very conservative approach to this," said Geraghty.

"The patients we will be using are people who've had the severest form of spinal injury . . . who have no movement or feeling in their legs.

"As well, it has to have been six months since the time of their original injury with no natural improvement in the spinal cord since the injury occurred."

With the research still preliminary, it does little to challenge arguments against pressing ahead with embryonic stem cell research.

"I don't think these fully differentiated nasal cells are going to replace stem cells," said Geraghty. "These cells may be good for some things and stem cells may be good for something else."

Yet the nasal cells have probably been the most successful cells in animal research for getting spinal cords functioning.

"In animals, these look like the most promising thing at the moment," he said.

"This is an important first stage in what will be ongoing research into how the nasal cells work in an effort to try to get the nerves in the spinal cord to regrow."

XINHUA NEWS AGENCY
July 21, 2002, Sunday 6:44 AM Eastern Time

Stem cell research in India makes progress

DATELINE: NEW DELHI, July 21

Indian scientists have made progress in research on **adult stem cells** in blood cells and eye tissue area, local media reported Sunday.

Hyderabad-based L.V. Prasad Eye Institute has successfully demonstrated direct applications of limbal tissue to treat visual disorders in humans, says Dr.V.K. Vinayak, an adviser of Department of Biotechnology. Focusing on neuro-degenerative disorders, the National Center for Brain Research is conducting research on converting adult animal **stem cells** to nerve cells and would make further endeavor in the field of embryonic **stem cells.**

On similar lines, National Center for Cell Science (NCCS) in Pune has undertaken research on human embryonic **stem cells,** Vinayak said.

"Scientists at NCCS have been successful in devising technology used for cryo-preservation of cord blood **stem cells** and are extending their expertise to hospitals for possible therapeutic exploration and setting up **stem cell** banks," he said.

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The Press Trust of India
July 21, 2002 Sunday

Stem Cell Research making encouraging strides in India

DATELINE: New Delhi, Jul 21

Research on **adult stem cells** in India in haematopoetic (blood cells) and limbal (eye tissue) areas has made encouraging strides.

The L V Prasad Eye Institute, based in southern Indian city of Hyderabad, has successfully demonstrated direct applications of limbal tissue to treat visual disorders in humans, says Dr V K Vinayak, Adviser, Department of Biotechnology. Focussing on neuro-degenerative disorders, the National Centre for Brain Research, Delhi, is conducting research on converting adult animal **stem cells** to nerve cells and would make further endeavors in the field of embryonic **stem cells,** he adds.

On similar lines, National Centre for Cell Science (NCCS) in Pune has undertaken research on human embryonic **stem cells,** Vinayak says.

"Scientists at NCCS have been successful in devising technology used for cryo-preservation of cord blood **stem cells** and are extending their expertise to hospitals for possible therapeutic exploration and setting up **stem cell** banks," says Nibedita Lenka of NCCS.

Other research works undertaken at NCCS include use of hematopoetic **stem cells** in gene therapy and culturing fetal hepatocytes for preparing bio-artificial liver support device in case of acute and chronic liver failure, she adds.

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The Sunday Telegraph (Sydney)
July 21, 2002, Sunday
SECTION: LOCAL; Pg. 17

Stem cells save Aussie babies

BYLINE: JUSTINE FERRARI

Cutting edge **stem cell** therapy has been used to save the lives of several children in Australia born without a working immune system. The youngest was a baby of two months.

Now aged six months, Tyran Greenhalgh had Severe Combined Immune Deficiency (SCIDS) syndrome, which affects about four babies born in Australia every year. Having no immune system made Tyran vulnerable. Common illnesses could leave him critically ill.

For the past 10 years, bone-marrow transplants have been used to treat children with SCIDS.

However, doctors at the Sydney Children's Hospital at Randwick are now using **stem cells,** the cells that grow into bone marrow.

Tyran's return to health turns a full circle for his family. In 1975, Tyran's grandmother Gail Geddes watched helplessly as her son Matthew died at the age of nine months with the same condition.

When Matthew was born, little was known about SCIDs and there was no readily available treatment. Bone-marrow transplants were in their infancy and could only be performed if the patient had a fully compatible brother or sister.

Tyran's mother, Mandy Greenhalgh, discovered when she was about 20 weeks' pregnant that she carried the gene for SCIDs, meaning her baby had a 50-50 chance of having the condition.

"It was very stressful through the whole pregnancy knowing he could have

it," Mrs. Greenhalgh said.

Of some comfort to her and her mother was that one of the doctors who treated Matthew 27 years ago was the doctor who treated Tyran.

Now director of the Sydney Children's Hospital's immunology department, Professor John Zeigler said **stem cells** had the potential to turn into different cells in the body for specific functions.

For Tyran's treatment, his father Ian received drugs to stimulate his bone marrow and the stem cells were harvested from his blood and transplanted into Tyran.

Tyran is now growing his own white blood cells designed to fight infection, and T cells and B cells, that make antibodies targeting specific infections.

This means he has every chance of a normal life.

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AAP NEWSFEED
July 19, 2002, Friday

Baby stem cells collected to help sick grandfather

DATELINE: ADELAIDE, July 19

An Adelaide couple has stored the **stem cells** of their newborn baby, hoping they might be used one day to help cure the child's grandfather of lekaemia.

The case was reported in the July edition of the South Australian Medical Review. But the Australian Medical Association said the couple had told their treating doctor this morning that they did not wish to be contacted or identified.

According to the publication, the 65-year-old grandfather was diagnosed with chronic lymphocytic leukemia (CLL) more than a year ago.

Since his diagnosis, his daughter and her husband have conceived a child.

Researching CLL during her pregnancy, the woman learned that **placental stem cells** might be helpful in treating her father's condition.

"We understand that placental **stem cells** can effectively treat young people," the woman's husband was quoted as saying in the medical review.

"But it is not clear whether they will be useful for my wife's father."

Despite these doubts, the couple went ahead with the procedure and had the placental material collected by their treating obstetrician.

The review said it was being stored indefinitely by researchers at a major public hospital and no commercial arrangement was involved.

The article also said the grandfather's life expectancy had been estimated at 14 years, with CCL considered relatively slow to develop.

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Pain & Central Nervous System Week
July 22, 2002
SECTION: EDITOR'S CHOICE; Pg. 4

BRAIN INJURY: Cord blood cells improve rats' neurological recovery, new study finds

Intravenous injections of cells from human umbilical cord blood improved the neurological and motor function of rats recovering from severe traumatic brain injury, researchers at Henry Ford Health Sciences Center (HFHSC), Detroit, and the University of South Florida (USF), Tampa, found.

The study appears in the journal Cell Transplantation (June 6, 2002), a special issue that focuses on emerging approaches in neural transplantation and brain repair. It is one of several articles exploring the therapeutic potential of human umbilical cord blood (HUCB) cells as an alternative to embryonic **stem cells.**

While studies of cellular therapies continue to grow in importance, the emphasis has been on neurological diseases like Parkinson disease and stroke, and, more recently, on spinal cord injury. **"This study is the first to suggest that human umbilical cord blood may be a novel way to treat traumautic brain injury, a significant cause of death and disability for adolescents and young adults," said report coauthor Paul R. Sanberg, PhD, DSc, director of the USF Center for Aging and Brain Repair.**

"The results certainly raise some interesting questions about the mechanisms of recovery," said coauthor Juan Sanchez-Ramos, PhD, MD, Helen Ellis professor of neurology and director of **stem cell** research at the USF Center for Aging and Brain Repair. "It appears that the growth factors and cytokines from cord blood help promote the brain's self-generated repair of damaged tissue."

"These findings were consistent with the therapeutic benefit we obtained

using cord blood to treat stroke in rats," said Michael Chopp, PhD, a neuroscientist at HFHSC and lead author of the report. This earlier study was published last November in the journal Stroke.

"Cord blood is readily available, noncontroversial and produces therapeutic benefit by stimulating endogenous restorative responses in the injured brain," Chopp said.

HUCB cells were injected intravenously into the tail veins of rats 24 hours after traumatic brain injury. At both 14 and 28 days after treatment, the rats receiving cell transfusions showed greater improvements in movement, balance and reflex responses than brain-injured rats receiving a placebo or no treatment.

The cord blood cells migrated to the region of the brain injury. A small portion took on the characteristics of immature neurons and other brain cells known as astrocytes. Some others integrated into the brain's blood vessels. Only a limited number of HUCB cells drawn to the area of brain injury actually expressed proteins typical of those in early neural cells.

Umbilical cord blood contains a small percentage of primitive **stem cells** - totally undifferentiated cells with the potential to develop into any one of the specialized tissues in the body, including blood, skin, muscle or nerve cells.

"It is unlikely that hastened recovery from the trauma could be solely attributed to such small numbers of **stem cells** transforming into neural cells," Sanchez-Ramos said.

Some HUCB cells that became part of brain tissue surrounding the injury expressed characteristics of endothelial cells lining the brain blood vessels. This suggests the injected cells may help regenerate injured vessels, Sanchez-Ramos said.

A second study in Cell Transplantation, by USF neuroscientist Tanja Zigova, PhD, reported that some undifferentiated HUCB cells transplanted into the developing brains of neonatal rats begin to appear like nerve cells and express certain proteins found only in neurons and glial cells. The findings suggest that at least some of the transplanted HUCB cells took on the characteristics of neural cells in response to cues from the young brain.

Researchers at the USF Center for Aging and Brain Repair are continuing studies to identify and expand the **stem-cell** portion of HUBC and to define how cord blood cells promote brain recovery.

The HUCB studies were suppported by Saneron CCEL Therapeutics, Inc., an affiliate of Cryo-Cell International, Inc., a company that collects and stores umbilical cord blood. A State of Florida High Tech Corridor grant also funded the research.

Stem Cell Week
July 22, 2002
SECTION: EXPANDED REPORTING; Pg. 12

SYSTEMIC LUPUS ERYTHEMATOSUS: Blood stem cell transplantation holds hope for autoimmune diseases

For patients with severe autoimmune diseases, **blood stem cell** transplantation may be promising therapy option. This process involves an infusion of healthy blood cells to replace the body's own malfunctioning ones and restore immune function. A recent case study, published in the journal Arthritis & Rheumatism, has shown this approach to be particularly effective in treating patients with the most serve form of systemic lupus erythematosus (SLE). A chronic rheumatic disease, SLE affects joints, muscles, kidneys, lungs, and other parts of the body by autoimmune attack. In the case of an 18-year-old female patient, a short, intensive course of blood **stem cell** transplant produced complete remission of the disease. Diagnosed with SLE at age 14, the patient had suffered bouts of pneumonia, requiring ventilation and resulting in serious lung impairment. Failing to respond to conventional drug therapy, she also continually battled infections, weight loss, and anemia. In February 2000, the young woman began the blood **stem cell** transplant therapy, as part of a study at the University of Vienna. She repeatedly received infusions of high-dose immunosuppressive agents followed by **stem cells** purified on the basis of a protein on the surface of cells called CD34. Within 9 days of receiving her transplant, the patient's blood cells began to regenerate - completely free of disease.

Fifteen months after completing her blood stem cell transplant regimen, the patient had maintained overall excellent health - without taking any medication. She showed no signs of SLE-related problems. Her lung, kidney, and ovarian functions were all normal. In addition, she had fully intact function on a standard measure of a person's ability to perform routine activities (Brunner M, Greinix HT, Greinix K, et al. Autologous blood **stem cell** transplantation in refractory systemic lupus erythematosus with severe pulmonary impairment, Arthritis & Rheumatism, June 2002;46(6)).

There have been numerous studies indicating the potential of blood **stem cell** transplants for patients with blood diseases and certain types of cancer. To date, researchers have studied only a small number of patients undergoing this therapy for autoimmune diseases. Consequently, the case of this young SLE patient is significant because it confirms blood **stem cell** transplantation as a potentially effective course of action for restoring healthy immune function. Researchers at the University of Vienna are currently conducting clinical trials to explore wider use of this therapy, as well as ways to apply it in the early stages of disease to prevent organ damage

Pain & Central Nervous System Week
July 22, 2002
SECTION: EXPANDED REPORTING; Pg. 11

CEREBRAL PALSY: Mature stem cell transplants linked to treatment

Whether transplantation of mature **stem cells** can help babies with cerebral palsy is the study focus of a Medical College of Georgia physician-scientist.

Dr. James E. Carroll, chief of the section of pediatric neurology, has received a 2-year grant from the National Institutes of Health to pursue whether brain damage that occurs during the birth of these babies can be repaired with transplants.

Cerebral palsy is a term used for brain damage that occurs before or during birth to about 1-2 babies per 1000 births. One-tenth of these babies incur the damage during birth, when complications such as protracted periods in the birth canal can deprive the baby of adequate oxygen. "The baby's brain is very resilient to low oxygen," Carroll said. "During delivery there is a certain period of time when the blood vessels are squeezed off, and it's not uncommon for babies to come out blue." But when those ischemic periods exceed 10 minutes, damage can occur.

In premature babies, the damage typically is in the white matter, including the supporting glial cells around the fluid-filled ventricles and the hippocampus, which controls memory. In full-term babies, damage occurs in the cortex, the outer, thinking portion of the brain. The difference in damage location results from changes in circulation as the brain matures.

Preliminary data on an animal model for stroke has shown that **mature stem cells from the bone marrow** will migrate to the site of brain injury, Carroll said, referencing the work of colleagues, Drs. David Hess and William D. Hill. Hess and Hill are looking for mechanisms to enhance this natural repair process.

Carroll is using a mouse model with ischemic injury to see whether putting

additional **stem cells** in the circulation can augment repair.

"There have been lots of strategies to help with this problem, but there is a need for other strategies," Carroll said. "Some strategies have centered around better care of babies prior to birth and after birth and that's a good thing. But other things that have not worked are the use of various agents given to protect the brain," he said of studies that worked in the laboratory but were not effective in human trials.

In his study model, bone marrow is removed from one group of mice that is genetically similar to the group that gets the transplant. Two major **stem cell** populations, hematopoietic and marrow stromal cells, are retrieved and tagged with a jellyfish protein that fluoresces green so they can be tracked. His goal in using two different cell lines is to see which is most effective; he believes it will be the marrow stromal cells.

The fluorescing cells are then transplanted into the vascular system of the other group of mice and monitored to see whether - as in the preliminary data - transplanted cells will find their way to the brain to help repair damaged brain cells and make new ones as well as supporting blood vessels. "The idea is that we would put cells into the right place and they would implant and function," Carroll said. "We don't know if that will happen."

He eventually wants to find an even more specific cell population, the oligodendrocyte cells, which make insulation for brain cells and are the most damaged in cerebral palsy. "There are culture techniques available that will allow us to develop this type of cell specifically and put it in the brain. That is really the next step and we are really interested in doing that."

If his laboratory studies work, he hopes to begin clinical trials on mature **stem cell** transplants in about 5 years.

Cerebral palsy results in a wide range of disability, from undetectable to severe physical disability. Some children also have accompanying learning and memory problems. "The numbers of people with this condition are not huge, but it can be a huge problem for those who have it," said Carroll, who believes that the transplant techniques being developed to help these babies have potential application in a large number of conditions.

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Sunday Herald Sun
July 21, 2002, Sunday
SECTION: EXTRA; Pg. 37

Baby cells mean misery for mums

BYLINE: Graeme O'Neill

EVIDENCE is emerging of cells produced by babies in the womb surviving in the mother's body for decades after the birth.

Doctors suspect they are responsible for a host of illnesses, but they may also save a woman's life by repairing damaged tissue.

These fetal cells have been found, in one case, to be active in a woman's body 27 years after she gave birth.

It has long been known that the cells of mothers and their unborn babies mix in blood in the placenta, but it was presumed the mum's immune system killed the cells from the infant soon after birth. In fact, some of them thrive, and can trigger serious health problems such as arthritis, thyroiditis and the collagen disorder scleroderma.

This, according to an article in the research journal Science, may solve a long-standing medical mystery: why women are more likely than men to develop certain illnesses that are impervious to the immune system.

AUS team has also unearthed some better news for women. In rare cases, fetal cells rebuild damaged organs.

This can result in entire segments of organs such as the liver and thyroid gland being made up of cells that were originally created by the fetus.

The mother -- or at least part of her -- would, in effect, be her child's offspring.

The first hint that cells from a fetus could survive long-term came in 1992

during work at the Children's Hospital in Boston to diagnose genetic disorders in unborn babies.

Dr. Diana Bianchi tested blood taken from 13 pregnant women.

As expected, cells created by a fetus were found in the women's blood.

What was not expected was that male Y-chromosomes would be found in all the samples -- only nine of the women were expecting boys.

Why would a woman who was not expecting a boy have male chromosomes floating around in her blood?

In this case, two of the women already had sons and the other two had terminated pregnancies without knowing the sex of the fetus.

It seemed fetal cells from earlier pregnancies had lived on.

But why would cells created by a child attack the mother?

Typically, these "left-over" cells are white blood cells involved in the immune system. They are programmed to kill cells produced by any other being.

A similar situation as to that experienced by some organ transplant patients may be occurring.

Rather than the patient rejecting the donor organ, the organ effectively tries to reject the patient. White, immune-system blood cells that remain in the organ when it is transplanted attack the recipient's tissues.

It is this continued assault by the fetal cells that can cause problems for women years after they give birth.

Studies carried out following Dr Bianchi's discovery show women with certain illnesses linked to the immune system -- auto-immune disorders -- generally have many more cells created by a fetus in their bodies than women without such health problems.

Scientists studying the severe disorder scleroderma, which causes skin and

organs to lose elasticity and harden, found male cells in the affected areas.

However, it would be wrong to blame health problems on baby boys.

The only way of detecting fetal cells in a woman's blood is by searching for the male Y-chromosome, so it is assumed cells from female fetuses may account for 50 per cent of cases in which mothers develop auto-immune disorders after pregnancy.

TWO research teams, one led by Dr Bianchi, the other by German researcher Dr. Michael Klintschar, have found high levels of fetal cells in women suffering from thyroiditis, which reduces production of the thyroid hormone, and which is much more common in women than in men.

Swiss researcher Dr Wolfgang Holzgreve recently linked left-over fetal cells to a common complication of pregnancy, pre-eclampsia, which causes dangerously high blood pressure and vomiting, and may prompt an emergency caesarean.

Pregnant women normally have about one fetal cell per million of their own in their bloodstream. In women with pre-eclampsia, the figure is about 1000 per million.

In a further development, it now appears some fetal **stem cells** may also survive in the mother's body.

These appear to be capable of living in the mother's bone marrow, and renewing themselves almost perpetually.

In one case, male cells were found in the bloodstream of a woman who had several sons, the youngest of them aged 27.

But living with cells in your body that were produced by your baby could be of benefit.

Dr Bianchi has reported the case of a woman with hepatitis C.

A biopsy revealed one part of her liver consisted entirely of male cells, suggesting **stem cells** from her son had repaired the damaged organ.

In another case, a mother had a large swelling, or goitre, removed from her thyroid gland, and a large segment was made of male cells -- presumably from her son.

This, Dr Bianchi says, suggests an unexpected bonus of pregnancy is that mothers receive a second population of **stem cells** capable of repairing damaged tissue.

Associated Press
July 28, 2002 Sunday 8:20 PM Eastern Time

Stem Cells Grow Eye Blood Vessels

BYLINE: RANDOLPH E. SCHMID; Associated Press Writer

Stem cells taken from bone marrow can grow new blood vessels in the eyes of mice, a development researchers say raises the possibility of treating some diseases that often lead to blindness in humans.

In tests in mice, the stem cells injected into the eye became incorporated into the eye's structure and formed new blood vessels.

If the process turns out to work in humans, the scientists hope to use it to treat eye diseases affecting the blood vessels in the retina. They include diabetic retinopathy and age-related macular degeneration, two leading causes of blindness. Dr. Martin Friedlander, who headed the research team at the Scripps Research Institute in La Jolla, Calif., said it may be possible to use the process to rescue sick blood vessels or, in modified form, inhibit the growth of abnormal vessels in the eye.

His research will be published in the September issue of the journal Nature Medicine.

Peter A. Dudley, director of the retinal diseases program the National Eye Institute, said it is "extremely interesting" that the team was able to take certain precursor stem cells that can form blood vessels and then target them.

He said it seems reasonable this could lead to human treatments. But he cautioned that the work only involved mice and that many details need to be worked out before moving on to humans.

Dr. John S. Penn, who teaches ophthalmology at Vanderbilt University, said the work adds to the fundamental understanding of biology, adding that the finding that the cells can home in on specific parts of the eye "is pretty cool stuff."

He also cautioned that the work is in mice and much work needs to be done before it can be applied to humans.

Stem cells are a type of cell that can differentiate into many different cells depending on what is needed. They form in the embryo and are also found in adult bone marrow.

Friedlander's team used a type of stem cell called an endothelial precursor cell taken from mouse bone marrow.

When these cells were injected into the eyes of mice, they attached to cells in the retina called astrocytes and then formed new blood vessels.

"What's exciting about this, and surprising to us, is they don't target mature vessels, they go where vessels are going to form," Friedlander said.

Newborn mice, for example, do not have blood vessels in their retina but have astrocytes forming a sort of template for future vessels, Friedlander explained.

In adult mice, he said, if the retina is injured, it encourages the development of astrocytes. By injecting the stem cells, the researchers can help stabilize a degenerating blood vessel system.

Friedlander said he was "flabbergasted" at the improvement when the stem cells were injected into the eyes of a type of mice that have eye degeneration and normally go blind within 30 days of birth.

Friedlander said he believes that because the stem cells target astrocytes, genetically modifying the stem cells before injection may make it possible to block the growth of unwanted blood vessels, which are also a factor in some eye disease.

He also suggested that the cells could be used as a drug delivery system for the eyes, something Penn said would be an exciting development.

Diabetic retinopathy is the leading cause of blindness in working age Americans, and almost all people who have had diabetes for more than 30 years will show signs of poor eyesight.

Age-related macular degeneration is a common cause of vision loss among people over age of 60. Both conditions are caused by damage to blood vessels of the retina.

The Daily Telegraph(Sydney)
July 29, 2002, Monday
SECTION: LOCAL; Pg. 7

Cells may cure some blindness

BLINDNESS caused by old age and diabetes may soon be curable using stem cells taken from adult bone marrow, say scientists who publish their research today in the science journal Nature.

Certain stem cells taken from bone marrow have been shown in mouse models to be effective in curing eye diseases such as diabetic retinopathy and deterioration of vision due to age. Both these are the leading cause of blindness and vision impairment.

The scientists from the Scripps Research Institute in California have found the groundbreaking development in a set of cells derived from bone marrow which produce red blood cells.

Within this set of cells are other cells called endothelial precursor cells, which are a form of stem cells which are capable of forming blood vessels.

Because both the diseases related to this form of blindness are related to damage of the blood vessels to the eye, it is believed the cells may work as well in humans.

The Associated Press
August 9, 2002, Friday, BC cycle

Study: Stem cell implants could create new blood vessels, save limbs

BYLINE: By EMMA ROSS, AP Medical Writer

Injecting patients' own stem cells into their leg muscles could create new blood vessels, eliminating pain from bad circulation and helping to prevent gangrene or amputations, new research indicates.

The study, described this week in The Lancet medical journal, is the first demonstration that implanting stem cells into humans can result in new blood vessel networks, a process called angiogenesis.

Experts say the findings offer hope to millions of people worldwide who suffer pain in their limbs because of clogged arteries but can't have an operation.

Controlling blood vessel growth is an emerging field of medicine. In the case of cancer, which spreads by sprouting its own blood vessel network, scientists are testing drugs to thwart angiogenesis. However, when parts of the body are starved of oxygen because blood vessels supplying them are blocked, doctors want to boost blood vessel growth - treatment they call therapeutic angiogenesis.

The main focus of research is on the heart, limbs and - in the future - brain. Heart attacks, limb amputations and strokes can result from severe circulation problems. Another target is sores that fail to heal.

Experiments so far have involved infusing human proteins needed for new blood vessel growth into the veins or injecting muscles with genes that make the proteins.

"This is truly a landmark paper because of its use of stem cells to induce angiogenesis," said Dr. William Li, president and medical director of the Boston-based Angiogenesis Foundation, who was not involved in the research.

"It's a brand new approach to treating limbs starved of blood supply," Li said. "They were able to eliminate rest pain in 80 percent of their patients. That is striking. You don't see that with other treatments."

The study was done by scientists at three Japanese universities: Kansai Medical University in Osaka, Kurume University School of Medicine in Kurume and Jichi Medical School in Tochigi.

It involved 45 people with severe blood circulation problems in their legs. About half had already had a bypass operation in their legs, nearly half had gangrene and 69 percent had diabetes. Many had sores that wouldn't heal, suffered pain in their legs even when sitting and were not candidates for surgery or other artery-widening techniques.

The first part of the experiment involved 25 patients in a pilot study to test how many people would be needed to demonstrate whether the treatment made a difference.

In the pilot study, bone marrow was extracted from the patients and stem cells injected into their worst leg. Saline solution was injected into the other leg.

The main study involved 20 other people in whom both legs were critically starved of blood flow. They had their bone marrow stem cells injected into one leg, randomly chosen, and regular blood injected into the other leg. Before the experiment, everyone had an angiogram, a scan that shows the blood vessel network.

The scientists used several measurements to gauge the success of the treatment.

The legs that got the stem cells had more improvement than the others on a test comparing blood pressure in the ankle with that in the arm before and after treatment. Similar results were seen in a second circulation test that measured differences in oxygen inside and outside tissues.

Pain while sitting down disappeared in the stem cell-injected legs of 16 of the 20 people in the main study, but 17 out of the 20 legs that got the blood injection remained painful. That improvement lasted for the six

months of the study.

X-rays before and after the cell implantation showed increased blood vessel networks in 27 of the 45 who got the stem cells in the two studies.

Toe amputations were avoided in 15 out of 20 people, and unhealed wounds improved in six out of the 10 patients who suffered from them.

Ira Herman, a professor of physiology at Tufts University who was not involved in the research, said the most impressive findings came from leg specimens of one patient who got stem cells in one leg and saline in the other but died half way through the trial of an unrelated heart attack. The examination found a striking increase in blood vessel numbers in the leg injected with stem cells.

"It's just remarkable," he said. "You can't help but be impressed by the collection of data."

One question that remains unclear is whether the stem cells actually became blood vessel cells or whether they simply released growth factors that prompted other cells to construct new vessels.

Dr. Frank Sellke, chief of cardiothoracic surgery at Harvard Medical School who was also not involved in the study, said the stem cell approach may have great potential.

"There is evidence that the bone marrow cells will actually seek out the most (starved) territory. They will circulate and go to where they are needed," he said.

On the Net:

The Angiogenesis Foundation, http://www.angio.org

"As to diseases ,make a habit of two things —
to help, or at least *do no harm.*"
— Hippocrates, *The Epidemics* —

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IN HUMAN PATIENTS:

Patient's Own Cells Aid Spinal Cord Repair
Eighteen-year old Melissa Holley, a paraplegic patient with a severed spinal cord, has been treated with her own immune cells, and has regained movement of her toes and bladder control.

Reference: *Globe and Mail* (Toronto), June 15, 2001.

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Adult Stem Cells Reduce Symptoms of Parkinson's
Symptoms of Parkinson's disease in a San Clemente, Calif., man have "largely disappeared" after doctors removed stem cells from his brain, grew them into neurons and transplanted the neurons back into his brain, the Washington Post reports. The procedure, described April 8, 2002 at a meeting of the American Association of Neurological Surgeons, marks the first in which doctors transplanted "adult neural stem cells" -- stem cells that can "morph into every kind of brain cell" -- to a human. The neural stem cells may allow patients with Parkinson's to "essentially grow their own cures," the Post reports. As part of the procedure, Michel Levesque, a neurosurgeon at Cedars-Sinai Medical Center in Los Angeles, removed 50 to 100 cells from the brain of the San Clemente patient and grew them in the lab for a few months. Levesque injected about six million of the cells, 35% of which were neurons, back into the man's brain. ...After a year, the man's symptoms were relieved by 83% ...

Reference: *American Health Line*, April 10, 2002.

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Adult Stem Cells Treat Multiple Sclerosis
Researchers have developed a combined therapy using a patient's own stem cells for treatment of severe cases of multiple sclerosis. Treatment decreased tissue damage in the patients, and had the capacity to completely suppress further tissue damage, an effect that appears to be sustained with time.

Reference: G.L. Mancardi et al., "Autologous hematopoietic stem cell transplantation suppresses Gd-enhanced MRI activity in MS," *Neurology* 57, 62-68; July 10, 2000.

Scientists reported April 16 that transplantation of stem cells from a patient's own blood could provide a new treatment for people with severe cases of multiple sclerosis. In research presented at the American Academy of Neurology's annual meeting, researchers at the University of Washington Medical Center in Seattle reported treating 26 patients with severe MS with their own adult stem cells. Conventional treatments had previously been unsuccessful for all of the patients. After the transplant of their own adult stem cells, 20 patients were stabilized, and 6 patients showed improvement in their condition. "This is good news," said Dr. George Kraft. "These patients had all been rapidly deteriorating over the past year, so to get them to a point where they are stabilized is great progress."

Reference: Liz Kay, "Stem Cell Therapy May Help Multiple Sclerosis", *Los Angeles Times*, April 17, 2002.

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Adult Stem Cells Successfully Treat Heart Disease

The first reports of successful treatment for heart disease using the patient's own adult muscle stem cells after heart attack are encouraging news. French physicians implanted skeletal muscle stem cells back into the patient; the encouraging result after eight months' follow-up underlines the potential of this new approach. Further clinical trials are now underway in Europe and the U.S. for other patients with heart disease. No human trials using embryonic stem cells have ever been reported.

A review of potential heart treatments notes that cell transplantation is a potential therapeutic approach for patients with chronic heart failure. Experimental transplantation of muscle cells showed that the grafted cells can functionally integrate with and augment the function of the recipient heart. The scientists note that skeletal muscle stem cells are abundant and can be grafted successfully into the patient's own heart even after genetic manipulation in vitro.

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- "Doctor Puts Arm Muscle Cells Into Patient's Heart," *Associated Press*, May 30, 2001.
- "First Percutaneous Endovascular Case of Heart Muscle Regeneration Completed with Bioheart's MyoCell(TM) Product," *PRNewswire*, May 30, 2001.
- R.M. El Oakley *et al.*, "Myocyte transplantation for cardiac repair: A few good cells can mend a broken heart," *Annals of Thoracic Surgery* 71, 1724 –1733, 2001.

Doctors in Germany report the successful use of a patient's own adult stem cells from bone marrow to regenerate tissue damaged after a heart attack. They injected the man's own bone marrow stem cells into his damaged heart muscle.

Ten weeks later, the damaged area of heart tissue had been reduced, replaced by new cells, and heart function had increased by 20-30 %. The authors conclude "transplantation of human autologous adult stem cells is possible under clinical conditions and that it can lead to regeneration of the myocardial scar after... infarction." They also point out that the therapeutic benefits can be ascribed to the adult stem cells. They plan to perform the same operation on 20 more patients in the coming months. The use of the patient's own adult stem cells from bone marrow or muscle to treat damage from heart attack is also in clinical trials in France and the U.S. (*Reuters Health*, July 23, 2001).

Reference: B.E. Strauer et al., "Myocardial regeneration after intracoronary transplantation of human autologous stem cells following acute myocardial infarction," *Dtsch Med Wochenschr* 126, 932-938; Aug. 24, 2001.

Surgeons at Newcastle's John Hunter Hospital north of Sydney extracted stem cells from patient Jim Nichol's bone marrow then injected them back into his heart wall to stimulate blood vessel growth in areas which lacked sufficient blood supply. Nichol was discharged from hospital on Tuesday and his condition will be monitored over the next six months by researchers who undertook the trial as part of an international experiment also being carried out in Hong Kong and China.

Reference: "Australia tests stem cells to beat heart damage", *Reuters* April 10, 2002

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Adult Stem Cells Used In Stroke Treatment
In a follow-up study, stroke patients who had received a transplant of human neuronal cells showed improved brain cellular function and engraftment of the implanted adult stem cell line. The cultured cell line was originally derived from an adult tumor (a "teratocarcinoma", sometimes called an "embryonal carcinoma" because it mimics some characteristics of embryonic cells; the tumor had been "tamed" and grown in culture a number of years.)

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- C.C. Meltzer *et al.*, "Serial [18F]Fluorodeoxyglucose Positron Emission Tomography after Human Neuronal Implantation for Stroke," *Neurosurgery* 49, 586-592; 2001.
- D. Kondziolka *et al.*, "Transplantation of cultured human neuronal cells for patients with stroke, *Neurology* 55, 565-569; Aug. 2000.

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Adult Stem Cells Help Restore Sight
Corneal stem cells have been used by doctors in Japan to restore useful vision to patients who were legally blind. Transplants of adult corneal stem cells were used for conditions in which normal cornea transplants were unsuitable. One year after treatment, over half of patients had marked improvements in vision.

Reference: K. Tsubota, *et al,* "Treatment of severe ocular-surface disorders with corneal epithelial stem-cell transplantation," *New England Journal of Medicine* 340, 1697-1703, June 3, 1999

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Umbilical Cord Blood Stem Cells Treat Sickle Cell Anemia
Umbilical cord blood stem cells have been used successfully to treat sickle cell anemia. The cord blood came from a matched sibling of the patient. The researchers note that routine collection of umbilical cord blood from siblings should be considered for sickle cell disease cases.

Reference: L. Gore *et al.,* "Successful cord blood transplantation for sickle cell anemia from a sibling who is human leukocyte antigen-identical: implications for comprehensive care," *Journal of Pediatric Hematology and Oncology* 22, 437-440; Sept-Oct 2000.

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Adult Stem Cells Treat Potentially Fatal Skin Disorder
A man with scleromyxedema, a rare and potentially fatal skin disease, is reported free of symptoms after receiving a transplant of adult stem cells taken from his own bone marrow. Like scleroderma, scleromyxedema causes the skin to thicken and become hard. Prior to the adult stem cell treatment, the patient could not completely close his eyes, and had lost the ability to eat. Three months after treatment the patient could once again close his eyes and open his mouth to eat. The results are reported in the August issue of *Archives of Dermatology*

References

- A.M. Feasel et al., "Complete remission of scleromyxedema following autologous stem cell transplantation," *Archives of Dermatology* 137, 1071-1072; Aug. 2001.
- "Stem Cell Transplant Treats Rare Skin Disorder," *Reuters Health*, August 17, 2001.

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Adult Stem Cells Used to Treat Children with Cartilage Defect
Bone marrow-derived stem cells have been used clinically to treat children with osteogenesis imperfecta, a condition that leads to multiple fractures, severe bony deformities, and considerably shortened stature. Three months after treatment, the three children showed changes indicating new dense bone formation. The report by researchers at St. Jude Children's Hospital in Memphis indicates the promising possibility for treatment of this as well as similar stem cell disorders.

Reference: E. M. Horwitz, *et al,* "Transplantability and therapeutic effects of bone marrow-derived mesenchymal cells in children with osteogenesis imperfecta," *Nature Medicine* 5, 309-313, March 1999

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Adult Stem Cells Successfully Treat SCIDS
As reported in April 2000 in the journal *Science*, French scientists restored the immune systems of 3 infants with severe combined immunodeficiency syndrome (SIDS, the "bubble boy syndrome") using gene therapy with *the patients' own bone marrow stem cells*. Researchers removed stem cells from the infants' bone marrow, added a working copy of the gene to the cells' DNA, and injected the repaired stem cells back into the infants. Since the procedure used the patients' own cells, there was no problem of transplant rejection. After treatment, the numbers and function of the patients' immune cells were restored to *normal levels*, and the children were living at home and developing normally with no further treatment

Reference: M. Cavazzana-Calvo, *et al.*, "Gene Therapy of Human Severe Combined Immunodeficiency (SCID)-X1 Disease," *Science* 288, 669-672, April 28, 2000).

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Adult Stem Cells Show Success Treating Autoimmune Diseases

Physicians at Chicago's Northwestern Memorial Hospital report initial success in using adult stem cells to treat two patients with Crohn's disease, a potentially disabling inflammatory bowel disease. One patient was said to be doing "phenomenally well" 2 ½ months after undergoing the procedure using the adult stem cells, which were extracted from her blood, leading doctors to try it on a second patient. Results in both patients were very encouraging, according to Dr. Richard Burt, who performed the procedures. Burt noted that results of similar procedures on multiple sclerosis patients have also shown progress, and that adult stem cell therapy on patients with lupus had repaired damage to their organs. According to Burt: " 'If you're able to use your own stem cells,' the embryonic stem cell issue is 'not just ethically moot, it's practically moot.' "

Reference: "Adult Stem Cells Hold Hope for Autoimmune Patients," *Reuters Health*, Aug. 13, 2001.

In Animal Studies:

Adult Stem Cells Repair Spinal Cord Damage
Several labs have shown adult stem cells capable of re-growth and reconnection in spinal cord injury, allowing functional recovery. Adult stem cell transplants "promote functional recovery of paraplegic adult rats and long-distance motor axon regeneration in their completely transected [severed] spinal cords," and showed "dramatic functional improvement and anatomical repair" (Ramon-Cueto et al; 2000).

Others, using transplanted adult stem cells or injection of growth proteins to stimulate existing adult stem cells, achieved re-growth of neurons and re-myelination (sheathing) of neurons.

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Adult Stem Cells Used in Stroke Treatment
Adult bone marrow or umbilical cord blood stem cells, delivered intravenously to brain tissue which has suffered stroke damage in rats, provide therapeutic benefit after stroke. The cells appeared to "home" to sites of damage.

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- J.Chen *et al.*, "Intravenous administration of human umbilical cord blood reduces behavioral deficits after stroke in rats," *Stroke* 32, 2682-2688; November 2001.
- J. Chen *et al.*, "Therapeutic benefit of intravenous administration of bone marrow stromal cells after cerebral ischemia in rats," *Stroke* 32, 1005-1011; April 2001.

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Adult Stem Cells Treat Heart Disease
Bone marrow stem cells injected into heart or which migrate to site of heart damage can regenerate heart tissue.

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Adult Stem Cells Successfully Treat Diabetes
Scientists "retrained" immune cells to reverse diabetes in mice. The autoimmunity that was previously directed against insulin-secreting cells was reversed, and adult stem cells in the mice formed insulin-secreting cells. The treatment was "...thus able to effect an apparent cure of established Type 1 diabetes in the [diabetic] mouse".
Reference: S. Ryu et al.; "Reversal of established autoimmune diabetes by restoration of endogenous ß cell function," *J. Clin. Invest.* 108, 63-72; July 2001

Pancreatic adult stem cells grown in culture formed insulin-secreting islets. When injected into diabetic mice, the mice survived without further need of insulin injections.
Reference: V.K. Ramiya et al.; "Reversal of insulin-dependent diabetes using islets generated in vitro from pancreatic stem cells," *Nature Medicine* 6, 278-282, March 2000.

THE GLOBE AND MAIL
CANADA'S NATIONAL NEWSPAPER ▪ FOUNDED 1844 ▪
GLOBEANDMAIL.COM ▪ FRIDAY, JUNE 15, 2001

Paraplegic regains movement after cell procedure

BY KRISTA FOSS

Israeli doctors who injected immune-system cells into the severed spinal cord of a paraplegic American teenager last year made a stunning announcement yesterday — she has now recovered movement in her toes and legs.

Within days of a car accident that left her numb and unable to move last summer, 18-year-old Melissa Holley was flown to Israel to become the first person to undergo the novel surgical treatment.

It is now generating hope for those with spinal-cord injuries around the world.

But Canadian scientists who are also developing therapies which harness the immune system to repair damaged spinal nerves — a feat once thought impossible — are expressing cautious optimism.

"The approach is exciting. The results are exciting. But there has to be caution," said John Steeves, a professor of neurosciences at the University of British Columbia and director of Collaboration on Repair Discoveries, a research group focusing on brain and spinal injuries.

"They [the Israeli researchers] have done three patients but the only one that has shown marked improvement is this girl."

Ms. Holley's treatment, which was developed by Proneuron Biotechnologies (Israel) Ltd., involved a concept that has gained momentum in spinal cord research.

If given a chance, researchers believe the body's own immune cells can repair damaged spinal nerves.

The nerve cells of the spine and brain are separated from the body's immune system by what's called the blood-brain barrier.

Researchers around the world are experimenting with transplanting the immune cells responsible for regenerating tissue in other parts of the body directly into injured spinal cords, in hopes they can heal the damaged nerve cells.

Professor Michal Schwartz of Israel's Weizmann Institute of Science is a leader in the field.

See SPINAL on page A7

HYOUNG CHANG/THE DENVER POST

Melissa Holley, 18, has movement in her toes and legs after novel surgical treatment in Israel.

Canadian MDs to test own version of therapy

SPINAL *from page A1*

Using animals with severed spinal cords, she pioneered a unique technique.

This involved harvesting immune cells called macrophages from the animals' own blood, activating them, and then injecting them in and around the damaged area of the spinal column.

It's still not clear whether Dr. Schwartz's therapy works because it changes how damaged nerve cells become inflamed or because it cleans up debris that can block regeneration around damaged cells, or whether it does both.

Nonetheless, Proneuron researchers took Dr. Schwartz's promising results with animals one step further, and turned them into a treatment for humans. In the early stages of testing the therapy, the company made the technique available to only those with acute spinal cord injuries less than seven days old.

Ms. Holley became the first patient to have the treatment last July when her grief-stricken father stumbled across the Proneuron Web site.

"She recovered very significant motor function in her legs, although she is not yet walking," Valentin Fulga, the founder of Proneuron, said yesterday.

It helps that Ms. Holley is young, highly motivated and receiving intense physical rehabilitation, said Jason Dyer, chief scientific officer of Neurotherapeutics Inc.

The company, based in Vancouver, is developing its own therapy using immune cells to repair injured spinal cords.

Dr. Dyer expects to test his company's version on patients within the next 18 months.

Having followed the research closely, Dr. Dyer is encouraged by the results from Israel.

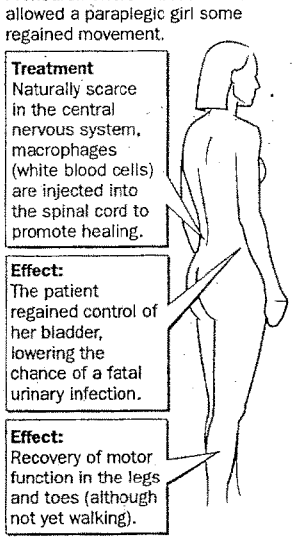
Nevertheless, he still has concerns.

"We need to worry about the patient numbers, what are the long term effects and whether she [Ms. Holley] will continue to get better or whether this is it," he said yesterday.

With a report from Reuters

Wiggle your toes...

Proneuron offers a treatment that allowed a paraplegic girl some regained movement.



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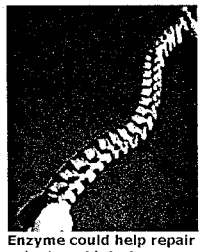
Spinal cord recovery hurdle cleared

Bacterial enzyme chews through nerve growth barrier.

11 April 2002

HELEN PEARSON



Enzyme could help repair spinal cord injuries.
© *GettyImages*

An enzyme that clears a path for growing nerves can help damaged spinal cord to repair itself, researchers have found. The enzyme could one day help to treat paralysing injuries, in conjunction with other therapies.

Damaged nerves in the spinal cord do not normally recover. The surrounding cells multiply to form a dense scar, and secrete a thicket of barrier molecules that nerves cannot cross.

Like a miniature lawnmower, the bacterial enzyme chondroitinase ABC trims back these obstructing molecules, Elizabeth Bradbury of King's College London and her team have shown[1]. Rats with damaged spinal cords injected with the enzyme partly recover from their injury.

Two months after treatment, severed nerves in the rats' spinal cord grew back towards the brain and limbs, Bradbury found. Most importantly, the disabled animals recovered a regular gait - although they did not regain normal touch and movement. "It shows the cells above the lesion are talking to those below," says Bradbury.

"It's a very interesting possibility," says neuroscientist Lars Olson of the Karolinska Institute in Stockholm, Sweden. The molecule-trimming enzyme may normally help bugs to chop up their food or invade other organisms, he suggests.

But many other obstacles must be overcome before complete spinal-cord repair can be achieved, Olson warns. Other groups are working on ways to mask or remove other inhibitory molecules that are released by dying nerves and their supporting cells.

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A physical bridge over an injury site might even be built to allow nerve fibres to cross, using grafts from other parts of the nervous system. Administering growth molecules could also give sprouting nerves a boost.

Olson hopes that early trials for these developing therapies might start within five years. Five in every 100,000 people in the United States - and similar numbers elsewhere - suffer spinal-cord injuries.

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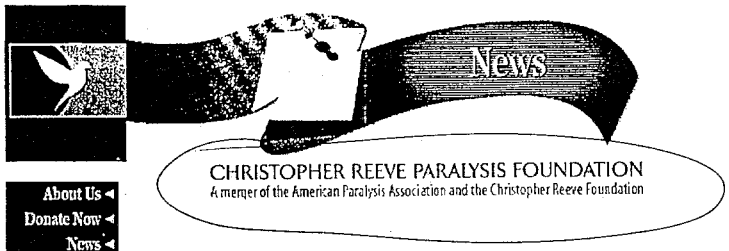

FOR IMMEDIATE RELEASE

August 14, 2000

Christopher Reeve Paralysis Foundation Funds Breakthrough Research
Researchers Convert Bone Marrow Stem Cells to Neurons; Discovery Holds Promise for Treating Spinal Cord Injury, Stroke and Other Brain Diseases

(SPRINGFIELD, NJ) - The Christopher Reeve Paralysis Foundation (CRPF) announced today that leading researchers in the field of spinal cord injury have developed the first successful procedure to convert cultured bone marrow stem cells exclusively into nerve cells. CRPF and the National Institutes of Health funded this research.

This critical advance now provides an abundant and accessible cellular reservoir to potentially treat a variety of neurological diseases, including spinal cord injury, stroke, brain trauma, and degenerative diseases such as Parkinson's, Alzheimer's and Lou Gehrig's diseases.

The results of the study, led by Dr. Ira Black, chair of the Department of Neurosciences at the University of Medicine and Dentistry of New Jersey (UMDNJ)-Robert Wood Johnson Medical School, and his colleague Dale Woodbury, are published in the August 15th issue of *The Journal of Neuroscience Research*. The work was performed in collaboration with Darwin Prockop and Emily Schwarz of MCP Hahneman University.

Dr. Black is a member of the CRPF Research Consortium on Spinal Cord Injury. The Consortium is a collaborative network of scientists who pool their wide-ranging expertise and work cooperatively to solve the multifaceted challenges of repairing the injured spinal cord. The Consortium is also

Marrow stromal cells form guiding strands in the injured spinal cord and promote recovery

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Contributed by Darwin J. Prockop, December 17, 2001

Marrow stromal cells (MSC) can be expanded rapidly *in vitro* and differentiated into multiple mesodermal cell types. In addition, differentiation into neuron-like cells expressing markers typical for mature neurons has been reported. To analyze whether such cells, exposed to differentiation media, could develop electrophysiological properties characteristic of neurons, we performed whole-cell recordings. Neuron-like MSC, however, lacked voltage-gated ion channels necessary for generation of action potentials. We then delivered MSC into the injured spinal cord to study the fate of transplanted MSC and possible effects on functional outcome in animals rendered paraplegic. MSC given 1 week after injury led to significantly larger numbers of surviving cells than immediate treatment and significant improvements of gait. Histology 5 weeks after spinal cord injury revealed that MSC were tightly associated with longitudinally arranged immature astrocytes and formed bundles bridging the epicenter of the injury. Robust bundles of neurofilament-positive fibers and some 5-hydroxytryptamine-positive fibers were found mainly at the interface between graft and scar tissue. MSC constitute an easily accessible, easily expandable source of cells that may prove useful in the establishment of spinal cord repair protocols.

Most, if not all, central nervous system neurons in mammals have the intrinsic capacity to regenerate a lost axon. The failure of axons to regenerate after spinal cord injury (SCI) has been attributed to growth-inhibitory molecules (1), lack of appropriate trophic support (2, 3), and reactions of the immune system (4). Glial cells produce growth-inhibiting molecules, such as Nogo (5, 6), MAG (7), tenascin (8), and chondroitin sulfate proteoglycans (9). Up-regulation of neurotrophic factors after SCI is limited (3). The role of the immune system in SCI is complex but may include nerve growth inhibitory as well as stimulatory events (4, 10). Davies *et al.* (11) demonstrated long-distance regeneration of adult dorsal root ganglion cells, transplanted into spinal cord pathways, if a micrografting technique was used to avoid local scarring. However, axon outgrowth was terminated or reversed upon contact with scar tissue. One approach to overcome some of the growth-inhibiting properties of the injured spinal cord is to transplant cells with protective and/or reparative properties to the site of injury. Recently, mouse embryonic stem cells, delivered into the injured spinal cord, were shown to differentiate into neurons, astrocytes, and oligodendrocytes and to improve motor function (12). However, recovery was limited. Also, the use of embryonic stem cells may not be generally accepted and heterologous transplantation may elicit graft rejection. Marrow stromal cells (MSC) constitute an alternative source of pluripotent stem cells. Under physiological conditions, they are believed to maintain the architecture of bone marrow and regulate hematopoiesis with the help of different cell-adhesion molecules and the secretion of cytokines, respectively (13). MSC grown out of bone marrow cell suspensions by their selective attachment to tissue culture plastic can be expanded efficiently (14, 15) and manipulated genetically (16). MSC are referred to as mesenchymal stem cells because they are capable of differentiating into multiple mesodermal tissues, including bone (17), cartilage (18), fat (17), and muscle (19). In addition, differentiation into neuron-like cells expressing neuronal markers has been reported (20–22), suggesting that MSC may be capable of overcoming germ layer commitment. Importantly, MSC can migrate along known migration pathways when injected into corpus striatum of rats (14). MSC migrated throughout forebrain and cerebellum, integrated into central nervous system cytoarchitecture, and expressed markers typical of mature astrocytes and neurons after injection into the lateral ventricle of neonatal mice (23).

We examined whether MSC expressing neuronal markers *in vitro* exhibited physiological properties characteristic of neurons. We then delivered MSC into the injured spinal cord to monitor survival, spread and differentiation of such cells, and their possible effects on the motor behavior of rats rendered paraplegic by SCI.

Methods

Primary Marrow Stromal Cell Cultures. MSC were collected from femurs and tibias of adult male Lewis rats (Harlan Breeders, Indianapolis) (16). Rats were euthanized with a mixture of 70% CO_2 and 30% O_2. Tibias and femurs were placed on ice in MEM with alpha modification (α-MEM; GIBCO/BRL) containing 20% FCS (Atlanta Biologicals, Norcross, GA), 2 mM L-glutamine (GIBCO/BRL), 100 units/ml penicillin, 100 μg/ml streptomycin, and 25 ng/ml amphotericin B (penicillin, streptomycin, and amphotericin; GIBCO/BRL). Epiphyses of femurs and tibias were removed, and the marrow was flushed out by using a syringe filled with medium. Bone marrow was filtered through a 70-μm nylon mesh and plated in 75-cm^2 flasks. About 24 h after plating, supernatant containing nonadherent cells was removed and fresh medium was added. After the cells had grown to near confluency, they were passaged two to five times by being detached (0.25% trypsin/1 mM EDTA for 5 min) and replated at a density of ~5,000 cells/cm^2.

Preparation of the Retroviral Vector, Production of Viral Particles, and Genetic Marking of MSC. A retroviral construct encoding green fluorescent protein (GFP) as an expression marker and aminoglycoside phosphotransferase as a neomycin (G418) selectable marker was prepared by using the LXSN vector (CLONTECH) (24). Phoenix amphotropic packaging cells (25) (ATCC) were transfected with the LXSN-GFP plasmid by using calcium phosphate precipitation. Viral supernatants were collected 48 h after the start of the transfection, filtered through a 0.45-μm filter, and stored at −80°C for further use. Phoenix packaging cells were analyzed at the time of viral harvest for GFP expression. One day before the infection of MSC with GFP-retrovirus, about 100,000 MSC were plated in 21.0-cm^2 plates. At the time

MEDICAL SCIENCES

Abbreviations: MSC, marrow stromal cells; 5-HT, 5-hydroxytryptamine; SCI, spinal cord injury; NF, neurofilament; GFP, green fluorescent protein; IR, immunoreactivity; GFAP, glial fibrillary acidic protein.

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Functional Recovery of Paraplegic Rats and Motor Axon Regeneration in Their Spinal Cords by Olfactory Ensheathing Glia

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Summary

Axonal regeneration in the lesioned mammalian central nervous system is abortive, and this causes permanent disabilities in individuals with spinal cord injuries. In adult rats, olfactory ensheathing glia (OEG) transplants successfully led to functional and structural recovery after complete spinal cord transection. From 3 to 7 months post surgery, all OEG-transplanted animals recovered locomotor functions and sensorimotor reflexes. They presented voluntary hindlimb movements, they supported their body weight, and their hindlimbs responded to light skin contact and proprioceptive stimuli. In addition, relevant motor axons (corticospinal, raphespinal, and coeruleospinal) regenerated for long distances within caudal cord stumps. Therefore, OEG transplantation provides a useful repair strategy in adult mammals with traumatic spinal cord injuries. Our results with these cells could lead to new therapies for the treatment of spinal cord lesions in humans.

Introduction

Complete transection of the adult mammalian spinal cord leads to irreversible and permanent loss of motor and somatosensory functions below the injury site. The lack of spontaneous anatomical and functional repair after spinal cord injury is due to the failure of neurons to regenerate their axons through the inhospitable extraneuronal environment of the mature CNS. These inhibitory environmental factors are associated with glial cell surfaces and the extracellular matrix and surround regenerating axons, preventing them from growing (Ramón y Cajal, 1928; Liuzzi and Lasek, 1987; Bovolenta et al., 1992; Schwab et al., 1993; McKerracher et al., 1994; Silver, 1994; Fitch and Silver, 1997; Pasterkamp et al., 1998; Zuo et al., 1998a; Miranda et al., 1999). The failure of injured axons to grow does not occur, however, in the adult mammalian olfactory bulb. This is a CNS structure where normal and sectioned olfactory axons are able to elongate and establish synaptic contacts with target neurons throughout adulthood (Graziadei and Monti Graziadei, 1980; Doucette et al., 1983). A remarkable difference between the olfactory bulb and "nonregenerating" CNS regions resides in the presence of olfactory ensheathing glia (OEG) in the former (Doucette, 1991). This unique glial cell type exhibits axonal growth-promoting properties (reviewed by Ramón-Cueto and Valverde, 1995; Ramón-Cueto and Avila, 1998) and enfolds growing olfactory axons, preventing their exposure to inhibitory molecules (Pasterkamp et al., 1998).

Over the past decades, several attempts have been made to find a repair strategy that circumvents and blocks the hostile CNS milieu, providing injured spinal cord axons with a supportive environment for their elongation (reviewed by Olson, 1997; Bregman, 1998; Fawcett, 1998). Some of these therapeutic approaches include the use of peripheral nerve bridges (Ramón y Cajal, 1928; David and Aguayo, 1981; Cheng et al., 1996), embryonic spinal cord tissue (Bregman et al., 1998), Schwann cell grafts (Xu et al., 1995; Guest et al., 1997; Menei et al., 1998), neurotrophic factor administration (Schnell et al., 1994; Xu et al., 1995; Grill et al., 1997; Menei et al., 1998), macrophage implantation (Rapalino et al., 1998), and blockade of myelin inhibition (Schwab et al., 1993; Bregman et al., 1995; Dyer et al., 1998; Thallmair et al., 1998), among others. Of these strategies, only some have been focused on the repair of completely transected spinal cords of adult mammals (Xu et al., 1995; Cheng et al., 1996; Guest et al., 1997; Menei et al., 1998; Ramón-Cueto et al., 1998; Rapalino et al., 1998), and two obtained partial recovery of paraplegic rats (Cheng et al., 1996; Rapalino et al., 1998).

The extraordinary growth-promoting properties of OEG have been used to repair selectively injured fibers of the adult rat spinal cord (Ramón-Cueto and Nieto-Sampedro, 1994; Li et al., 1997; Navarro et al., 1999), and to enhance the regenerative effect of Schwann cell–filled guidance channels after complete spinal cord transection (Ramón-Cueto et al., 1998). However, the functional and anatomical repair abilities that OEG have by themselves in completely transected spinal cords have not yet been tested. Here, we report that OEG transplants, with no other additional treatments, promote functional recovery of paraplegic adult rats and long-distance motor axon regeneration in their completely transected spinal cords. This constitutes a dramatic functional improvement and anatomical repair after complete transection of the adult mammalian spinal cord.

Results

Spinal cord transection in all animals (OEG-transplanted and nontransplanted) resulted in a flaccid paralysis of both hindlimbs immediately after injury. Two weeks after transection, all OEG-transplanted (n = 9) and all nontransplanted rats (n = 12) dragged their hindlimbs, while the forelimbs propelled the animals. Two months post injury, none of the rats (OEG-transplanted and nontransplanted) supported their body weight. However, two of

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Manipulating A Single Gene Dramatically Improves Regeneration in Adult Neurons: Finding May Lead to New Approaches for Treating Brain and Spinal Cord Damage

For release: Sunday, July 01, 2001

Increasing the expression of a single gene that is important during development dramatically improves the ability of adult neurons to regenerate, a new study shows. The finding suggests that intrinsic properties of neurons play an important role in controlling neuronal regeneration and may lead to new approaches for treating damage from stroke, spinal cord injury, and other neurological conditions.

The study examined how genetically engineering adult neurons to produce larger amounts of a type of protein called integrin affects nerve fiber growth. This approach is one of the first to examine "the critical missing half of the regeneration equation: the properties of adult neurons, rather than the environment of the adult brain," says study investigator Maureen L. Condic, Ph.D., of the University of Utah School of Medicine in Salt Lake City. The work was supported by the National Institute of Neurological Disorders and Stroke (NINDS) and will appear in the July 1, 2001, issue of the *Journal of Neuroscience*.[1]

Most neural regeneration studies in the past have manipulated factors in the environment of the adult nervous system to try to influence neuron growth. Studies have shown that nerve fibers can regenerate in the brain and spinal cord of newborn animals, but regeneration does not normally occur in the brain or spinal cord of older animals. Recent studies have linked neuronal regeneration to integrin proteins, which function as receptors that enable neurons to interact with specialized molecules in the surrounding environment during development. Neurons taken from developing animals typically have very high levels of integrin, but neurons from adult animals have very little of this protein.

In this study, Dr. Condic used a modified adenovirus to insert extra copies of a gene for one kind of integrin protein into sensory neurons taken from adult rats. A second group of neurons received extra copies of a different integrin gene. The additional genes produced levels of integrin in the adult neurons that were comparable to those in newborn animals. The neurons were cultured in conditions similar to those of the adult central nervous system. Dr. Condic then measured the amount of nerve fiber growth displayed by the adult neurons with extra integrin genes and compared it to the growth of neurons from newborn rats and of adult neurons that had received a non-integrin gene. She found that increasing the amount of either of the integrin proteins dramatically increased the amount of nerve fiber growth in the adult neurons. The increase in growth was more than ten times greater than that in any other published study of regeneration by adult neurons. The adult neurons with the extra integrin genes were able to extend nerve fibers profusely even when growth-inhibiting proteins were present in the culture. The amount of growth was indistinguishable from that of neurons from newborn animals.

The magnitude of the integrin proteins' effects on the adult neurons was very surprising, Dr. Condic says. In the past, many scientists believed that the inherent limitations on growth of nerve fibers from adult neurons were too complex to be significantly affected by altering a few genes. In this study, however, the effect of increasing just one gene was striking. "It's as though you have a '57 Chevy on blocks in the front yard, and it has all the necessary components except for its wheels," says Dr. Condic. "If you give the wheels back, which are the car's usual way of interacting with the environment, it's ready to go." Integrin proteins are like the tires of the car - they connect with the surrounding surface to enable neurons to extend nerve fibers, she explains.

The finding complements studies of factors in the nervous system environment that improve regeneration. Effective therapies will probably employ a multi-pronged approach that alters environmental factors as well as the inherent properties of the neurons, Dr. Condic says. However, it should be much easier to regulate gene expression in specific neurons than to change the environment of the brain. "The nervous system is a very big place, and right now we don't have the technology to modulate the total environment of the brain," Dr. Condic explains. Because the nervous system is so complex, there is also a risk that changes to the environment of the brain could inadvertently harm neurons outside of the damaged area and result in problems such as epilepsy or increased sensitivity to pain.

It may eventually be possible to modify integrin genes with a type of "switch" that is controlled by drugs or other chemicals and inject those genes into a damaged area of the brain, says Dr. Condic. Doctors could then add and subtract the chemical to turn the genes on and off, allowing them to precisely control the amount of nerve fiber growth in that region of the brain. However, an approach of this type is still theoretical, and more research is needed before scientists can predict whether such a technique might work in humans.

Journal of Neuroscience Research 66:1187–1197 (2001)

Spinal Cord Reconstruction Using NeuroGel™ Implants and Functional Recovery After Chronic Injury

Stéphane Woerly,[1*] Van Diep Doan,[1] F. Evans-Martin,[3] Christopher G. Paramore,[2] and Jean D. Peduzzi[3]
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There is currently a lack of effective ways to achieve functional tissue repair of the chronically injured spinal cord. We investigated the potential of NeuroGel™, a biocompatible polymer hydrogel, to induce a reconstruction of the rat spinal cord after chronic compression-produced injury. NeuroGel™ was inserted 3 months after a severe injury into the post-traumatic lesion cavity. Rats were placed in an enriched environment and the functional deficits were measured using the BBB rating scale. A significant improvement in the mean BBB scores was observed. Rats without enriched environment and severely injured rats with an enriched environment alone showed no improvement; however, 7 months after reconstructive surgery using NeuroGel™, a reparative neural tissue had formed within the polymer gel that included myelinated axons and dendro-dendritic contacts. NeuroGel™ implantation into a chronic spinal cord injury therefore resulted in tissue reconstruction and functional improvement, suggesting that such an approach may have therapeutic value in the repair of focal lesions in humans. J. Neurosci. Res. 66:1187–1197, 2001.
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Key words: spinal cord; contusion injury; NeuroGel™; hydrogel; recovery; regeneration; myelin

The devastating effects of spinal cord injury are paradoxical, because despite evidence that the central nervous system (CNS) is capable of regeneration, minimal repair is actually observed. The capacity for post-injury, long-distance axonal elongation (David and Aguayo, 1981), spontaneous remyelination of axons (Salgado-Ceballos, 1998), and the sprouting and long-term persistence of axonal sprouts (Li and Raisman, 1995; Wang et al., 1996) are well documented. In addition, spontaneous cellular reorganization at the lesion site (Guth et al., 1985; Brook et al., 1998) and synaptic reorganization of intact projections (Nacimiento et al., 1997) indeed occur after injury. Furthermore, neurotrophic growth factors (Logan et al., 1994; Frisen, 1997; Goss et al., 1998) and their receptors are produced, and regeneration-promoting genes are expressed (Schwaiger, 1998). This paradox is accentuated by the finding that a larger repair attempt occurs with more severe injuries (Beattie et al., 1997). The question therefore remains: is it possible to reconstitute the cellular components of the chronically injured spinal cord and promote axonogenesis and recovery?

In adult inframammalian vertebrates, the success of axonal regeneration in crossing the lesioned spinal cord is attributed to the concomitant wound repair effort that results in the reconstitution of the lesion with vascular, ependymal and glial processes (Lamer et al., 1995) that in turn depend on the presence of an acellular framework that directs the entire cell repair process. This naturally occurring tissue engineering process is the basis for a novel approach for the repair of spinal cord lesions that uses polymer matrices as support, migration channels, and adhesive surfaces for cells.

At Organogel, we have focused on hydrogel-based therapies with NeuroGel™, a polymer hydrogel (i.e., a water-saturated cross-linked hydrophilic copolymer, see inset of Fig. 3C) of [*N*-2-(hydroxypropyl) methacrylamide] (HPMA) to optimize wound repair and functional tissue restoration (for a review see Woerly, 2000). The significant number of pores within NeuroGel™ and their interconnection aid in the migration of cells into the hydrogel, although its topological organization enables cells to grow, develop, and reorganize to form a three-dimensional tissue configuration. In addition, the viscoelastic properties of NeuroGel™, are similar to those of nervous tissue and thus facilitate its integration at the host site after implantation. Through the hydrogel network, its diffusion properties, which have been shown to be similar to those of the developing spinal cord, facilitate the move-

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ELSEVIER

Tissue-Engineered Spinal Cord

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LIMITED SUCCESS has been reported in restoring function to spinal cord-injured rodents. Lower limb paralysis caused by complete spinal cord transection in neonatal rats less than 14 days of age may resolve, presumably because of the plasticity of the still-developing central nervous system (CNS).[1,2] Less success has been achieved in functional repair of the injured adult spinal cord. Implants of immobilized nerve growth factor (NGF)[3] appear to enhance the regrowth of ascending sensory axons across spinal cord gaps in adult rats. Limited but progressive improvement (over a 6-month period) of hind limb function in spinal cord-transected adult rats has been observed over a 6-month period after bridging the transected cord with multiple intercostal nerve grafts.[4]

In addition, much has been learned recently about the biology of stem cells. Stem cells isolated from the brain and the spinal cord of both neonatal and adult mice reportedly retain the potential to differentiate into neurons, astrocytes, and oligodendrocytes.[5,6] Undifferentiated stem cells have been reported to propagate in culture by adding epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF) to the growth medium.[5] Recent reports suggest that transplantation of immortalized neuronal stem cells into the spinal cord and cerebral cortex led to differentiation of such cells into site-specific neuronal and glial cells and also some functional recovery of the associated defects seen in spinal cord injury,[7] Sly disease,[8] and the myelin degenerative disorder found in the shiverer (shi) mouse.[9] Thus, neuronal stem cells propagated in vitro appear to retain the developmental plasticity necessary to respond to local environmental cues. We postulated that resected segments of the spinal cord could be regenerated in adult rats by implanting spinal cord progenitor cells associated with an appropriate scaffolding or matrix.

MATERIALS AND METHODS

Tissue Harvest and Cell Culture

Cells were harvested from the spinal cords of adult female Fisher rats using a modification of the methods reported by Weiss et al[5] and Shihabuddin.[6] Under sterile conditions, the spinal cord was removed intact from the spinal column, and the gray matter was dissected away from surrounding white matter and placed in cold phosphate-buffered saline (PBS) with 50 mU/mL penicillin and 90 mg/mL streptomycin (Gibco, Grand Island, NY, USA). The tissue was then collected by centrifugation at 1200 rpm for 5 minutes and resuspended in 10 mL of 0.05% trypsin (wt/vol) for an additional 5 minutes at 37°C. Trypsinization was stopped by adding 10 mL of Dulbecco's Minimal Essential Medium (DMEM)/F-12 (Gibco), containing 10% heat-inactivated fetal bovine serum (FBS) (Gibco). The cells were then dispersed by trituration using progressively narrow fire-polished, reduced-bore pasteur pipettes. Dispersed cells were collected by centrifugation at 1200 rpm for 5 minutes, the supernatant removed, and the resulting pellet resuspended in 15 mL of DMEM/F-12 medium containing 33 mmol glucose (Sigma, St Louis, Mo, USA), .09 mg/mL transferrin (Sigma), .02 mg/mL insulin (Sigma), .055 mmol putrecine (Sigma), 27 nmol selenium (Sigma), 10 nmol progesterone (Sigma), 20 ng/mL EGF (Peprotech, Rocky Hill, NJ, USA), and 20 ng/mL bFGF (Collaborative Biomedical, Raynham, Mass, USA).[10] The primary cell suspension was then incubated at 37°C in 5% CO_2, with media changes every 3 days. Cells were passaged every 7 to 9 days by collecting the nonadherent cell aggegates at 1200 rpm for 5 minutes and aspirating the spent growth medium. Cell suspensions were prepared by trituration, and the cells were split 1:2.

Cultured cells were infected with neural cell-specific p29-Green Fluorescent Protein chimera[11] (GFP^{p29}) 2 days prior to implantation. Replication-deficient Ad5-p29 constructs were created by fusing green fluorescent protein (GFP) to the carboxyl terminus of p29. Adenoviral vectors have proved useful for long-term expression of delivered gene products in the CNS of rodents and primates.[12,13] In brief, the 825-bp Fsp I-Hinf 1 fragment from p29 cDNA was blunted with Klenow and ligated into the blunted Hind III site of the pEGFP N-one expression vector (Clonetech, Palo Alto, Calif, USA). In-frame insertion was confirmed by DNA sequencing. The Bam HI-Not I fragment containing the GFP^{p29} chimera was ligated into the Bam HI-Not I sites of the AdpREC shuttle vector. The Pvu I-linearized AdpREC shuttle construct was cotransfected with Cla I linearized Ad5-bgal into HEK293 cells using lipofectin according to manufacturer's instructions. Expression of the GFP^{p29} chimera was confirmed by visual inspection and fluorescence microscopy (Fig 1) and by Western blot analysis using

From the Center for Tissue Engineering, Departments of Anesthesiology (M.P.V., B.D., L.J.B., Y.C., F.O., C.S.Y., C.A.V.), Departments of Pathology (M.P.V.), Physiology (J.L.L., S.J.S.), and the Molecular Endocrinology Laboratory (J.L.L., S.J.S., A.P.F.), University of Massachusetts Medical School, Worcester, Massachusetts, USA, and Department of Surgery (J.P.V.), Massachusetts General Hospital, Boston, Massachusetts, USA.

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SOURCE: Theratechnologies Inc.; Celmed Biosciences Inc.

Adult Stem Cells Used to Repair Damage from Parkinson's Disease

Researchers studying technique for possible treatment of other nervous system conditions

MONTREAL, Quebec, April 8 /CNW/ - Scientists from Celmed BioSciences, a subsidiary of Theratechnologies, reported today at the annual meeting of the American Association of Neurological Surgeons (AANS) in Chicago that adult neural stem cells taken from a patient's own central nervous system have been successfully used to treat Parkinson's disease. Their research suggests this method of using adult stem cells may possibly be useful in treating a variety of other neurological conditions.

The research was conducted by Celmed's researchers, Dr. Michel F. Lévesque, Vice President, Medical Affairs, also neurosurgeon at the prestigious Cedars-Sinai Medical Center, in Los Angeles, California, and Dr. Toomas Neuman, Program Director, Neurodifferentiation, at Celmed BioSciences USA.

Dr. Lévesque and Dr. Neuman isolated adult neural stem cells from a patient, induced them to differentiate into the desired nervous system cells, and implanted them back into the patient's brain. One year after the procedure, the patient's symptoms were reduced by more than 80%. Dr. Lévesque has been authorized by the FDA to conduct a Phase II clinical trial for Parkinson's disease, using cell therapy derived from autologous neural stem cells, once certain animal studies are completed and approved. This will be the first study of its kind in the world evaluating the benefits of autologous cell therapy for this disease.

The research demonstrates that adult stem cells can be coaxed to become the crucial cells that produce dopamine and that those cells can function after implant. Dopamine is an essential brain chemical, which is deficient in people who suffer from Parkinson's disease.

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Using patient's own blood-producing stem cells from bone marrow

Posted at 06:56 a.m. PST; Wednesday, February 24, 1999

MS patient progressing well after stem-cell transplant

Background and Related Info.

by Warren King
Seattle Times medical reporter

Susan Stross, left, who underwent a stem-cell transplant for her MS, exercises her arm with the help of physical therapist Stacia Lee.

Greg Gilbert
©The Seattle Times

The long, slender fingers still bend partially downward, but Susan Stross has made friends with her right hand again.

Carefully, slowly, Stross writes a check, pen held tightly, precisely guiding, letter by letter. Picking up change - even stubborn, skinny dimes - is not such a chore anymore. Food "does not go flying" now.

Now Stross, 34, has some hope again. Now there is promise that after 15 years of a downward spiral with multiple sclerosis (MS), a stem-cell transplant will at least keep her stable.

Seven months since her transplant at the Fred Hutchinson Cancer Research Center, Stross smiles brightly over her progress.

"Before, it seemed like I would take two steps forward and three steps back. Now, it's two steps forward and another two steps forward and another two steps forward," says Stross in the living room of her Capitol Hill apartment.

A former language teacher and competitive swimmer, Stross was among the first 30 MS patients in the world to receive a stem-cell transplant - a sort of bone-marrow transplant of her own cells.

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Using genetically repaired bone marrow stem cells

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'Bubble Boy' Cured in British Gene Therapy First

Last Updated: April 03, 2002 07:51 AM ET

Print This Article

LONDON (Reuters) - British doctors have successfully used gene therapy for the first time to cure a Welsh toddler born without an immune system, the Great Ormond Street Hospital for Children said on Wednesday.

The London hospital said 18-month-old Rhys Evans had been cured of the fatal genetic condition X-linked Severe Combined Immunodeficiency Disease (X-SCID), commonly known as "baby in the bubble" syndrome.

"This is the first time gene therapy has cured a child in Britain," the hospital said in a statement.

The disease meant Rhys was born without an immune system and was highly susceptible to potentially fatal infections.

He was forced to live in a totally sterile environment, isolated from other children, and spent much of his life in hospital.

Doctors removed some of Rhys' bone marrow and genetically modified it to add a correct copy of the faulty gene which caused X-SCID. The marrow was then re-injected into his system.

Dr. Adrian Thrasher, who led the team which carried out the procedure, said the success of Rhys' treatment was very exciting.

"Gene therapy is about turning understanding into real cures for real children," he said.

Rhys' mother Marie said the treatment had made a huge difference for her son.

"We see him now playing with other children and it is just amazing," she told the BBC.

The Evans case, which followed the opening of a gene therapy laboratory at the hospital last September, is one of the few clinically successful examples of gene therapy in the world.

French researchers claimed the first success for gene therapy in 2000 when they treated two infant boys with X-SCID.

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World first as man has stem cells injected into heart

SYDNEY: Newcastle man Jim Nichol, aged 74 and a veteran of three bypass operations, is at the centre of a world-first trial using adult stem cells to repair his damaged heart.

Researchers from Newcastle's John Hunter Hospital revealed yesterday that on Monday they took bone marrow from Mr Nichol's hip, extracted stem cells from the marrow and injected the cells into the muscle of his heart.

If the experiment works the way they expect, the injected stem cells will begin secreting growth factors which will stimulate the growth of blood vessels in Mr Nichol's heart, easing his constant chest pain and reducing his need for medication.

It was the first clinical trial of a procedure that doctors hope could help almost a third of all patients with end-stage coronary artery disease.

Cardiologist Suku Thambar, of the Hunter Medical Research Institute heart and lung research program, said the procedure targeted what were known as "no-option patients".

"This is trial which is seeking to examine the efficacy of the patient's own adult bone marrow-derived stem cells to increase the blood vessel growth in the heart," he said.

"It involves a group of patients . . . who have got vessels which are not amenable to the conventional methods of improving blood supply such as angioplasty or coronary artery bypass surgery."

Safety and feasibility studies were completed overseas.

Dr Thambar said Mr Nichol had been discharged from hospital in a stable condition.

However, it would be some months before it became clear whether the procedure was working.

The trial comes after news that a man in the United States had apparently recovered from Parkinsons

American Diabetes Association.

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Adult Islet cell transplants for diabetes

61st Scientific Sessions June 22-26, 2001 • Philadelphia, Pennsylvania

Abstract #: 33-LB
Abstract Type: Late Breaker Poster Session (6:00 PM - 7:30 PM)
Abstract Category: Transplantation
Abstract Schedule: 7:30 PM-6:00 PM , 6/24/01

Glycemic Outcome Post Islet Transplantation

EDMOND A RYAN, JONATHAN RT LAKEY, RAY V RAJOTTE, GREGORY S KORBUTT, BRAEY W PATY, NORMAN M KNETEMAN, DAVID BIGAM, AM JAMES SHAPIRO

Islet transplantation is now feasible, but longer term results are still scarce. We have transplanted 15 patients and now present an update (as of 1st April, 2001) on their glycemic control using a steroid-free immunosuppression regimen. Patients were transplanted with freshly prepared islets as previously described.[br]Five women and ten men, age 39.9 [plusminus] 8.2 yrs (mean [plusminus]SD), with a duration of diabetes of 28.8 [plusminus] 10.5 years were transplanted in a consecutive series. All required more than 9000 islet equivalents/kg to become insulin independent which necessitated two procedures in eleven patients and three procedures in four subjects. Acute complications of the procedure included bleeding (n=2), minor portal vein thrombosis (n=1), and a puncture of the gall bladder (n=1). All of these settled with conservative therapy. All patients became insulin free and all are continuing to have measurable C-peptide. Four patients have had a deterioration of glycemic control and are now taking insulin after being off insulin for a median 3 (range 1.5 - 15) months. All four patients have stable glucose values without the major problems of hypoglycemia or lability that was present pre-transplant and are requiring approximately one-half their pre-transplant daily doses. One other patient is using insulin intermittently and is on oral hypoglycemic agents. Nine patients have a normal HbA1c and are off insulin for a median of 8 months (range 1 - 24). HbA1c pre- and post-transplant for all patients was 8.6 [plusminus] 1.3% versus 6.2 [plusminus] 0.7%. Only two patients have a HbA1c over 7% (7.1 and 7.4) and the most recent HbA1c for the 11 patients not requiring insulin is 5.9 [plusminus] 0.5%.[br]Complications of the immunosuppressive therapy encountered include hypercholesterolemia (9 of 15), two subjects had a rise of serum creatinine and three more a rise of urine protein excretion. Five had a problem with acne.[br]Islet transplantation using the steroid-free immunosuppression is continuing to give long-term function, and in the majority of patients glucose control is excellent.

(Now in further U.S. clinical trials, with excellent results.)

Important Note:

There is a strict embargo on the science being presented at the American Diabetes Association's Annual Scientific Sessions. This applies to all information included in the abstracts (abstracts found in hard copy via the Abstract Book and online via the Association's Web site, www.diabetes.org) and other presentations. An embargo means that information from any abstract or presentation may not be announced, publicized or distributed before the embargo date and time. Specific embargo information is as follows:

- General Posters and Publish Only papers are embargoed until 10:00 a.m. EDT, Saturday, June 23
- President's Posters are embargoed until 6:00 p.m. EDT, Sunday, June 24
- All other papers are embargoed until immediately following their presentation

Harvard University Gazette
SCIENCE / RESEARCH

Current Issue:
July 19, 2001

Diabetes

Dr. Denise Faustman prepares reagents for treating diabetic mice, a novel therapy that has led to the reversal of disease and regeneration of the missing insulin secreting cells. (Staff photo by Kris Snibbe)

Adult stem cells effect a cure

Diabetes cure may reduce need for embryo cells

By William J. Cromie
Gazette Staff

The permanent reversal of Type 1 diabetes in mice may end the wrenching debate over harvesting stem cells from the unborn to treat adult diseases. Researchers at Harvard Medical School killed cells responsible for the diabetes, then the animals' adult stem cells took over and regenerated missing cells needed to produce insulin and eliminate the disease.

"It should be possible to use the same method to reverse Type 1 diabetes in humans," says Denise Faustman, the associate professor of medicine who leads the research. Setting up a trial for patients has already begun at Massachusetts General Hospital in Boston.

Type 1 diabetes is an "autoimmune" disease in which the body's blood cells attack its own organs and tissues. Such maladies include rheumatoid arthritis, multiple sclerosis, lupus, and more than 50 other ailments. Faustman believes that many of them may be similarly cured by poisoning the offending cells and letting adult stem cells regrow replacement organs.

"Once the disease is out of the way, adult stem cells regenerate normal

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Researchers claim stem-cell breakthrough

Last updated: 16-08-01, 10:12

Australian scientists said today they may have found a way to successfully treat brain, nerve and spinal injuries by harvesting adult neural stem cells.

Conditions such as Parkinson's and Alzheimer's could also be reversed after researchers at the prestigious Walter and Eliza Hall Institute of Medical Research in Melbourne claimed an international breakthrough.

> **"We can now look at ways of being able to stimulate it [the stem cell] into making new nerve cells with the possibility of replacing damaged or lost nerve cells in the adult brain"**
>
> Mr Perry Bartlett

They isolated large volumes of neural stem cells capable of regenerating into new tissue, nerves and muscle, according to research published in the international journal *Nature Today*.

The discovery could also end the ethical controversy surrounding stem-cell research on cloned human embryos, which are destroyed when the cells are extracted.

Research team head Mr Perry Bartlett said the work had proved the versatility of adult stem cells beyond a doubt.

"It's really taken us this last nine or 10 years to be able to find what the cell looks like, and having found it, we can now look at ways of being able to stimulate it into making new nerve cells with the possibility of replacing damaged or lost nerve cells in the adult brain," he said.

"It's important in the sense that there's been a debate about whether stem cells from adult tissues, whether that be brain or blood or elsewhere, do have the potential of embryonic stem cells to give rise to various tissues".

The Australian researchers said they were the first in the world to extract mouse neural stem cells pure enough for scientists to be able to experiment with their versatility.

Race an issue in Australian territory election

If adult stem cells could be used to restore nerve function lost through diseases such as Parkinson's or Alzheimer's, it would also get around the likely problem of cloned embryonic stem cells being rejected by the body's immune system, Mr Bartlett said.

AFP

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From The Irish Times

Walter and Eliza Hall Institute of Medical Research

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Note: Animal studies show that even embryonic stem cells from cloned embryos can be rejected. Stem cells from the patient's own body are not.

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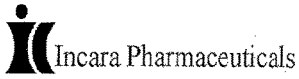

For Immediate Release:

Human Hepatic Stem Cells Disclosed at Keystone Symposium

Incara holds license to discovery with promise of treating liver disease

Research Triangle Park, N.C., March 22, 2002 – Human hepatic (liver) stem cells – unique cells capable of multiplying and giving rise to mature liver cells – have been described in a poster presented at the Keystone Symposium on Stem Cells: Origins, Fates and Functions in Keystone, Colorado. The authors of the poster are Dr. Nicholas G. Moss, Eliane Wauthier and Dr. Lola M. Reid of the University of North Carolina at Chapel Hill School of Medicine. Incara Pharmaceuticals Corporation (Nasdaq:INCR) is supporting the research and has a license to its results. Incara is applying discoveries in the field of liver biology to the development of cell therapies for liver diseases.

The poster describes the identification, expansion and antigenic characterization of human hepatoblasts, hepatic stem cells that are highly proliferative cells that are the immediate progenitors for hepatocytes and bile duct cells, the major cellular components of the liver. The research also identified more primitive stem cells that are precursors to hepatoblasts and represent an even earlier stage in liver development. In addition, the authors provide details of expansion conditions for the two types of liver stem cells, enabling large numbers of them to be generated in culture.

"This research extends our earlier discoveries in rats and the discoveries of others in mice and establishes the existence of the liver stem cell in humans," said Dr. Reid, Professor, Department of Cell and Molecular Physiology, and of the Program in Molecular Biology and Biotechnology, at the University of North Carolina at Chapel Hill. "In addition, this is the first report in any species of a more primitive stem cell in the development of the liver."

"We congratulate Drs. Moss and Reid on this advancement in the field of human liver biology," said Clayton I. Duncan, Chief Executive Officer of Incara. "We believe our program for transplantation of liver cells might provide a life-saving treatment for patients with liver failure. Currently, many patients have limited alternatives."

Incara is investigating the transplantation of human liver cells as a treatment for liver failure. The company is currently preparing an IND to be filed with the FDA to begin initial Phase 1 clinical trials for treatment of adults with end-stage liver diseases. Later clinical trials are expected to include children with life-threatening genetic diseases.

The Straits Times (Singapore)
July 16, 2002 Tuesday

China 'has cloned 30 human embryos';

Its 200-cell embryos, the largest grown anywhere, can be harvested for stem cells that are key to medical research

BEIJING - China has cloned more than 30 human embryos, a feat that has made it the first country in the world to have an abundant supply of embryonic stem cells (ESCs), according to reports.

China's cloning techniques will soon be revealed in a major scientific journal, reported Britain's Sunday Times.

Scientists elsewhere have also cloned human embryos but none have survived as long as the Chinese ones. For example, the Massachusettes-based Advanced Cell Technology recently made a similar attempt but failed because its embryos were only able to divide into a few cells.

But in China, it was said that embryos were grown to a 200-cell stage, large enough to harvest ESCs, which many believe are of great medical use.

At least five laboratories in China are known to be engaged in the research and all have made great strides, reported the New Scientist website.

One researcher said to have harvested ESCs was identified as Professor Lu Guangxiu of the Xiangya School of Medicine in southern China's Hunan province. She said the purpose of her work was only to develop a way of growing spare body parts from ESCs for use in extending human life. The re-creation of a human was furthest from her mind, she said.

Life-saving cloning, or therapeutic cloning, aims to minimize the rejection of a transplant by cloning cells from the patient's own body, reported The Guardian.

Dr Lu is believed to have used a refined version of the technique used by British scientists to produce Dolly the sheep five years ago.

The scientist, who runs a fertility clinic, has easy access to human eggs, into which donor cells are injected to grow embryos. She could ask her patients to donate theirs for her research. She admitted that her research team was 'partly funded by the revenue from her own clinic and partly by the state'.

China has been investing heavily in the area of biotechnology recently and there are no laws to control embryo research, unlike in Western countries such as the United States, which is promoting a worldwide ban of all human cloning.

Like Prof Lu, all the Chinese researchers have asserted that their intention is only to create genetically matched cells to make tissues for transplant patients, as well as for research purposes.

Professor Yang Xiangzhong, a biotechnologist at Connecticut University, knows of some details of Prof Lu's work and predicts that she will produce human transplant tissue within five years.

He told The Sunday Times: 'She has embryos, money and the backing of the Chinese government. 'These are credible people. I have encouraged them to publish in peer-review journals so that they receive credit and the world knows about their accomplishments,' he said.

Sunday Times (London)
July 14, 2002, Sunday
SECTION: Overseas news; News; 5

China leads race for first human clone

BYLINE: Lois Rogers Medical Correspondent

China, the most populous country in the world, is leading the race towards human cloning. One of its top research scientists reports producing more than 30 cloned human embryos. The scientist, Professor Lu Guangxiu, says she wants to pave the way for cloned "spare parts" that would extend the lives of millions.

Her breakthrough brings closer, however, the prospect of scientists producing an entire cloned baby - a goal that is officially opposed throughout the world but is privately regarded by most embryo researchers as irresistible. Details of the new Chinese technique, which is being developed in secrecy, are due to be published shortly by a leading western scientific journal, believed to be Nature. It is the first time Chinese embryo researchers have had their work recognized by the West and is viewed as a major coup.

Other teams of scientists have claimed to have cloned human embryos but only one - Advanced Cell Technology (ACT) - has published details. None of ACT's clones have survived as long as the Chinese embryos.

Two licenses have so far been issued in Britain to allow researchers to try to create human stem cells, at the Centre for Genome Research in Edinburgh, and Guy's hospital in London. Neither centre has so far announced any major successes.

Lu, 62, is professor of reproductive medicine at Xiangya School of Medicine at Changsha in Hunan province, where she leads the cloning team. She says she has been told not to discuss her work ahead of publication in

the scientific press, but she has told other workers in the field that she believes it will revolutionize medicine.

Her team has used a refinement of the cloning technique that led to the birth of Dolly the sheep five years ago. Lu's success has been attributed by western rivals to her access to an almost unlimited supply of human eggs, and China's less stringent legal controls.

Each year 20,000 hopeful Chinese mothers attend her clinic in Changsha for fertility treatment. Unwanted eggs are harvested by Lu's researchers for experimentation.

"She has a production line," said a leading cloning expert in America.

Lu has financial backing from the Chinese government through its commercial investment arm, China International Trust and Investment Corporation (Citic), which owns an empire of banks, factories and airlines worth Pounds 28 billion. Citic has bought a majority stake in her clinic and is helping Lu patent her work internationally to protect its enormous financial potential.

Larry Yung, the son of Citic's founder and a key figure in the company, owns a string of racehorses and fast cars and is one of the world's richest men. Birch Grove, his East Sussex home, which once belonged to Harold Macmillan, features a shooting estate and an 18-hole golf course..

One of the few people to know the details of Lu's work is Xiangzhong Yang, a Chinese-born professor of biotechnology at Connecticut University. He predicted she would be able to produce human tissue for transplant operations within five years. "She has embryos, money and the backing of the Chinese government," he said.

Lu, who speaks no English, has been working for decades in parallel with her western counterparts, painfully deciphering scientific publications with the aid of a dictionary.

She says she was able to produce China's first test-tube baby in 1988 - 10 years after the world's first IVF baby, Louise Brown, was born in Britain. She then announced her first cloned mouse in 1995, three years before a

team in Hawaii proclaimed what was apparently the world's first such achievement.

The professor claims to have produced her first cloned human embryo in 1999, two years ahead of ACT, the American firm usually acknowledged as the pioneer in the field. Lu's researchers are now attempting to create cell cultures from embryos that could be grown into specialized human tissue, such as liver, heart, or brain, which could then be used for repairing damaged organs.

Lu's progress has been aided by different cultural attitudes: the Chinese believe life begins only at birth. Because childlessness carries a heavy stigma, many couples turn to IVF, yet a strict one-child policy means many unused eggs are produced that are readily donated for research.

Lu is a member of the people's consultative congress, one of China's ruling bodies, which allows her to argue her case for research funding.

Alan Handyside, professor of developmental biology at Leeds University, was among British specialists who recently attended a scientific meeting in China. He said the nation's vast supply of human eggs was a key to its success.

"Nobody here can get hold of anything like their numbers," he said. "There are a lot of people involved in the work and they are making a great deal of progress."

While limited research on eggs and early embryos is permitted in Britain, America is still considering whether to ban human cloning research altogether because of arguments from Catholics and other protesters who believe that cloning destroys the unique status of human life at conception.

ACT said cloning work in the West was held back by stricter controls and the nervousness of investors. "I had heard about this work in China," said Robert Lanza, its medical director. "They are bound to be ahead of us because they have access to eggs. Nobody wants to invest in the work here because it might be outlawed at any time.

"It is a real tragedy. I have calculated that two people die of heart disease, Parkinson's or diabetes - all curable with stem cells - every minute that we delay research on this."

Lu's cloning techniques differ from some others because she leaves the egg's own nucleus inside the cell when the new "adult" cell nucleus is inserted to create the clone. In so doing, she claims to minimize damage to the egg's delicate structure. The original nucleus is then removed hours later.

The technique has allowed her to grow cloned embryos for periods of up to 10 days, when they become masses containing several hundred cells but before they start to show the characteristics that would eventually form a baby. ACT has managed to grow an embryo to only six cells.

The Boston Globe
July 25, 2002, Thursday ,THIRD EDITION
SECTION: NATIONAL/FOREIGN; Pg. A15

WOMAN CARRIES HUMAN CLONE, GROUP SAYS

BYLINE: By Raja Mishra, Globe Staff

A fringe religious movement's South Korea-based scientific team yesterday said they had implanted a cloned human embryo in a woman, the latest of a string of similar uncomfirmed experiments to emerge from the underground field of human cloning.

The Raelian Movement's chief scientist refused to confirm details of the team's report, but said that they soon would make an announcement that numerous scientists and governments around the world have been dreading.

"The only thing I can tell you is that, yes, we have done implantations and the next announcement will be the birth of a baby," said Dr. Brigitte Boisselier, director of Clonaid, the scientific wing of the Swiss-headquartered Raelian Movement, which believes humans are clones of God-like aliens destined to revisit Earth. Four months ago, a maverick Italian scientist also announced he had implanted a cloned embryo, and since has said that five female patients under his care have been implanted.

No mother has delivered a cloned human but several rogue groups, including the Raelians, appear bent on becoming the first to cross this controversial ethical barrier. If any of the recent claims are true, several clone babies are due this winter.

None of the claims have been confirmed by independent scientists, but many fertility specialists believe these groups possess the ability to create cloned babies. They fear all the infants would suffer grievous health problems caused by the cloning process, in which eggs are filled with adult DNA, grown to embryo stage, then implanted in females.

That procedure, called reproductive cloning, is different than therapeutic cloning, where stem cells are plucked from week-old cloned embryos that sit in laboratory dishes. Most scientists support therapeutic cloning, convinced the resulting stem cells can be used to cure a range of diseases.

The latest reproductive cloning report emerged in the Korean press, which reported that BioFusion Tech, a South Korean firm owned by the Raelian Movement, had implanted a clone. The Raelians also run Clonaid, which oversees BioFusion.

BioFusion officals yesterday said three women had been part of their experiment, conducted outside of South Korea, and one returned to the country pregnant.

"She has a clone embryo which was implanted into her about two months ago," BioFusion spokesman Kwak Gi-Hwa told the Agence France-Presse wire service. "The operation was carried out outside South Korea and therefore, the government has no right to meddle with it. She would leave the country if the authorities continue harassing us."

The Korean government is investigating the matter, reported the Korea Times. Human cloning remains legal in South Korea; a bill that would ban the practice awaits parliamentary approval.

In the United States, Congress has been unable to pass cloning legislation, with lawmakers divided over whether to criminalize all cloning or just reproductive cloning. Though reproductive cloning remains legal in many nations, it is a field dominated by rumor and unsubstantiated claims.

In February, Kentucky fertility specialist Panayiotis Zavos told the Globe his team had selected 10 infertile couples for a human cloning project, predicting success by late this year or early 2003. He refused to comment yesterday, and it's unclear whether he has succesfully implanted any embryos.

In April, Italian doctor Severino Antinori said that a patient was eight weeks pregnant - the first such claim. Speaking to the Chicago Tribune in June, Antinori said he'd overseen five pregnancies, with at least one birth expected in December.

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THIS STORY HAS BEEN FORMATTED FOR EASY PRINTING

Clone research quietly builds in world's labs

By Raja Mishra, Globe Staff, 6/21/2002

Once the province of a handful of marginalized scientists, the cloning of human embryos is becoming increasingly common in laboratories around the world, with several scientific teams regularly producing cloned embryos and many more labs preparing to follow suit.

Many researchers believe that multiple US labs are quietly preparing to create microscopic human embryos to harvest their stem cells, which can be used to grow new organs and tissues for disease treatment. None of the mainstream researchers want to create a cloned human, but the science is still controversial.

Opponents unsuccessfully pushed for a ban on so-called therapeutic cloning in the US Senate last week, hoping to prevent repeats of the headline-grabbing experiment by Advanced Cell Technology Inc. of Worcester last fall, the first published account of human cloning in hopes of getting stem cells.

Cloning experiments already have proliferated abroad, notably in China and England, according to interviews with researchers. Many US scientists are simply waiting for some political calm before embarking on their own human cloning work, scientists said.

The burgeoning human embryo cloning experiment underscores the gap between public perception and scientific reality. Although the public remains divided over the wisdom of cloning human embryos - even if only to develop treatments for disease - many scientists consider cloning an inevitable and essential component of 21st century medicine.

"You're not going to be able to put a lid back on the jar or put the genie back into the bottle," said Michael Lysaght, director of Brown University's biomedical engineering program, who monitors trends in regenerative medicine.

The United States has no laws regulating human embryo cloning. The failure of the Senate cloning ban left many US scientists cautiously optimistic about the field's future, even as they watch their foreign colleagues race ahead.

Some researchers anticipate new accounts of human embryo cloning experiments being published in the near future. MIT biology professor Rudolf Jaenisch said he has reviewed several of these accounts, which describe the experiments in detail.

The University of Connecticut's Dr. Xiangzhang Yang, another cloning specialist, said he has

been briefed on the human cloning work in "half a dozen labs" in China, and is urging his colleagues there to seek publication of their work in Western peer-reviewed journals. At least one of the labs successfully cloned a human embryo before Advanced Cell Technology, said Yang, and all have conducted embryo cloning experiments numerous times.

In England, where embryo-related research has won government approval, a London academic teaching hospital and a Scottish research institute have obtained government licenses to conduct embryo cloning experiments, according to officals at the Human Fertilization and Embryology Authority, the British government agency that monitors embryo research. In addition, Scotland-based cloning pioneer Ian Wilmut, whose work produced Dolly, a lamb and the first cloned mammal, also has applied for a license.

To date, only ACT has published a paper describing human embryo cloning, in an obscure Internet journal. Many scientists thought the study premature because ACT scientists could not extract stem cells from the cloned embryos - the goal of human embryo cloning researchers. In addition, scientists seek more efficient cloning techniques since the majority of attempts fail.

Scientists overwhelmingly oppose implanting cloned embryos in women to produce babies, called reproductive cloning. Several maverick researchers claim to have implanted women, though no proof exists. However, many mainstream scientists worry that such attempts could proliferate as cloning becomes widespread and researchers become more proficient.

In therapeutic cloning, which seeks medical cures, genetic material from a patient is placed into a hollowed-out egg, then artificially stimulated to grow, creating an embryo genetically identical to the patient. Researchers hope to extract stem cells from these week-old embryos, then mold the flexible cells into easily-used replacement tissue for patients. But the process destroys the embryo, ethically troubling many.

In the United States, these ethical qualms have complicated research. Last month, the University of California at San Francisco admitted, after media inquiries, its researchers conducted a cloning experiment that failed. The work was kept quiet to avoid political controversy, explained UCSF administrators. Until then, ACT was the only group to publicly admit to embryo cloning.

Many biotech specialists believe other US labs and companies have cloning experiments underway.

"I suspect there are more groups than we know who are actually working on therapeutic cloning," said Jean-Francois Formela, a Boston-based general partner with Atlas Venture, an investment firm specializing in technology, which nonetheless remains skittish about pouring money into cloning science.

The ethical controversy has kept many other interested US researchers away, at least for now.

Johns Hopkins University stem cell pioneer Dr. John Gearhart, when asked whether he planned human embryo cloning work, said, "Yes, but I do not know when we would [or] could begin."

Agence France Presse
July 21, 2002 Sunday

Cloning on six couples to start this year: British press

DATELINE: GLASGOW, July 21

Six couples trying to become the parents of the first **clones** will be flown to an unnamed developing country by a leading fertility expert before the end of the year, a Scottish weekly said Sunday.

One of the six couples, Americans Bill and Kathy -- who did not want to reveal their surname -- told The Sunday Herald that the experiment will be led by American fertility expert Panos Zavos.

"We want children so badly and we have tried so hard and for so long. No one has tried as hard as Kathy has to have children," Bill, a high school teacher in his fifties, told the paper. Kathy, a sales representative in her mid-40s, spent a total of 24 months on IVF treatments and for 17 months of this time she was taking injectable drugs, the paper said.

The couple would also be considered too old to adopt in the US, the weekly said.

"We do not know where it is going to be or when, but it's imminent," Kathy told the weekly.

The couple attended the Andrology Institute of America, a fertility clinic run by Zavos in the southern US city of Kentucky, and were selected for the process, the paper said.

In Kathy and Bill's case, the child produced would be a **clone** of the mother and would be made up almost entirely of Kathy's DNA, the weekly said.

Some of the couples have requested a baby boy, in which case a **clone** of the father will be made by taking the nucleus from one of his cells, it added.

"This is a typical couple. They want their own children,' Zavos told the

paper.

He was originally working on a joint cloning bid with the Italian Severino Antinori, but the two doctors fell out over unsubstantiated claims by Antinori of his cloning success.

In April the Rome-based doctor told a Gulf News journalist at a genetics conference in Abu Dhabi that a woman on his programme was eight weeks pregnant with a cloned embryo.

Antinori later refused to confirm whether or not this is the case.

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Human embryo created through cloning

WASHINGTON (CNN) --**Scientists at a technology company said Sunday they have created human embryos through cloning, drawing criticism from President Bush and lawmakers and raising new ethical questions.**

Advanced Cell Technology Inc. of Worcester, Massachusetts, said the experiment was aimed not at creating a human being but at mining the embryo for stem cells used to treat disease.

Stem cells are a kind of master cell that can grow into any kind of cell in the body. The company's study was also published in an online scientific journal.

"I'm just trying to help people who are sick, and really that's our focus," said Dr. Michael West, the company's president and CEO. He called the development "the first, halting steps" toward a new area of medicine.

Speaking on CNN's "Late Edition with Wolf Blitzer," West disputed the suggestion the work amounted to the creation of a human being.

"We're talking about making human cellular life, not a human life," West said.

"A human life, we know scientifically, begins upwards, even into two weeks, of human development, where this little ball of cells decides, 'I'm going to become one person or I am going to be two persons.' It hasn't decided yet."

West said the breakthrough in what he called "therapeutic cloning" could lead to advances in fighting a variety of ailments, including Parkinson's disease and diabetes.

He said his company was not interested in cloning human beings and did not create the embryos for reproductive purposes.

Immediate criticism

The news drew immediate criticism from some lawmakers.

"I think that people are concerned about the ethical problems here," Sen. Richard Shelby, R-Alabama, said on NBC's "Meet the Press." He said he expected lawmakers would soon take up the issue.

"I believe it will be a big debate, but at end of day I don't believe we'll let cloning of human embryos," Shelby said.

"I find it very, very troubling, and I think most of Congress would," Sen. Patrick Leahy, Democrat of Vermont,

said on NBC.

A White House spokeswoman reaffirmed President Bush's opposition to human cloning.

"The president has made it clear that he is 100 percent opposed to any type of cloning of human embryos," said spokeswoman Jennifer Millerwise. "The president supported the House legislation to ban human cloning which passed overwhelmingly."

Last summer, the House of Representatives voted to ban human cloning and set penalties of up to 10 years in prison and a $1 million fine for those convicted of attempting to clone humans.

The measure was never taken up by the Senate, so it never became law.

Sen. Richard Durbin, D-Illinois, said he hoped the Senate could find a compromise that would allow some cloning research to continue, without opening the door to the creation of human beings through clones.

"We in the Senate have to draw that line so it's a reasonable line, so we can continue medical science and breakthroughs, without crossing that line into something none of us want to see," he said on CNN's "Late Edition."

'Lifesaving therapies'

In the study, published in the online Journal of Regenerative Medicine, scientists removed the DNA from human egg cells and replaced it with DNA from a human body cell. The egg cells began to develop "to an embryonic state," according to a press release from the company.

Of the eight eggs, two divided to form early embryos of four cells and one progressed to a six-cell stage before it stopped dividing.

"These are exciting preliminary developments," said Robert P. Lanza, vice president of medical and scientific development at ACT and one of the authors of the paper.

"This work sets the stage for human therapeutic cloning as a potentially limitless source of immune-compatible cells for tissue engineering and transplantation medicine.

"Our intention is not to create cloned human beings," Lanza said, "but rather to make lifesaving therapies for a wide range of human disease conditions including diabetes, strokes, cancer, AIDS and neurodegenerative disorders such as Parkinson's and Alzheimer's disease."

Though he described the advance as a "very primitive development," the director of the Center for Bioethics at the University of Pennsylvania deemed it a "significant" one.

"When you get to the point where you've made a human embryo, even for research purposes ... it's a line that's crossed," Arthur Caplan told CNN.

The medical ethicist said an argument could be made for using the technology to create cells that could be used to treat diseases.

"If you could make cell lines from these creations and turn them into something that the body wouldn't reject ... that would be a wonderful breakthrough in terms of being able to offer cures to people."

Earlier this year, Italian fertility doctor Severino Antinori and U.S. researcher Panos Zavos announced plans to clone humans. They said hundreds of couples had volunteered for controversial procedure.

The announcement was criticized by officials in several countries, and Italian authorities threatened to ban Antinori from practicing medicine if he goes ahead with the experiment.

Another organization, Clonaid, moved its research into human cloning outside of the United States after being investigated by the federal government.

Clonaid was founded by members of a religion called the Raelian movement, which believes extraterrestrial scientists created life on Earth and that cloning is a way of achieving eternal life.

The Food and Drug Administration investigated the company after its research director, Brigitte Boisselier, told a congressional hearing the company wanted to clone a human in the United States.

Find this article at:
http://www.cnn.com/2001/TECH/science/11/25/human.embryo.clone/index.html

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Reuters Medical News — for the Professional

Cloning Scientists Seek Permission to Work on Human Embryos

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Introduction

LONDON (Reuters) Apr 11 - The scientists who cloned Dolly the sheep said on Thursday they plan to seek permission to experiment on human embryos for medical purposes.

In a move expected to raise concerns from some religious groups, the Roslin Institute will apply for a license to the Human Fertilization and Embryology Authority (HFEA), the British government body that regulates embryo research.

"It will be several weeks before we put in a final application," said Roslin spokesman Dr. Harry Griffin. "It will be a few months before we know whether the proposal will be approved."

The Roslin Institute stunned the world in 1996 when it created Dolly, the first animal to be cloned from an adult cell. Since then, Britain, which has the world's most liberal policy on stem cell research, has said the cloning of human embryos for research should be allowed to proceed under strict conditions.

Last year Britain became the first country explicitly to allow the creation of embryos as a source of stem cells.

Dr. Griffin acknowledged that while some people will always feel such research is not appropriate, the issues have been subject to a lengthy debate in Britain. Roslin would be operating within a strictly defined legal and ethical framework, he said.

There was no immediate comment from the HFEA, but sources close to the authority said Roslin's proposed application appeared to be within the remit of British law on embryo research.

Reports last week that Italian fertility specialist Severino Antinori had managed to achieve a pregnancy in a woman as a result of human cloning prompted widespread skepticism among scientists.

Dr. Antinori was said to have made the claim in response to a question during a lecture in Abu Dhabi but has refused to confirm or deny media reports or clarify exactly what he said.

Critics of human embryo cloning say it represents the first step on a slippery slope to reproductive cloning, which is illegal in many countries, including Britain.

EXPAND STORY

BC-Britain-Dolly Scientists,0412

Creators of Dolly to request permission to test human embryos

LONDON (AP) _ The creators of Dolly, the world's first cloned sheep, will soon seek permission to carry out experiments on human embryos, one of the scientists said.

The Roslin Institute, near Edinburgh, Scotland, will apply to the government's fertility authority for a license in the next few months to investigate ways of harvesting human stem cells that are found in the growing embryo, said Professor Ian Wilmut, head of the institute's gene expression and development division.

``It is a significant shift for us and a natural way to go,'' Wilmut said late Wednesday.

Experts believe stem cells have the potential to treat degenerative diseases such as Parkinson's and Alzheimer's.

The Roslin Institute, which drew worldwide attention after Dolly was born in 1996, also is considering how it could apply its technique, cell nuclear replacement, to human embryos.

The scientists are proposing to establish methods for deriving human embryonic stem cells by using surplus embryos or embryos created specifically for the purpose by IVF.

Last month, embryo stem cell research in Britain moved into high gear when regulators granted the first licenses allowing scientists to extract the cells from donated spare IVF embryos and experiment with them.

Several groups around the world have already started research on embryonic stem cells _ blank-slate cells found in early stage embryos that go on to form every type of specialized cell in the body. However, Britain has the most open laws governing the controversial area of research and is widely tipped to lead the emerging field.

Doctors hope they will be able to cure or treat hundreds of diseases by extracting stem cells from embryos and directing them to develop into any type of tissue needed for transplant.

Britain is the only country so far to have legalized human cloning for stem cell research.

In another world first, Britain is setting up a national stem cell bank, similar to a blood bank, to store stem cells and make them available to researchers.

Meanwhile, Dolly the sheep recently developed arthritis at the relatively early age of 5 1/2 years, stirring debate that the current cloning procedures might be flawed.

In fact, Dolly's problem could raise new doubts about cloning animals for use in human transplantation and about cloning humans themselves.

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EXPAND STORY **DJ Australia Co Plans To Produce Human Embryos For Research**

Dow Jones International News Service via Dow Jones

MELBOURNE (AP)--An Australian company said Friday it plans to begin producing cloned human embryos later this year for use in medical research.

Stem Cell Sciences has rights to the cloning technique used by Scottish scientists to create Dolly the sheep in 1997, said executive director Peter Mountford.

"Our objective is to therapeutically clone diseased embryos," said Mountford.

The patented cloning technique involves inserting human cells into animal eggs or leftover human eggs from in vitro fertilization clinics.

The egg's original genes are then removed and the cloned embryo allowed to develop.

Mountford said the planned research would use cells donated by people suffering from genetic diseases to create cloned embryos with diseased cell lines.

"It would allow us to screen millions of drugs against these diseased cells," he said.

Mountford said his company wouldn't consider allowing an embryo to develop into a cloned person.

"I think it would be an outrageous thing to do," said Mountford.

The planned research will likely take place in Australia or Britain, depending on moves by Australian authorities to regulate therapeutic cloning.

The Australian government is in the process of formulating nationwide laws dealing with therapeutic human cloning and stem cell research. A parliamentary committee has recommended a moratorium on therapeutic cloning.

In Britain, the government allows strictly regulated therapeutic human cloning.

(END) Dow Jones Newswires 08-03-02

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Cloned-Fetus Rumor Stirs Talk

Report on Italian Doctor's Claim Cannot Be Confirmed

By Rick Weiss
Washington Post Staff Writer
Saturday, April 6, 2002; Page A02

Scientists, ethicists and politicians around the world became caught up in a flurry of electronic chatter yesterday triggered by an unconfirmed report that an Italian fertility doctor had helped a woman become pregnant with the world's first human clone.

The doctor, Severino Antinori, a renowned medical maverick and director of a human reproduction research center in Rome, could not be reached to comment on the report, which appeared in Gulf News, a Middle Eastern newspaper. The paper quoted Antinori as saying that a woman in a human cloning program he had started was eight weeks pregnant.

A woman who answered the telephone at Antinori's clinic yesterday said the doctor was unavailable and would not be releasing any further information. "Science needs silence, or science will not get done," said the woman, who did not identify herself.

The high incidence of miscarriages, malformed newborns and premature deaths among the few mammals that have been cloned has led most experts to conclude that human cloning is dangerous and unethical.

It's possible that the pregnancy claim, reportedly made Wednesday in veiled comments at a scientific meeting in the United Arab Emirates, amounts to nothing more than a publicity stunt -- or that the newspaper misconstrued Antinori's statements.

But the editor who handled the article at Gulf News, an English-language daily, stood by the story when contacted by The Washington Post last night. And several people familiar with Antinori's tumultuous history agreed that of the few researchers who have said they intend to clone a human, Antinori is probably the most likely to try.

In 1994, Antinori helped a 62-year-old Italian woman get pregnant. At 63, she became the oldest woman ever to give birth. Experiments in which he cultivated infertile men's immature sperm inside rodent testicles also stirred controversy.

Last year, Antinori said he was launching a human cloning effort with Panos Zavos, a Kentucky reproductive scientist and entrepreneur. In February, Zavos reportedly declared that an effort was about to begin on 10 couples -- some of them Americans -- in an undisclosed country.

Responding to queries yesterday, Zavos released a statement on one of his Web sites saying "we are not prepared to confirm or deny" that a clonal pregnancy had been achieved.

Antinori made his comments at a genetic engineering and cloning meeting held this week in Abu Dhabi, according to Gulf News. Answering a question about cloning, he reportedly said: "Our project is at a very advanced stage. One woman among the thousands of infertile couples in the program is eight weeks pregnant."

He appears not to have said explicitly that the fetus is a clone.

The Senate is considering legislation that would ban human cloning. There is strong support for a ban on the cloning of babies, but the bill's fate is uncertain because it would also ban the creation of cloned human embryos for research that could lead to cures for disease.

The American Society for Reproductive Medicine yesterday reiterated its opposition to the cloning of babies but warned Congress against overreacting to the rumors. "It is possible that some policymakers and advocates will want to use the claims of irresponsible scientists to bolster their case for an overly broad prohibition on scientific research," the ASRM said in a statement. "We caution policymakers not to be rushed into approving overreaching legislation."

But Richard Doerflinger of the U.S. Conference of Catholic Bishops yesterday urged Congress to enact a law banning human cloning. "If we don't want it happening in this country, we need to ban it."

Staff researcher Lynn Davis and special correspondent Sarah Delaney contributed to this report.

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Ottawa Citizen

April 14, 2002 Sunday Final Edition

SECTION: News; Pg. A6

LENGTH: 377 words

HEADLINE: Second scientist set to **clone** humans: Project to go ahead despite concerns over malformations

SOURCE: The Sunday Times

BYLINE: John Follain

DATELINE: ROME

BODY:
ROME -- A former associate of Dr. Severino Antinori, the controversial Italian fertility expert, has revealed his own plans to create cloned children for a dozen couples this summer.

Dr. Panayiotis Zavos also disclosed that he had severed relations with Dr. Antinori after differences over how to approach cloning.

Despite continuing controversy over Dr. Antinori's claims last week that one of his patients was eight weeks' pregnant with a cloned fetus, Dr. Zavos plans to pursue his own project -- even though there is widespread concern that the technique could lead to severely malformed children. Dr. Zavos hopes to implant his first cloned embryos at two secret locations by August. Based in Lexington, Kentucky, he has described 2002 as "the year of the **clone.**" In addition to himself and Dr. Antinori, the Raelians, a religious cult, also claim to have cloned embryos and plan to produce cloned babies.

Dr. Zavos, who heads the Andrology Institute of America, said this weekend: "The status is looking good, and we're ready to execute. We have selected the final 10 or 12 couples, and it's a matter of time now. But you must realize this is a very sensitive area, and we must proceed very carefully."

Last August, Dr. Zavos and Dr. Antinori appeared together before a panel at the National Academy of Sciences in Washington, D.C. to defend their plans.

However, Dr. Zavos said that he broke away from the Italian professor five months ago. He declined to give detailed reasons but said: "I worry a great deal about Severino and the way he is approaching the subject."

A source close to the team said: "No one from the original team works with him any more. No one trusts Severino and no one can make science with him."

Dr. Zavos was skeptical over Dr. Antinori's claim earlier this month in comments to a Middle Eastern news agency to have made a woman pregnant with a cloned fetus. Dr. Antinori gave no evidence to support his claim.

Dr. Antinori declined to comment. But in an interview with an Italian magazine last week, he said that his patient, thought to be a rich Arab, would give birth to a "completely healthy" baby and that 85 per cent of its genetic makeup would come from the father and 15 per cent from the mother.

LOAD-DATE: April 14, 2002

California School Attempted to Clone Human Embryos

By David P. Hamilton and Antonio Regalado

The Wall Street Journal, 5/24/02

Cell biologists at the University of California in San Francisco, beginning three years ago, conducted a closely guarded, large-scale effort to clone human embryos for therapeutic purposes, in research supported by state funds and the biotechnology firm Geron Corp.

Led by embryologist Roger Pedersen, the apparently unsuccessful project was designed to find new ways to derive stem cells, not to clone people. Stem cells are amazingly versatile cells drawn from week-old embryos that can be tranformed into any type of tissue in the body, making them potentially useful for treating degenerative diseases such as diabetes.

UCSF is the most prestigious institution to attempt so-called therapeutic cloning, which to date has only been publicly attempted at Advanced Cell Technology Inc., a small biotechnology company, and by researchers in China. Those other efforts have drawn fire from some ethicists, religious leaders and politicians who consider the work dangerous and unethical. The U.S. Senate in the next few months plans to debate whether cloning -- of either cells or people -- should be outlawed.

Dr. Pedersen's work would be among the first known attempts by a respected scientist to try to clone embryos for this purpose. UCSF officials stand behind Dr. Pedersen's work, which they say is important and should continue when researchers are ready.

Last summer, a university spokeswoman denied that anyone on campus was then engaged in cloning using human eggs, but

declined to say whether such work had occurred in the past. Geron's chief executive, Thomas Okarma, has also denied funding embryo-cloning research -- largely for semantic reasons, he now says. Dr. Pedersen has repeatedly declined to describe the nature of his studies.

Documents obtained from UCSF under the California Public Records Act, however, reveal that Dr. Pedersen sought official permission from the university to begin his embryo-cloning experiments in mid-1998. UCSF administrators now say that one round of such experiments took place during the first six months of 1999. After an 18-month hiatus, the work resumed for an additional five months in early 2001.

Dr. Pedersen, who left the university last year to move his research to the University of Cambridge in the United Kingdom, said in a brief e-mail comment yesterday that such cloning studies "continue to be important," because they offer hope of unraveling the mysteries of embryonic development.

Keith Yamamoto, vice dean for research at the UCSF medical school, said the university kept its silence in order to respect Dr. Pedersen's desire not to discuss his work publicly until it was ready for scientific publication.

No researchers at UCSF are currently engaged in embryo-cloning work, Dr. Yamamoto said, though he added that the university has protocols in place should anyone wish to pursue the research. UCSF has recently established a major program in developmental and stem-cell biology, under whose auspices the university recently launched an effort to derive its own lines of stem cells using discarded embryos from fertility clinics.

Dr. Pedersen's cloning effort, described in several hundred pages of documents provided by UCSF, was largely an attempt to

produce stem cells that are genetically identical to another individual. According to the documents, Dr. Pedersen's research team of about 10 people arranged to receive eggs from donors at the UCSF fertility clinic and other participating clinics. The team only used eggs that had failed to be fertilized when mixed with sperm, though it drew up plans, still unused, to obtain fresh eggs as well.

Those eggs were moved to another lab, where Dr. Pedersen's team used micro-manipulating instruments to place the DNA of adult human cells inside them. That process "reprograms" the cells, causing them to grow as if they were developing embryos. Ideally, such embryos would develop after a week to 10 days into largely featureless clumps of 100 or so cells called blastocysts, from which scientists can extract stem cells.

At one point, the team envisioned working with as many as 1,000 human eggs a year. Neither Dr. Yamamoto nor anyone else familiar with the research would say how many eggs the research team worked on, though Dr. Okarma of Geron emphasized that the eggs were assumed to be "dead," because they were resistant to fertilization.

For much the same reason, in fact, Dr. Okarma argued that Dr. Pedersen's "failed" experiments weren't designed to create cloned embryos at all. While many of the UCSF documents do refer to "early embryos" created as a result of the research, Dr. Okarma said that those clumps of cells were defective and highly unlikely ever to develop into a fetus under any circumstances, and therefore shouldn't be called embryos at all.

He added that the early work was intended more to shed light on the way the egg reverts the inserted DNA to an embryonic state than to yield new stem cells. Ideally, scientists might have

learned how to duplicate that process without the use of an egg cell, which might eventually make it possible to convert any adult cell into an embryonic stem cell.

Dr. Pedersen, a pioneer in stem-cell research, was clearly aware of the sensitive nature of his work, writing in a 1998 letter to a university administrator of "its potential for visibility and controversy." On the advice of the university's human-subjects committee, he took the unusual step of informing the UCSF chancellor's office and the dean of the medical school about the study. The study was reviewed several times by that committee, other administrators and a university bioethicist, all of whom eventually approved.

Carrying out the work posed other difficulties. UCSF was forced to steer around a law passed by Congress in 1995 barring any use of federal funds for studies in which embryos are destroyed, which it managed by supporting Dr. Pedersen's research with state and private funds.

Maintaining the fire wall between federal and other funds proved challenging, however, and last summer the university announced it was moving Dr. Pedersen's stem-cell laboratory to an undisclosed off-campus location, and the work cloning embryos was halted.

Geron didn't fund similar cloning work anywhere else, Dr. Okarma said. Partly as a result of Dr. Pedersen's failure to produce growing embryos, Geron has soured on cloning technology
and now considers it something of a sideshow, compared with other avenues of stem-cell research.

Wall Street Journal
May 24, 2002

U.S. university sought to clone human embryos

By Andrew Quinn

SAN FRANCISCO, May 24 (Reuters) - The University of California-San Francisco confirmed on Friday that it had hosted a large-scale drive to clone human embryos for therapeutic purposes, the first major public institution to acknowledge pursuing the controversial research.

The UCSF project, which began three years ago and has since been temporarily shelved, sought to derive embryonic stem cells for medical research, not to clone human beings.

But the university's research work, which was reported on Friday by the Wall Street Journal, looked likely to fuel debate in the U.S. Senate where lawmakers are considering moves to outlaw all human cloning.

``The general point is these experiments and others like them underscore for us the importance of proceeding forward and not criminalizing science," said Keith Yamamoto, vice dean for research at the the university's medical school.

UCSF's announcement makes it the first major U.S. university to acknowledge an embryo cloning program, which thus far has only publicly been undertaken by Advanced Cell Technology, a biotechnology firm.

The UCSF project was led by embryologist Roger Pedersen, a leading scientist who subsequently relocated to Britain to escape the increasingly inflamed U.S. debate over the morality of cloning and stem cell research.

Pedersen's work on therapeutic cloning was funded with state money and by the biotechnology company Geron Corp. in order to comply with a 1995 law which bars the use of federal funds for studies in which embryos are destroyed.

According to UCSF, Pedersen's research group conducted two sets of embryo-cloning experiments, one in early 1999 and another in early 2001.

The scientists sought to transplant the DNA of adult human cells into eggs from donors at the university fertility clinic, a process aimed at producing blastocysts -- the earliest stage of embryonic development -- from which stem cells could be harvested.

The goal was to obtain stem cells genetically identical to the adult DNA donor and could then be used to develop possible treatments for everything from Alzheimer's and Parkinson's diseases to diabetes, cancer and spinal injuries.

Pedersen said the cloning approach to stem cell research could ``prove uniquely valuable for developing human therapies."

``An obvious benefit would be obtaining embryonic stem cells that were immunologically compatible with individual patients," he said in a UCSF news release.

NO CONCLUSIVE RESULTS

University officials said the project failed to produce conclusive results and had been shelved -- at least for now.

But while no therapeutic cloning research is currently under way at UCSF, officials said the university, already at the

forefront of U.S. stem cell research, stood ready to resume the cloning studies if conditions permit.

``The field of human embryonic stem cell research is in its infancy and will require years of study in laboratories throughout the world," said Yamamoto said. ``The best chance for achieving success is to engage and fuel the public research enterprise."

University officials said they had not publicized the project out of deference to Pedersen, who felt ongoing research should not be made public until it had definitive results.

But the Wall Street Journal's account of the university's cloning efforts, based on documents obtained under the California Public Records Act, looked likely to spur new debate on the ethics of human cloning.

That debate is already well under way in Washington, where the Senate looks likely to take up competing legislation that would either bar all cloning outright or allow therapeutic cloning for medical research.

Foes of cloning say it is immoral to create an embryo only to destroy it. But advocates of therapeutic cloning say it is a promising avenue of stem cell research that could lead to treatments for a wide range of diseases.

The House of Representatives last year passed a bill, strongly backed by President George W. Bush and anti-abortion groups, that would ban all types of human cloning. The Senate debate is being heavily lobbied and is the source of a number of emotional advertising campaigns.

Yamamoto said therapeutic cloning projects like that at UCSF

promised too many scientific benefits, particularly in the research of human genetic disease, to be scrapped without serious consideration of the consequences.

``We understand almost nothing about the early stages of most human genetic diseases. We wait for symptoms, and often by that time there lots of things have gone wrong," he said.

``(With this research) we might be able to find diagnostics very very early that would tell us whether or not the disease is there .... and potentially even therapeutic treatments."

Reuters, 5-24-02

University of California-San Francisco Acknowledges Tests on Human Cloning

By Paul Jacobs, San Jose Mercury News, Calif. Knight Ridder/Tribune Business News

May 25--The University of California-San Francisco acknowledged Friday that scientists there conducted experiments in"therapeutic cloning"-- the controversial procedure that would be banned by legislation now before Congress.

The work was conducted from 1999 to 2001 in the laboratory of Roger Pedersen, a leading embryonic stem cell researcher who left the university last year for England because of fears his research would be restricted in the United States.

The experiments were funded by Geron, a biotechnology company in Menlo Park, with matching money from BioSTAR, a university-run program.

In the experimental procedure -- also called"somatic cell nuclear transfer"-- Pedersen's team replaced the genetic material in human eggs with the genetic material from the cells of adult donors. The same technique has been used in animals to create offspring genetically identical to the adult -- like Dolly, the cloned sheep.

The university scientists' eventual aim was to create an early stage human embryo from which stem cells could be harvested for study and use in treating patients with disorders like Parkinson's and heart disease.

The UC research, first disclosed in Friday's Wall Street Journal, becomes the second instance to come to light in which scientists in the United States attempted to apply the cloning technology to human cells.

Last year, scientists at Advanced Cell Technology in Massachusetts kicked up an international controversy when they claimed to have cloned an early-stage human embryo. Since then, scientists in China have made similar claims.

The Journal story relied on hundreds of pages of documents, obtained under the California Public Records Act, from which specific experimental results had been excised.

A university press release issued Friday said the San Francisco campus is not now conducting studies of therapeutic cloning but that it does have"research protocols in place that would permit scientists to resume the studies."

The statement quoted Pedersen as saying that stem cells derived from the nuclear transfer technology "should prove uniquely valuable for developing human therapies.

An obvious benefit would be obtaining embryonic stem cells that were immunologically compatible with individual patients." Pedersen also said studying the stem cells produced in this way should provide insights into how adult cells might be reprogrammed for use in cell therapy that does not rely on the use of human embryos.

Last year, President Bush announced he would allow federal research money to be used to study stem cells from surplus embryos that would otherwise be discarded by fertility clinics. But he limited the spending to 60 or so existing stem cell lines to avoid further destruction of embryos. Two of those

stem cell lines -- each from individual embryos but without using nuclear transfer technology -- were developed by Pedersen's group at UC-San Francisco.

Bush, however, has opposed the creation of human embryos using the nuclear transfer technology for reproductive or therapeutic purposes. And Congress is now considering whether to ban the procedure outright or to limit its use to the production of early stage embryos as a source of cells for therapy.

Pedersen apparently was unable to obtain sustainable stem cell lines using the nuclear transfer or"cloning"method. The experiments were reviewed in advance by the university's Committee on Human Research, as well as a UC-San Francisco bioethicist and the executive committee of the school of medicine.

"The field of human embryonic stem cell research is in its infancy, and will require years of study in laboratories throughout the world,"said Keith Yamamoto, the vice dean for research at the UC-San Francisco School of Medicine."It is critical that scientists be given the opportunity to carry out a broad-based, deep examination of multiple experimental strategies, particularly at this early stage in the evolution of the field."

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EXPAND STORY

Furor Rises on Cross-Species Cloning

--- Fusing Human DNA and Egg of a Cow Creates Embryo and World Debate ----- By Antonio Regalado and Meeyoung Song Staff Reporters of The Wall Street Journal

The Asian Wall Street Journal via Dow Jones

SEOUL -- Embryologist Park Se Pill received an urgent telephone call Monday from his office at Maria Biotech Co. here. Twenty people carrying picket signs and shouting through amplifiers had gathered outside the company, a spinoff of Maria Infertility Hospital, South Korea's largest fertility clinic.

"We denounce Maria Hospital's unethical research of mixing humans and animals," yelled the protesters. One was dressed as a cow.

The costume wasn't incidental. Last summer, researchers in Dr. Park's laboratory launched what he terms a "top secret" project to create cross-species embryos by combining human DNA with cow eggs.

Using 15,000 bovine eggs stored in a freezer, technicians here spent long hours hunched over microscopes, slipping human genetic material into hollowed-out cow eggs at a lightning pace and producing hundreds of cloned embryos, none quite entirely human due to remaining traces of cow DNA. The goal: to generate human embryonic stem cells, not human offspring, for research or perhaps for novel transplant treatments.

This week's protesters were late to the picket lines. The interspecies work at Dr. Park's lab was put on hold in December because of public complaints. But similar efforts continue elsewhere in Asia and the U.S., where researchers are turning to animal eggs, such as those from cows and rabbits, because they are easier to obtain than human ones.

Researchers for a U.S. company, Advanced Cell Technology Inc. of Worcester, Massachusetts, were the first to disclose, in 1998, that they had put human DNA into a cow egg, an announcement that earned them their own visit from cow-masked protesters. The work then moved underground and overseas, but hasn't stopped. Dr. Park's project in Korea appears to be the most extensive effort yet described to produce human embryos through cloning. In cloning, the egg's DNA-containing chromosomes are removed, then replaced by the chromosomes of an adult cell.

Even now, proliferating cross-species research is confronting policy makers world-wide, sometimes with contradictory results. In the U.K., making cloned human embryos using the eggs of women is allowed, but cross-species cloning is banned. In Japan, the reverse holds.

While cross-species cloning isn't outlawed in the U.S., it is challenging the U.S. Patent and Trademark Office. In addition to an application on human embryos cloned using cow eggs from Advanced Cell Technology, the agency has received similar applications from a separate South Korean team at the College of Veterinary Medicine at Seoul National University.

Although the agency's policy is to reject any patent that claims rights to human beings or human embryos, former Patent Commissioner Q. Todd Dickinson says human-animal mixtures require high-level policy discussions to decide where to draw the line. Mr. Dickinson says patent examiners can attend regular meetings to help them understand which biotechnology inventions are "human" and which aren't.

Combining animal eggs and human DNA is "forcing people who thought they have a settled view of the

embryo to reassess their views," says R. Alta Charo, a bioethicist at the University of Wisconsin, Madison.

For opponents of cross-species research, the experiments confirm fears of ever-larger-scale efforts to manufacture human embryos for research purposes. The National Right to Life Committee, an antiabortion group in Washington, has been airing radio ads calling cloning research a "nightmare project" that will lead to "human embryo hatcheries" in the hope of influencing a pending U.S. Senate vote to ban the cloning of human embryos for stem cells.

In Seoul, a city set aglow by night with the neon crosses of evangelical churches, passions are also on the rise. Kim Ji Yeon, a coordinator at the People's Solidarity for Participatory Democracy, the largest nongovernmental organization in South Korea, says a coalition of Christian and other groups is demanding that the government quickly enact rules to prevent experiments like those at Maria Biotech.

"This is an act that ruthlessly cuts down the hopes of citizens who want bioethics to be observed, as well as the [hopes of the] majority of scientists who have a conscience," says Ms. Kim.

South Korean policy makers haven't implemented rules but may do so by midsummer, says Jung Sung Chul, a section chief at the Korean National Institute of Health. That will likely involve a ban on reproductive cloning, but researchers are pressing for a green light for experiments such as those that rely on animal eggs. "It's a question of the freedom of science," Dr. Jung says.

Dr. Park, who trained in the U.S. under cattle-cloning pioneer Neal First at the University of Wisconsin, says that before the cross-species fusion experiments were discontinued at Maria Biotech, his team had grown embryos that lived for as long as a week. But the lab hasn't yet been able to make stem cells from the cloned embryos, he says.

The embryos tend to grow well up to a point, but then growth sputters, Dr. Park says. The key problem, he suspects, is scrambled signaling between the new human nucleus and energy-producing structures known as mitochondria that remain in the cow egg. Mitochondria have their own DNA, which isn't replaced in the nucleus-swapping cloning procedure.

With enough practice, some scientists expect that barrier can be overcome. "By doing it over and over again, we are going to solve that problem," predicts Dr. Park. He adds that the basic research will pave the way for human-embryo cloning using human eggs, which he says the company has so far held off doing because of ethical concerns. "Someday," he says, "if our government permits it, we will be ready."

But if creating humanlike embryos in animal eggs works, the technique could be rapidly adopted by a large number of research groups. Recently, stem-cell researchers in the U.S. have been abuzz with reports from China that interspecies embryos have successfully yielded stem cells. Sheng Huizhen, a U.S.-trained biologist now at Shanghai No. 2 Medical University, has presented work showing how stem cells were derived from embryos created by fusing human tissue with the egg cells of rabbits. That work is now being studied by members of President George W. Bush's Council on Bioethics.

Leon Kass, the University of Chicago philosopher who leads that panel, says he couldn't comment on the interspecies experiments until his group produces its report on cloning, which is due out this summer.

Egg-switching experiments also are finding other, less controversial uses in animal conservation. Hwang Woo Suk of the College of Veterinary Medicine at Seoul National University is leading an effort to clone a Siberian tiger named Nang-Nim.

Housed at Seoul Grand Park, the city's sprawling zoo, the tiger was captured in North Korea and lent to the South in 1999, but cloning her has so far failed.

After making embryos using more easily acquired lion and house-cat eggs, Dr. Hwang first tried growing Nang-Nim clones inside two lionesses. But big cats need to be sedated, which can pose problems, and the effort ended badly. Dr. Hwang says he is pressing forward with a new effort to replicate Nang-Nim within the womb of a nonfeline species. Which type of animal he has chosen is a secret.

--- Ox + Cow = ?

Other interspecies cloning experiments on endangered species:

-- Researchers are trying to clone African wildcats using house-cat eggs

-- In 2001, a wild ox was cloned and brought to term in a domestic cow but died shortly after birth

-- Researchers are exploring whether the sexually finicky giant panda can be cloned using other bears as surrogates

WJAviaNewsEDGE :PAGE: A1
:SUBJECT: BIOT DRUG HEAL SKOR SCI

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February 2, 2002

SECTION: This Week, Pg. 4

LENGTH: 686 words

HEADLINE: Take a thousand eggs

BYLINE: Sylvia Pagan Westphal (Boston)

HIGHLIGHT: Mass-produced **clones** could soon be rolling off the production line

BODY:

A CHIP that will automatically create hundreds of cloned embryos at a time is being developed by a Californian biotech company, "New Scientist" has learned.

If it lives up to its promise, the chip should help make cloning cheap and easy enough for companies to mass-produce identical copies of the best milk or meat producing animals for farmers. It might even be used for cloning human embryos.

The chip automates the laborious process of nuclear transfer, the key step in cloning. At present it takes hours of painstaking work with a microscope to remove the nucleus of an egg cell and replace it by fusing the denucleated egg with another cell. "If somebody's got something like that, obviously it would make everybody's life easier," says Tanja Dominko of Advanced Cell Technology, the Massachusetts company that caused a stir late last year when it announced that it had created cloned human embryos.

In animals, cloning is still very wasteful. At best, around half of cloned embryos develop to the point where they can be implanted, and only a tenth of these survive to birth. Often more than a hundred nuclear transfers must be carried out to create a single **clone.**

Scientists usually start with a batch of 150 eggs, and denucleate them one at a time before moving on to the next step. That means eggs can be left sitting around for several hours, a delay that may reduce success rates.

But the nuclear transfer array developed at Aegen Biosciences, by the company's founders Richard Kuo and Gregory Baxter, could handle hundreds or even thousands of eggs at once. Kuo says they can routinely denucleate 30 to 50 sea urchin eggs at a time. They plan to start testing cow eggs in the next few weeks.

The prototype is a thin silicon slice a few centimetres across etched with hundreds of tiny wells, one for each egg. The trick is to spin the chip in a centrifuge, forcing the eggs' dense nuclei through a small hole at the bottom of each well. About 90 per cent of the eggs can be successfully denucleated this way, Kuo says.

Kuo and Baxter are now working on the next step, which is to fuse a donor cell with the denucleated egg. A lid with appropriately positioned donor cells will be placed on top of the eggs. "Then they're ready to fuse," says Kuo, although he won't reveal details of the method. After fusion, eggs that develop far enough could be implanted manually into an animal's womb as normal.

"If it works with cow (eggs), that would be very neat," says Rudolph Jaenisch of MIT, who

studies problems with cloning. But just because it works with sea urchins doesn't guarantee that it will work with the eggs of other species, he warns.

And Randall Prather of the University of Missouri, whose team recently announced the cloning of miniature pigs, says the chip won't help solve other problems, such as ensuring that the eggs you use have been kept in the right conditions. He thinks it might also be too expensive for many labs.

Kuo admits there is much work still to be done on the chip, but he believes it's worth the effort. One could submit different batches of eggs to various treatments, to find out which conditions improve success rates in cloning, he says. Such studies could also help researchers identify the factors in eggs that reprogram the added nucleus.

If the chip does improve success rates in animals, it is likely to be used to create cloned human embryos, where the problem is not dealing with many eggs at a time but getting hold of sufficient numbers of eggs. Companies such as Advanced Cell Technology hope to obtain embryonic stem cells from cloned embryos but have had only limited success (New Scientist, 1 December 2001, p 4).

The chips might also appeal to the mavericks who want to carry out human reproductive cloning despite all the warnings about the risks. The warnings are based on the health problems seen in the few **clones** that do survive, which have also prompted the FDA to ask companies not to sell food from **clones** until it has been proved to be safe.

For more science news see http://www.newscientist.com

LOAD-DATE: January 31, 2002

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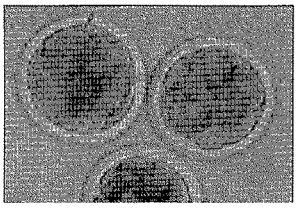
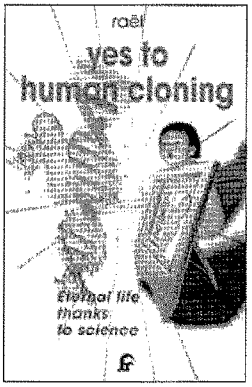
Welcome to CLONAID™ – the first human cloning company ! CLONAID™ was founded in February 1997 by Raël who is the leader of the Raelian Movement, an international religious organization which claims that life on Earth was created scientifically through DNA and genetic engineering by a human extraterrestrial race whose name, Elohim, is found in the Hebrew Bible and was mistranslated by the word "God". The Raelian Movement also claims that Jesus was resurrected through an advanced cloning technique performed by the Elohim.

Raël has handed over the CLONAID™ project one year ago to Dr Brigitte Boisselier, Raelian Bishop, who is now CLONAID's™ Managing Director. Dr. Brigitte Boisselier has founded a new company that is now carrying out the CLONAID™ projects as well as other projects presented herein. The name and the location of this company are currently kept secret for obvious security reasons.

Human clone embryos





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Three years ago, Raël, the well-known spiritual leader of the Raelian Movement, the world's largest UFO-related organisation counting 55,000 people in 84 countries, founded Clonaid, the first company offering to clone human beings. In this book, he explains how today's cloning technology is the first step in the quest for eternal life.

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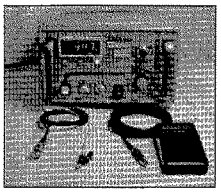
CLONAID's™ main goal is to give life to the first human clone. On top of that CLONAID™ is offering a range of services like creating personal stem cells, INSURACLONE™, OVULAID™ and CLONAPET™ . A more detailed description of these services can be found in the "Services" section. Last but not least, CLONAID™ is also selling an embryonic cell fusion system RMX568 that our scientists have developped themselves. Thanks to this new device we have achieved extraordinary results in creating hundreds of blastocysts already as can be seen in the "Products" section.



CLONAID™ , the first company in the world to offer human cloning, expects to have over a million customers worldwide interested in its services as well as many laboratories to seek partnership with in this venture.

"Cloning will enable mankind to reach eternal life. The next step, like the Elohim do with their 25,000 years of scientific advance, will be to directly clone an adult person without having to go through the growth process and to transfer memory and personality in this person. Then, we wake up after death in a brand new body just like after a good night sleep!" Raël

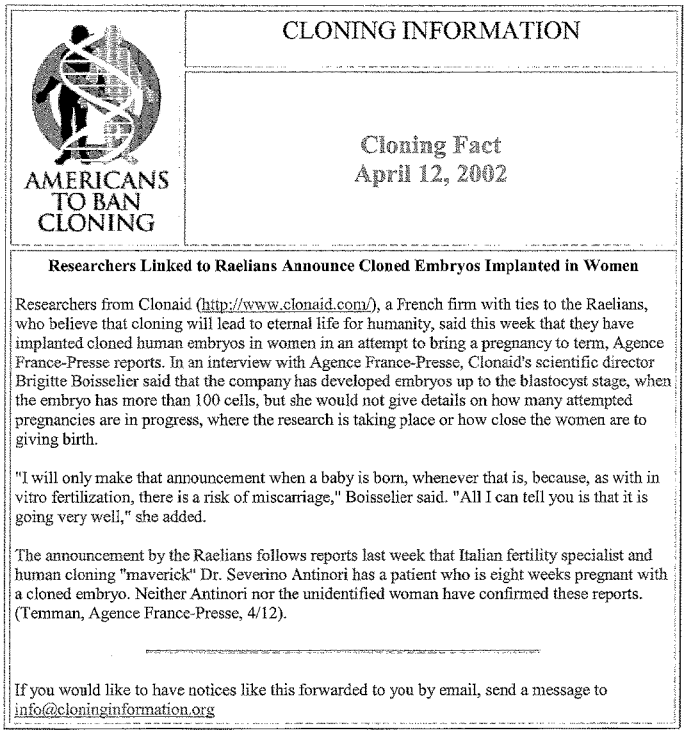
If you are interested in CLONAID™ or any of its services please contact us at help@clonaid.com.

For any media interview please contact Nadine Gary, Public relations, Phone: +1-702-497-9186

ourselves, the next step will be to transfer our memory and personality into our newly cloned brains, which will allow us to truly live forever. Since we will be able to remember all our past, we will be able to accumulate knowledge ad infinitum.

Thus today, man's ultimate dream of eternal life, which past religions only promised after death in mythical paradise, becomes a scientific reality. Raël, with exceptional vision, allows us an extraordinary glimpse into an amazing future and explains how our nascent technology will revolutionize our world and transform our lives. For example, he describes how nanotechnology will make agriculture and heavy industry redundant, how super-artificial intelligence will quickly perform human intelligence, how eternal life in a computer will be possible whitout the need for any biological body, and much, much more.

And as Raël says, don't be mistaken in thinking that this is 22nd-century science fiction. All this will happen within the next 20 years! This is a book written to prepare us for an unimaginably beautiful world, turned into a paradise, where no one needs work anymore!



CLONING INFORMATION

Cloning Fact
April 12, 2002

Researchers Linked to Raelians Announce Cloned Embryos Implanted in Women

Researchers from Clonaid (http://www.clonaid.com/), a French firm with ties to the Raelians, who believe that cloning will lead to eternal life for humanity, said this week that they have implanted cloned human embryos in women in an attempt to bring a pregnancy to term, Agence France-Presse reports. In an interview with Agence France-Presse, Clonaid's scientific director Brigitte Boisselier said that the company has developed embryos up to the blastocyst stage, when the embryo has more than 100 cells, but she would not give details on how many attempted pregnancies are in progress, where the research is taking place or how close the women are to giving birth.

"I will only make that announcement when a baby is born, whenever that is, because, as with in vitro fertilization, there is a risk of miscarriage," Boisselier said. "All I can tell you is that it is going very well," she added.

The announcement by the Raelians follows reports last week that Italian fertility specialist and human cloning "maverick" Dr. Severino Antinori has a patient who is eight weeks pregnant with a cloned embryo. Neither Antinori nor the unidentified woman have confirmed these reports. (Temman, Agence France-Presse, 4/12).

If you would like to have notices like this forwarded to you by email, send a message to info@cloninginformation.org

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April 12, 2002 Friday

SECTION: Domestic, non-Washington, General News

LENGTH: 457 words

HEADLINE: Raelians launch first attempts at human cloning

BYLINE: FRANCIS TEMMAN

DATELINE: WASHINGTON, April 11

BODY:
Scientists from Clonaid, a firm linked to the Raelian movement, say they have implanted the first cloned human embryos in women in the hope of bringing the first human **clone** into the world.

"We have developed human embryos up to the blastocyst stage" -- a stage generally about five or six days after fertilization at which the embryo is made up of more than 100 cells, French researcher Brigitte Boisselier, Clonaid's scientific director, told AFP in a telephone interview.

"When they are well-developed, we implant them." But she cautioned: "When I say that we are doing this, we are doing it, but I cannot tell you where we are in terms of an actual birth."

She would not give further details about the process being conducted in a secret location, and declined to confirm whether the attempted pregnancies were successful or how many were in progress.

"I will only make that announcement when a baby is born, whenever that is," Boisselier said, "because, as with in vitro fertilization, there is a risk of miscarriage.

"All that I can tell you is that it is going very well."

Earlier this week, Clonaid revealed that a 59-year-old man in the terminal phase of an incurable disease has asked Raelians to **clone** him.

A previous cloning candidate, US lawyer Mark Hunt, dropped an effort to have his dead baby cloned, after having invested 500,000 dollars, due to the storm of press coverage and public outcry.

Inspectors from US government regulatory agency the Food and Drug Administration raided the Raelian's secret laboratory in West Virginia, Hunt's home state, and seized documents.

The Raelians, who claim 55,000 followers worldwide, believe that life on Earth was established by extraterrestrials who arrived in space ships 25,000 years ago and that humans themselves were created by cloning.

The movement's founder, Rael -- the former French journalist Claude Vorilhon -- lives in Quebec. He describes himself as a prophet in the line of Moses or Mohammed and claims that cloning will enable humanity to attain eternal life.

The Raelians' efforts mirror other cloning attempts around the globe.

The English-language daily Gulf News reported on April 3 that a maverick Italian fertility expert, Severino Antinori, announced to a conference that one of his patients was eight weeks pregnant with a **clone.**

The details have not been confirmed either by Antinori or the unidentified woman.

And British scientists have received the go-ahead to **clone** human embryos for research, raising the prospect of Britain establishing the world's first bank of human stem cells as early as next year.

US President George W. Bush Wednesday endorsed legislation to make human cloning illegal in the United States.

LOAD-DATE: April 12, 2002

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Courier Mail

April 11, 2002, Thursday

SECTION: WORLD; Pg. 12

LENGTH: 422 words

HEADLINE: Dying man in bid for clone

SOURCE: AP/AFP

BODY:
WASHINGTON: A 59-year-old man in the terminal phase of an incurable disease had asked the **Raelian** movement to clone him, the human cloning company Clonaid has revealed.

"The new candidate is a wealthy 59-year-old man who is single and has no children. He is suffering from an incurable disease," said Nadine Gary, a spokeswoman for Clonaid -- a firm linked to the religious group, which bases its beliefs on encounters with extra-terrestrials. The news broke as opponents of cloning research began a push to outlaw all forms of human cloning, including experiments aimed at helping patients produce their own tissue and organ transplants.

In a speech at the White House today, President George W. Bush is expected to ask the Senate to pass legislation that would ban all human cloning experiments. Supporters of the Bill were planning their own gatherings, replete with movie stars, ethicists, religious leaders and scientists.

The House of Representatives has already passed a comprehensive ban on human cloning, including so-called therapeutic cloning that involves making a very early embryo from a patient's cells and using it as a source of stem cells.

The latest Clonaid effort is being directed by French chemist Brigitte Boisselier, 45, the scientific director of the organisation, and carried out in a new laboratory in a secret location, according to the **Raelians.**

The man, whose identity has not been disclosed, "will bequeath half of his wealth to the surrogate mother who will give birth to his clone, and the other half to the newborn child", they said in a statement.

The movement has several surrogate mothers at the present time, including Ms Boisselier's daughter Marina, Ms Gary said.

"As soon as the baby is born, the man will stop taking medication, which will most likely put an end to his life because the side effects and suffering caused by the disease are unbearable," she said.

A previous cloning candidate, US lawyer Mark Hunt, dropped an effort to have his dead baby cloned, after having invested $US500,000 ($956,000), due to the storm of press coverage and public outcry.

Inspectors from US government regulatory agency the Food and Drug Administration raided the **Raelian's** secret laboratory in West Virginia,

Mr Hunt's home state, and seized documents.

The **Raelians,** who claim 55,000 followers worldwide, believe that life on Earth was established by extra-terrestrials who arrived in flying saucers 25,000 years ago, and that humans themselves were created by cloning.

LOAD-DATE: April 10, 2002

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Biotech Week
April 3, 2002
SECTION: EXPANDED REPORTING; Pg. 23

INTERNATIONAL RAELIAN MOVEMENT:
Rael announces a new candidate for human cloning

Rael, leader of the International Raelian Movement, recently announced during a press conference in London that Clonaid, the company claiming to be in the process of giving birth to the first human clone, has a new project and a new candidate for cloning.

Last year, American lawyer Mark Hunt gave up on the project to clone his 2-year-old deceased son after strong pressures from the U.S. Food and Drug Administration and, as a result, closed the laboratory that he was renting in the U.S.

The new candidate is a wealthy 59-year-old man who is single and has no children. He is suffering from an incurable disease and will bequeath half of his wealth to the surrogate mother who will give birth to his clone and the other half ! to the newborn child.

As soon as the baby is born, the man will stop taking medication which will most likely put an end to his life because the side effects and suffering caused by the disease are unbearable. The new Clonaid laboratory is in a secret location.

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Los Angeles Times

June 30, 2001 Saturday Home Edition

SECTION: Part A; Part 1; Page 12; National Desk

LENGTH: 299 words

HEADLINE: THE NATION;
;
Group's Human **Cloning** Efforts Hit FDA Snag

BYLINE: AARON ZITNER, TIMES STAFF WRITER

DATELINE: WASHINGTON

BODY:
An obscure religious group said Friday that it would move its efforts to clone a human being offshore after the Food and Drug Administration paid a surprise visit to its laboratory and warned that **cloning** could not be done without agency permission.

Brigitte Boisselier, who leads the Raelian Movement's **cloning** project, said FDA officials discovered the secret location of the lab and made an inspection in mid-April. She said that technicians there were working with biological material from cows, which is legal. "They couldn't find a human egg, and so they couldn't shut us down," Boisselier said. "In fact, the lab is still running here in the U.S., and we are still doing things that are legal."

FDA spokesman Lawrence Bachorik said Boisselier had signed an agreement "not to attempt **cloning** in the United States and not to do research using human eggs in the United States until the legality of human **cloning** is ascertained" by Congress or federal courts.

Human **cloning** is barred in several states, and Congress is now deciding whether to make it a federal crime.

The Raelian **cloning** effort received wide attention in March, when Boisselier discussed it at a congressional hearing. She told lawmakers that the group had established a laboratory, hired staff and intended to work toward **cloning** a boy who had died of a heart defect at the age of 10 months.

Boisselier, who is a chemist, said the group may go to federal court to challenge the FDA's jurisdiction over **cloning.**

Neither Boisselier nor the FDA would give the location of the lab.

Raelians are led by Frenchman Claude Vorilhon, who took the name Rael after claiming that he witnessed a UFO landing in 1973. He says that aliens created humanity and that humans must in turn create life through **cloning.**

The Associated Press

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June 29, 2001, Friday, BC cycle

SECTION: Washington Dateline

LENGTH: 435 words

HEADLINE: Doctor agrees not to try human **cloning,** for now

DATELINE: WASHINGON

BODY:
A researcher who had been preparing to work on human **cloning** has agreed not to attempt an experiment or research until the legality of the effort is determined, the Food and Drug Administration reported.

FDA spokesman Lawrence Bachorik said Friday that his agency has inspected a lab set up by Brigitte Boisselier in an effort to attempt human **cloning.**

She signed a statement committing not to attempt human **cloning** and not to do research using human eggs until the legality of human **cloning** is determined, Bachorik said. Lawmakers have been preparing legislation to outlaw human **cloning.** In the meantime, FDA has insisted that no experiments can go forward without its approval.

That hasn't discouraged a religious organization called the Raelian Movement, which argues that life on Earth was created by extraterrestrial scientists.

Its leader, Rael, started a lab - directed by Boisselier - where he vowed to clone a human somewhere in the United States.

Another group, led by an Italian fertility doctor, is promising to find another country where **cloning** is legal. Both teams say they have people ready to volunteer for the first human effort.

In its issue due on newsstands Monday, U.S. News & World Report says that a federal grand jury in Syracuse, N.Y., is investigating the Raelian lab.

Bachorik declined to say where the lab is located. Boisselier formerly taught chemistry at Hamilton College in Clinton, N.Y.

Boisselier told a House energy and commerce subcommittee in March that her lab had received a letter from FDA warning that it would be against the law to proceed with **cloning** without permission.

At that time she said she did not know whether the company operating the lab, Clonaid, would proceed

anyway.

She dismissed safety concerns, saying the problems have all come in **cloning** animals and do not apply to potential human **cloning.** She said she was working with a father who was devastated by the death of his son and wants to clone him.

The FDA says any human **cloning** experiments in the United States would need its approval and, based on safety concerns, the agency would not approve any applications at this time.

Clones are created when the genetic material from a single cell is injected into an egg cell that has had its genes removed. The resulting baby would be like an identical twin born years later.

Ethicists note that the clone would not be a copy of the original person. He or she would grow up in a different environment at a different time, said Arthur Caplan, director of the Center for Bioethics at the University of Pennsylvania.

LOAD-DATE: June 30, 2001

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Genomics & Genetics Weekly

April 12, 2002

SECTION: EXPANDED REPORTING; Pg. 14

LENGTH: 638 words

HEADLINE: CLONING: Commercial cloning of pets two years away, company said

BODY:
The day when Fluffy the cat or Spot the dog can be commercially cloned is only about two years off, according to the company that funded the first cloning of a cat.

But the ethical and moral debate about pet cloning is well under way.

Sausalito, California-based Genetic Savings & **Clone** already announced its work with Texas A & M University's veterinary medicine school in College Station to **clone** a cat was successful with the December 22, 2001, birth of a female domestic shorthair called "cc" for "copycat."

Lou Hawthorne, chief executive officer of Genetic Savings & **Clone,** said researchers expect to successfully **clone** a dog by the end of the year. Commercial cloning of cats and dogs is expected within two years. While the cost at first will probably be somewhere in the low five figures, it will eventually drop into the low four figures, he said.

"We're committed to affordable cloning for pet species. But we can't lose money on it," said Hawthorne, whose company will have spent $5 million on the project by the time a dog is cloned. "We're looking at factory methodologies ... automating aspects of cloning that are not automated right now."

The company has hundreds of gene samples from pets already stored, at a cost of $895 for a healthy animal and $1395 for a sick or dead animal.

Hawthorne said he doesn't think the cloning of pets will create a technical stepping stone to human cloning, which the company is against.

But since the announcement of cc's birth, animal activists, bioethicists and others have expressed concerns about what pet cloning could do to efforts to reduce the number of unwanted animals at shelters and create change in the use of animals for research.

During a conference call organized by the company, Hawthorne debated these various issues with two professors.

David Magnus, assistant professor of bioethics at the University of Pennsylvania, said he believed the company is misleading its customers by creating the idea that their pets can be brought back in some way.

"You're telling them you can help make it better by not letting go of their pets," Magnus said. "For a lot less money you can rescue an animal" at a shelter.

Hawthorne said he believes cloning will make a pet owner's grieving process more manageable.

"We're crystal clear a **clone** is not a reincarnation," he said. "There will be differences in behavior, intelligence and temperament."

Brandy Norton, a company customer who had a Maltese named Chopin for 17 years, said she sees cloning as a chance to recapture her special pet.

"I realize it's not going to be the same dog," said Norton, who lives in Palm Springs, California, and did purchase another puppy after her dog died. "I hope personality is genetically based."

Lori Gruen, an assistant professor of philosophy at Wesleyan University in Connecticut, said she worries about whether there is enough external oversight of Genetics Savings & **Clone** and similar companies as they develop this new technology.

"If this technology is going to go ahead, you must have a commitment on the part of the company to do as much as it can to reduce (the unwanted animal) population," she said.

Hawthorne said his company is committed to reducing this population, as it funds clinics that spay pets as part of its research.

The kitty **clone** was the only success after transferring 87 cloned embryos into eight female cats. Other mammals cloned before include sheep, cattle, goats, pigs and mice.

The work was an offshoot of the Missyplicity Project, a $3.7 million effort to **clone** a mixed-breed pet dog named Missy.

This article was prepared by Genomics & Genetics Weekly editors from staff and other reports.

http://www.NewsRx.net

LOAD-DATE: April 5, 2002

PR Newswire
July 22, 2002, Monday 7:00 AM Eastern Time

Raelians Are First to Commercialize A Cloning Machine

DATELINE: NEW YORK, July 22

The following was released today by the Raelian Religion:

CLONAID, the company created by Rael to clone the first human being, is now selling the first cloning machine developed and manufactured by a team of Korean Raelian scientists. Nicknamed RMX 2010, this machine, which allows cellular fusion, can also be purchased on the internet for only $9,199 see http://www.clonaid.com).

RAEL said: "Not only are we hoping to be the first to clone a human being, but we also want to contribute so that the cloning efforts can multiply everywhere on the planet, helping to cure all diseases and improve the human race. The fact that the U.S. has refused to pass an anti-cloning law is a huge victory, in addition to the fact that 5 countries are now fully engaged in cloning: China, Sweden, UK, Israel and Saudi-Arabia. All the countries that ban cloning end up exiling their 'brains' and as a result will fall far behind and that's too bad for them."

For all interviews with Rael, please contact his press attache:

Sylvie Chabot at 514-366-3734
pr@rael.org
http://www.rael.org/press

SOURCE Raelian Religion

CONTACT: Sylvie Chabot of the Raelian Religion, +1-514-366-3734, pr@rael.org

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International

Leading IVF Doctor Might Support Cloning

By Mike Wendling
CNSNews.com London Bureau Chief
June 13, 2002

London (CNSNews.com) - Cloning skeptics reacted harshly Thursday to comments made by a leading in-vitro fertilization doctor who said he might support reproductive cloning in humans to allow infertile couples to have children.

Professor Robert Edwards, who pioneered IVF treatment in the late 70s, said that if the abnormalities seen in cloned animals can be avoided, he would favor creating human clones.

Edwards told the London *Daily Telegraph* that there was a "glimmer of hope" of overcoming the abnormalities in recent work on rabbits. If the research is successful, he said it might then be possible to help an infertile couple to have a cloned child.

Edwards' work led to the birth of the first IVF baby, Louise Brown, in July 1978. Since then, more than 1 million IVF babies have been born worldwide and the technique has become a standard practice.

In 1998, Queen Elizabeth honored him for his research in the field. Edwards is currently retired, but anti-cloning activists said Thursday that he still holds influence among scientists studying infertility.

"He is the king of IVF scientists," said Josephine Quintavalle, director of Comment on Reproductive Ethics (CORE). "From this we can see that a lot of enthusiasm for cloning is going to translate into reproductive cloning. A lot of prestigious scientists agree with him."

CORE supporters have mixed views on IVF treatments, with some agreeing with them within certain guidelines and some opposing them altogether, Quintavalle said. But she noted that many treatments wouldn't be needed if factors that decreased fertility such as smoking, obesity age of childbirth were to be addressed.

"If you looked at the causes of infertility and addressed them, you'd be left with only a handful of cases where IVF and other treatments would be needed to produce a child," she said.

Quintavalle said that no matter how safe cloning could be made in animals, applying the same techniques to humans would be treading into unknown territory.

"We might not feel too worried about killing a cow halfway through gestation if a fetus is too big ... but are we going to look for women to experiment on in these ways?" she asked.

The problems of testing cloning techniques on humans were also raised by scientific watchdog agency

Genewatch UK. Genewatch spokeswoman Dr. Helen Wallace said reproductive cloning would be a "pretty dangerous experiment."

"Even if you could correct the problems with cloning in animals, which I seriously doubt, you would still have to perform an experiment with the risk of significant suffering in humans," she said.

In addition to the scientific problems, Wallace said there are "broader social issues" at stake, including whether it would be desirable to essentially choose the genetic makeup of children by copying parents.

In the *Telegraph* interview, Edwards said he admired some of the work of controversial Italian doctor Severino Antinori, including Antinori's fertility treatments on women who were beyond their natural reproductive years.

"He did a very nice piece of work on getting pregnancies in ladies up to the age of 62," Edwards reportedly said. "Some people might think that is bad but the ladies themselves don't think it's bad and I think the ladies who want their desperate last chance of pregnancy in their 50s are to be supported."

Antinori claims that three women worldwide are pregnant with cloned embryos - claims that other scientists have said are baseless. Edwards said he recently talked with Antinori about the alleged clones and expressed doubts about the current state of cloning technology.

"I have told him my own opinion is that I wouldn't object to him saying he was going to clone a child, provided all the embryos after cloning are as normal as those after normal conception," Edwards said. "He can't say that at the moment. No one can."

Implanting a human clone into a woman's uterus is banned in the U.K., and all human cloning research is currently on hold pending an appeal by the Pro-Life Alliance. The Alliance is hoping to use its lawsuit to expose loopholes in the U.K.'s cloning ban and force a full-scale debate in Parliament.

"It is impossible not to compare the seriousness with which cloning has been confronted in the U.S.A., in comparison to the shoddy efforts to allow it in by the back door in our country," an Alliance spokesman said.

E-mail a news tip to Mike Wendling.

Send a Letter to the Editor about this article.

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Scientists Say "Therapeutic Cloning" Creates a Human Embryo
July 26, 2001

** President Clinton's National Bioethics Advisory Commission, in its 1997 report *Cloning Human Beings*, explicitly stated:

> "The Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo, with the apparent potential to be implanted in utero and developed to term."

** The National Institutes of Health Human Embryo Research Panel also assumed in its September 27, 1994 Final Report, that cloning results in embryos. In listing research proposals that "should not be funded for the foreseeable future" because of "serious ethical concerns," the NIH panel included cloning:

> "Such research includes: . . . Studies designed to transplant embryonic or adult nuclei into an enucleated egg, including nuclear cloning, in order to duplicate a genome or to increase the number of embryos with the same genotype, with transfer."

** A group of scientists, ethicists, and biotechnology executives advocating "therapeutic cloning" and use of human embryos for research -- Arthur Caplan of the University of Pennsylvania, Lee Silver of Princeton University, Ronald Green of Dartmouth University, and Michael West, Robert Lanza, and Jose Cibelli of Advanced Cell Technology -- confirmed in the December 27, 2000 issue of the *Journal of the American Medical Association* that a human embryo is created and destroyed through "therapeutic cloning":

> "CRNT [cell replacement through nuclear transfer, another term for "therapeutic cloning"] requires the deliberate creation and disaggregation of a human embryo."

> " . . . because therapeutic cloning requires the creation and disaggregation ex utero of blastocyst stage embryos, this technique raises complex ethical questions."

** On September 7, 2000, the European Parliament adopted a resolution on human cloning. The Parliament's press release defined and commented on "therapeutic cloning":

> ". . . 'Therapeutic cloning,' which involves the creation of human embryos purely for research purposes, poses an ethical dilemma and crosses a boundary in research norms."

** Lee M. Silver, professor of molecular biology and evolutionary biology at Princeton University, argues in his 1997 book, *Remaking Eden: Cloning and Beyond in a Brave New World*:

> "Yet there is nothing synthetic about the cells used in cloning . . . . The newly created embryo can only develop inside the womb of a woman in the same way that all embryos and fetuses develop. Cloned children will be full-fledged human beings, indistinguishable in biological terms from all other members of the species."

** The President and CEO of the biotechnology firm that recently announced its intentions to clone human embryos for research purposes, Michael D. West, Ph.D. of Advanced Cell Technology, testified before a Senate Appropriations Subcommittee on December 2, 1998:

> "In this . . . procedure, body cells from a patient would be fused with an egg cell that has had its nucleus (including the nuclear DNA) removed. This would theoretically allow the production of a blastocyst-staged embryo genetically identical to the patient . . . ."

** Dr. Ian Wilmut of PPL Technologies, leader of the team that cloned Dolly the sheep, describes in the Spring 1988 issue of *Cambridge Quarterly of Healthcare Ethics* how embryos are used in the process now referred to as "therapeutic cloning":

> "One potential use for this technique would be to take cells -- skin cells, for example -- from a human patient who had a genetic disease . . . . You take this and get them back to the beginning of their life by nuclear transfer into an oocyte to produce a new embryo. From that new embryo, you would be able to obtain relatively simple, undifferentiated cells, which would retain the ability to colonize the tissues of the patient."

** As documented in the *American Medical News*, February 23, 1998, University of Colorado human embryologist Jonathan Van Blerkom expressed disbelief that some deny that human cloning produces an embryo, commenting: "If it's not an embryo, what is it?"

Order Code RL31358

Report for Congress

Received through the CRS Web

Human Cloning

Updated May 2, 2002

Judith A. Johnson
Specialist in Life Sciences
Domestic Social Policy Division

Human Cloning

Summary

On November 25, 2001, a Massachusetts company, Advanced Cell Technology (ACT), announced that it had created the world's first cloned human embryos. The cloned embryos survived only for a few hours. ACT has indicated that it intends to use such embryos to derive stem cells in producing new therapies for diseases like diabetes and Parkinson's disease. The possibility of using cloning technology not just for therapeutic purposes but also for reproducing human beings raises profound moral and ethical questions.

President Bush announced in August 2001 that for the first time federal funds will be used to support research on human embryonic stem cells, but funding will be limited to "existing stem cell lines." President Bush indicated that he is strongly opposed to human cloning, and that federal funds will not be used for the cloning of human embryos for any purpose, including stem cell research. The Bush Administration established The President's Council on Bioethics on November 28, 2001, "to consider all of the medical and ethical ramifications of biomedical innovation." In January 2002 the 18-member Council held its first meeting and Chairman Leon Kass announced that the first topic to be addressed would be human cloning. At the second (February 2002) and third (April 2002) meetings the discussion of human cloning and stem cell research was continued.

On January 18, 2002, the National Academies released its report entitled *Scientific and Medical Aspects of Human Reproductive Cloning*. The panel recommends that the U.S. ban human reproductive cloning that is aimed at creating a child. It suggests the ban should be legally enforceable and carry substantial penalties rather than rely on voluntary actions. It should be reconsidered within 5 years, but only if compelling new data on safety and efficacy are presented and a national dialogue on the social and ethical issues suggests that a review is warranted. However, the panel concluded that research using cloning procedures to produce stem cells should be permitted because of the considerable potential for developing new therapies and advancing biomedical knowledge. This position is in agreement with a previous National Academies' report entitled *Stem Cells and the Future of Regenerative Medicine* which was released on September 11, 2001.

On July 31, 2001, the House passed H.R. 2505 by a vote of 265-162. The bill would ban the process of human cloning as well as the importation of any product derived from an embryo created via cloning. The provisions mean that cloning could not be used for reproductive purposes or for research on therapeutic purposes, which has implications for stem cell research. The Senate is expected to debate the various legislative proposals concerning human cloning in May 2002. S. 1899 (Brownback) is the companion bill to H.R. 2505. On April 10, 2002, President Bush announced his support for S. 1899 and 40 Nobel Laureates, who are in favor of nuclear transplantation technology for research and therapeutic purposes, announced their opposition to the Brownback bill. Senators Arlen Specter, Dianne Feinstein, Orrin Hatch and Edward Kennedy introduced S. 2439 on April 30, 2002. S. 2439 would prohibit human reproductive cloning while allowing cloning for medical research purposes, including stem cell research. This report will be updated as needed.

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Human Cloning

Background

The term "cloning" is used by scientists to describe many different processes that involve making copies of biological material, such as a gene, a cell, a plant or an animal. The cloning of genes, for example, has led to new treatments developed by the biotechnology industry for diseases such as diabetes and hemophilia. In the context of this report, a human embryo produced via cloning involves the process called somatic[1] cell nuclear transfer (SCNT). In SCNT, the nucleus of an egg is removed and replaced by the nucleus from a mature body cell, such as a skin cell. In cloning, the embryo is created without sexual reproduction.

Concern over the possibility of producing a human clone increased with the announcement on February 24, 1997, that scientists in Scotland had used SCNT in 1996 to produce the first cloned adult mammal, Dolly, the sheep. Scientists at the Roslin Institute in Edinburgh removed the nucleus from a sheep egg and replaced it with the nucleus of a mammary gland cell from an adult sheep. The resulting embryo was then transferred to the uterus of a surrogate sheep. A total of 277 such embryos were transferred, but only one lamb was born.[2] Analyses of Dolly's genetic material confirmed that she was derived from the sheep mammary cell. Proponents maintain that cloning could be used for a number of significant agriculture applications, including the improvement of livestock.

On November 25, 2001, Advanced Cell Technology (ACT) of Massachusetts announced that it had created the world's first human embryos produced via cloning; the results were published the following day in an electronic journal.[3] ACT used two techniques to produce human embryos — SCNT and a second process called parthenogenesis. ACT researchers obtained eggs from seven women, ages 24 to 32, who were paid $3000 to $5000. In the SCNT approach, scientists removed the nucleus from 19 eggs and replaced it with a nucleus from another adult cell. For 11 of the eggs, the nucleus came from a skin cell, for the remaining eight eggs, from cells which cling to the egg and are called cumulus cells. None of the eggs that received a skin cell nucleus divided; seven of the eggs with the cumulus cell nucleus began to divide. Two embryos divided into four cells each, and one embryo divided into six cells before division stopped. In parthenogenesis, an egg cell is treated with

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[1] A somatic cell is a body cell, as opposed to a germ cell, which is an egg or sperm cell.

[2] Wilmut, I., et al. Viable Offspring Derived From Fetal and Adult Mammalian Cells. *Nature*, v. 385, February 27, 1997. p. 810-813.

[3] Cibelli, J.B., et al. Somatic Cell Nuclear Transfer in Humans: Pronuclear and Early Embryonic Development. *Journal of Regenerative Medicine*, v. 2, November 26, 2001. p. 25-31.

chemicals causing it to divide without being fertilized by a sperm. ACT exposed 22 human eggs to the chemicals. After 5 days, six eggs had matured into a larger mass of cells before division stopped. None of the embryos developed by ACT through cloning divided sufficiently to produce stem cells.

The stated goal of ACT's work is not to produce a cloned human baby (which requires implantation of the cloned embryo into a woman's uterus), but human embryonic stem cells.[4] Other research groups have derived stem cells from mice and cattle using SCNT. ACT intends to derive stem cells from human embryos to develop new therapies for diseases such as diabetes and Parkinson's disease. Some scientists believe that stem cells transplanted into a patient could treat disease or injury by replacing damaged tissue. If the cell nucleus used in SCNT is from the patient, the stem cells would be genetically identical to the patient, recognized by the patient's immune system, and avoid any tissue rejection problems that could occur in other stem cell therapeutic approaches. Because of this, many scientists believe the SCNT technique may provide the best hope of eventually treating patients using stem cells for tissue transplantation. A California biotechnology company, Geron Corporation, is also working on stem cells created via SCNT.[5]

Ethical and Social Issues

The possibility of using cloning technology not just for therapeutic purposes but also for reproducing human beings raises profound moral and ethical questions. In response to the creation of Dolly and concerns about the potential application of cloning humans, on February 24, 1997, President Clinton asked the National Bioethics Advisory Commission[6] (NBAC) to review the ethical and legal issues associated with the use of cloning technology; NBAC reported its findings and recommendations on June 9, 1997.[7] NBAC recommended a continuation of the moratorium on the use of federal funding in the support of any attempt to create a child by SCNT, and an immediate request to all non-federally funded investigators to comply voluntarily with the intent of the federal moratorium. NBAC also recommended that federal legislation be enacted, with a 3- to 5- year sunset clause, to prohibit anyone from attempting to create a child through the use of SCNT in a research or clinical setting. The NBAC found it morally unacceptable to attempt to clone humans for the purpose of human reproduction because scientific data from

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[4] For more information about stem cells, see CRS Report RL31015, *Stem Cell Research*, by Judith A. Johnson.

[5] Weiss, R. Embryo Work Raises Spector of Human Harvesting. *Washington Post*, June 14, 1999. p. A01.

[6] NBAC was established by Presidential Executive Order 12975 on October 3, 1995, to provide guidance to federal agencies on the ethical conduct of current and future human biological and behavioral research. A September 16, 1999 executive order extended the NBAC charter until October 2001. NBAC has been replaced by the President's Council on Bioethics, which was described by the Bush Administration in its August 9, 2001 policy decision on human embryonic stem cell research. The President's remarks on embryonic stem cell research are available at:
[http://www.whitehouse.gov/news/releases/2001/08/20010809-2.html].

[7] National Bioethics Advisory Commission. *Cloning Human Beings*. June 1997.

animal experiments indicate the method is not safe for mother or baby. In addition to concerns about physical safety, the NBAC report pointed out that SCNT raises issues about the individuality, autonomy, objectification and kinship of the resulting children.

Cloning, if allowed for human reproduction, could affect society's perception of what it means to be a human being. Uncertainties over a cloned individual's personal uniqueness or freedom to create one's own identity may haunt him or her. Relatives or friends could have specific expectations regarding the cloned individual's talents and abilities. Others might ill treat or discriminate against a cloned individual. Some worry that cloning would lead to diminished respect for human life in general, and for cloned individuals in particular, since the cloned person might simply be replaced with another clone. Others point out, however, that this altered perception does not occur today with identical twins, who are naturally produced clones. Cloning human embryos also raises difficult questions about the rights of parents to control their own embryos and other issues concerning reproductive rights and privacy. Some observers believe that it would be ethical to clone human embryos to help infertile couples conceive. Lastly, the possibility of human cloning is offensive to the religious and other deeply held beliefs of many people.

On January 7, 1998, a Chicago scientist, Dr. Richard Seed, announced his intention to clone a human being. In response, bills were introduced in Congress that would have banned human cloning indefinitely or imposed a moratorium. The legislation was opposed by a number of medical organizations, the biotechnology industry and many scientists and was not enacted. Others expressing an interest in reproductive cloning include: (1) Clonaid, a company directed by chemist Brigitte Boisselier and formed by the Raelians, a group that believes humans are descendants of extraterrestrials and that cloning can allow humans to become immortal; and, (2) Panos Zavos, of the University of Kentucky, and Severino Antinori, director of a fertility clinic in Rome, who are working together to help infertile couples have children via cloning. In April 2002, there were unconfirmed reports in the media that both Clonaid and Severino Antinori had implanted cloned human embryos in women. Dr. Severino claims there are 3 such pregnancies of 6 to 9 week duration; 2 in Russia and 1 in an Islamic state. His claim has been disputed by his former partner, Panos Zavos. The Clonaid group would not reveal any further details about their cloning attempts.

Brief History of Federal Policy Involving Human Embryo Research

Currently no U.S. laws or regulations would prohibit all cloning research. However, federal funding of *any* type of research involving human embryos, starting with *in vitro* fertilization (IVF) then later cloning and stem cells, has been blocked by various policy decisions dating back 25 years. Following the birth of the first IVF baby, Louise Brown, in July 1978, the Ethics Advisory Board (EAB) was tasked with

considering the scientific, ethical, legal, and social issues surrounding human IVF.[8] The EAB released its report on May 4, 1979, which found that IVF research was acceptable from an ethical standpoint and could be supported with federal funds. The EAB's recommendations were never adopted by HHS, the EAB was dissolved in 1980, and no other EAB was ever chartered. Because federal regulations that govern human subject research (45 CFR 46) stipulated that, at the time, federally supported research involving human IVF must be reviewed by an EAB, a so-called "de facto moratorium" on human IVF research resulted. Other types of embryo research ensuing from the development and use of IVF, such as cloning and stem cells, were therefore also blocked. The de facto moratorium was lifted with the enactment of the National Institutes of Health (NIH) Revitalization Act of 1993 (P.L. 103-43, Section121(c)) which nullified the regulatory provision (45 CFR 46.204(d)) requiring EAB review of IVF proposals.

In response, the NIH established the Human Embryo Research Panel to assess the moral and ethical issues raised by this research and develop recommendations for NIH review and conduct of human embryo research. The NIH Panel released a report providing guidelines and recommendations on human embryo research in September 1994. It recommended that some areas of human embryo research be considered for federal funding, including SCNT, stem cells and (under certain limited conditions) embryos created solely for the purpose of research.[9] The NIH Panel also identified areas of human embryo research it considered to be unacceptable, or to warrant additional review. It determined that certain types of cloning[10] without transfer to the uterus warranted additional review before the Panel could recommend whether the research should be federally funded. However, the Panel concluded that federal funding for such cloning techniques followed by transfer to the uterus should be unacceptable into the foreseeable future. The Panel's report was unanimously accepted by the NIH Advisory Committee to the Director (ACD) on December 2, 1994.

After the ACD meeting on December 2, 1994, President Clinton directed NIH not to allocate resources to "support the creation of human embryos for research purposes." The President's directive did not apply to research involving so-called "spare" embryos, those that sometimes remain from clinical IVF procedures performed to assist infertile couples to become parents. Nor did it apply to human parthenotes, eggs that begin development through artificial activation, not through fertilization. Following the Clinton December 2, 1994 directive to NIH, the agency

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[8] The EAB was created in 1978 by the Department of Health Education and Welfare (HEW), the forerunner of the Department of Health and Human Services (HHS). The EAB was formed at the recommendation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The National Commission operated from 1974 to 1978 and issued 10 reports, many of which formed the basis of federal regulations for research involving human subjects (45 CFR 46).

[9] National Institutes of Health. *Report of the Human Embryo Research Panel*, September 27, 1994.

[10] These were **blastomere separation**, where a two- to eight-cell embryo is treated causing the cells (blastomeres) to separate; and, **blastocyst division**, in which an embryo at the more advanced blastocyst stage is split into two.

proceeded with plans to develop guidelines to support research using spare embryos. However, these plans were halted on January 26, 1996, with the enactment of P.L. 104-99 which contained a rider that affected FY1996 funding for NIH. The rider prohibited HHS from using appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. This same rider, often referred to as the Dickey amendment, has been attached to the Labor, HHS and Education Appropriations Acts for FY1997 through FY2002.[11] Current language, Section 510 of the FY2002 Labor, HHS and Education Appropriations Act, prohibits HHS from using FY2002 appropriated funds for:

> (1) the creation of a human embryo or embryos for research purposes; or,
>
> (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and Section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). For purposes of this section, the term "human embryo or embryos" includes any organism, not protected as a human subject under 45 CFR 46 ... that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes [sperm or egg] or human diploid cells.

One month after the Dolly announcement, on March 4, 1997, President Clinton sent a memorandum to the heads of all executive departments and agencies making it "absolutely clear that no federal funds will be used for human cloning." This action extended the congressional ban beyond HHS to all federally supported research. Clinton also urged the private sector to adopt a voluntary ban on the cloning of human beings. The *NIH Guidelines on Stem Cell Research*, published by the Clinton Administration in August 2000, would not have funded research in which: human stem cells are used for reproductive cloning of a human; human stem cells are *derived* using SCNT; or, human stem cells that were derived using SCNT are *utilized* in a research project.

Bush Administration Policy Regarding Human Embryo Research

On August 9, 2001 President Bush announced that for the first time federal funds will be used to support research on human embryonic stem cells, but funding will be limited to "existing stem cell lines." In the speech, President Bush stated that he strongly opposes human cloning. Although not mentioned specifically in the August 9 speech, a fact sheet on the White House website states that federal funds

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[11] The original rider, introduced by Representative Jay Dickey, is in Section 128 of P.L. 104-99; it affected NIH funding for FY1996 contained in P.L. 104-91. For subsequent fiscal years, the rider is found in Title V, General Provisions, of the Labor, HHS and Education Appropriations Acts in the following public laws: FY1997, P.L. 104-208; FY1998, P.L. 105-78; FY1999, P.L. 105-277; FY2000, P.L. 106-113; FY2001, P.L. 106-554; and FY2002, P.L. 107-116.

will not be used for "the cloning of human embryos for any purpose."[12] In his speech, President Bush announced his intention to name a President's council, chaired by Dr. Leon Kass of the University of Chicago, "to consider all of the medical and ethical ramifications of biomedical innovation." The President's Council on Bioethics, was established for a period of up to 2 years by Executive Order 13237 on November 28, 2001. The White House announced the other 17 members of the council on January 16, 2002.

The first meeting of the President's Council on Bioethics was held on January 17-18, 2002, in Washington, D.C.[13] Dr. Kass announced that the first topic to be addressed by the Council would be human cloning. At the Council's second meeting, the terminology of cloning was discussed in order to reach a consensus on the terms used to describe the two types of cloning: reproductive vs. therapeutic or research cloning. Although all Council members voted in opposition to reproductive cloning, they could not come to an agreement on articulating the precise nature of their objection, whether solely on safety grounds or which of the various moral objections were most important. On the issue of therapeutic cloning, what the Council prefers to call research cloning, the Council also could not come to agreement. Dr. Kass proposed that the Council's final report should reflect both the arguments supporting cloning for the purpose of medical treatment and those against. He asserted that the report should also provide the soundest arguments for each position and indicate how many Council members supported each viewpoint.

The third meeting of the Council was held on April 25 and 26, 2002. The Council heard presentations on the scientific and therapeutic promise of embryonic stem cells from John Gearhart of Johns Hopkins University and the potential of adult stem cells from Catherine Verfaillie of the University of Minnesota. In an informal vote, almost half of the 18 members of the Council voiced their support for the therapeutic use of human cloning. A final report by the Council on human cloning is expected by the end of the summer of 2002.[14]

A year ago in March 2001, the Food and Drug Administration (FDA) sent letters to the research community stating that the creation of a human being using cloning is subject to FDA regulation under the Public Health Service Act and the Food, Drug and Cosmetic Act.[15] FDA stated that such research could only occur when an investigational new drug application (IND) is in effect. Some legal scholars believe that there is no legal basis for the regulation of cloning by FDA.[16] They find little

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[12] The White House Fact Sheet on embryonic stem cell research is available at: [http://www.whitehouse.gov/news/releases/2001/08/20010809-1.html].

[13] A transcript of the first meeting and papers developed by staff for discussion during the meeting can be found at [http://www.bioethics.gov].

[14] Shehzad, N. President's Bioethics Advisors Resolve to Avoid "Media Circus" as They Work on Cloning Advice." *Washington Fax*, April 30, 2002.

[15] The FDA position statement and letters to the research community are available at [http://www.fda.gov/cber/genetherapy/clone.htm].

[16] Weiss, R. Legal Barriers to Human Cloning May Not Hold Up. *Washington Post*, May

(continued...)

evidence to support FDA's position that cloned human embryos are "drugs." However, the biotechnology industry and the American Society for Reproductive Medicine believe FDA has the authority to regulate cloning and legislation is unnecessary because FDA regulation is preferred to any new action by Congress.[17]

On January 18, 2002, the National Academies released its report entitled *Scientific and Medical Aspects of Human Reproductive Cloning.*[18] The panel recommends that the U.S. ban human reproductive cloning that is aimed at creating a child. Based on the results of animal cloning experiments, the panel is concerned for the safety of both the woman and the fetus and judged the procedure to be too dangerous for use in humans at the present time. It recommends that the ban should be legally enforceable and carry substantial penalties rather than be based on voluntary actions. It should be reconsidered within 5 years, but only if compelling new data on safety and efficacy are presented and a national dialogue on the social and ethical issues suggests that a review is warranted. However, the panel concluded that research using SCNT to produce stem cells should be permitted because of the considerable potential for developing new therapies and advancing biomedical knowledge. This position is in agreement with a previous National Academies' report entitled *Stem Cells and the Future of Regenerative Medicine* which was released on September 11, 2001.[19]

Legislation

On July 19, 2001, the House Judiciary Subcommittee on Crime approved the Human Cloning Prohibition Act of 2001, H.R. 2505 (Weldon), by voice vote. The bill would ban the process of human cloning as well as the importation of any product derived from an embryo created via cloning. The provisions mean that cloning could not be used for reproductive purposes or for research on therapeutic purposes, which has implications for stem cell research. The bill includes a criminal penalty of imprisonment of not more than 10 years and a civil penalty of not less than $1 million.

On July 24, 2001, the House Judiciary Committee approved H.R. 2505 by a vote of 18 to 11 and defeated a substitute measure by a vote of 11 to19. The substitute was identical to H.R. 2608 (Greenwood), which would ban *only* human reproductive cloning; the ban would sunset after 10 years. H.R. 2608 has the same criminal and civil penalties as H.R. 2505 when cloning is used "with the intent to initiate a

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[16] (...continued)
23, 2001. p. A1.

[17] Ibid.

[18] The National Academies are the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council. The report on human cloning is available at:
[http://www.nap.edu/catalog/10285.html?onpi_topnews_011802].

[19] The National Academies' report on stem cell research is available at: [http://www.nap.edu/catalog/10195.html?onpi_topnews_091101].

pregnancy." The Bush Administration announced its support for H.R. 2505 on July 24, 2001.

On July 31, 2001, the House passed H.R. 2505 by a vote of 265-162. Prior to the vote on H.R. 2505, the House defeated a substitute amendment, H.Amdt. 285, which is identical to H.R. 2608, by a vote of 178 to 249. During debate, supporters of H.R. 2505 argued that a partial ban on human cloning, such as H.R. 2608, would be impossible to enforce. Critics of H.R. 2505 argued that SCNT creates a "clump of cells" rather than an embryo, and that the measure would curtail medical research and prevent Americans from receiving life-saving treatments created overseas.

On December 3, 2001, the Senate considered an amendment proposed by Senator Lott that would have imposed a 6-month moratorium on all human cloning research; an attempt to attach the amendment to a bill (H.R. 10) on pension contribution limits failed (Senate Roll Call vote 344).

The Senate is expected to debate the various legislative proposals concerning human cloning before the Memorial Day recess in late May.[20] S. 1899 (Brownback), the Human Cloning Prohibition Act of 2001, was introduced on January 28, 2002; it is the companion bill to H.R. 2505. S. 1899 currently has 30 cosponsors and is very similar to S. 790, a bill introduced by Senator Brownback in April 2001. At a White House press briefing on April 10, 2002, President Bush again stated his support for a prohibition on all forms of human cloning and endorsed Senator Brownback's bill.

On the same day as the White House briefing, the American Society for Cell Biology released a statement, signed by 40 Nobel Laureates, in favor of nuclear transplantation technology for research and therapeutic purposes and in opposition to the Brownback bill.[21] The statement asserts that S. 1899 "would impede progress against some of the most debilitating diseases known to man."

Former President Gerald Ford stated his strong opposition to both H.R. 2505 and S. 1899 in a April 25, 2002, letter to President Bush.[22] In the letter, Ford indicates that during his administration, the controversy over recombinant DNA research was "successfully addressed with 'careful thought' and the implementation of safety regulations."[23] Former President Ford "expresses full support for therapeutic cloning, arguing a prohibition of this technology 'would adversely impact scientific research and should not become law.'"[24]

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[20] Glendenning, D. Cloning Bill Options Set For Senate Floor Debate Before Memorial Day, Daschle Aide Says. *Washington Fax*, April 1, 2002.

[21] The American Society for Cell Biology statement by the 40 Nobel Laureates is available at: [http://www.ascb.org/publicpolicy/Nobelletter.html].

[22] Hafner, L. Revised Feinstein/Kennedy Cloning Bill Has Criminal and Civil Penalties, Requires Research Review. *Washington Fax*, May 2, 2002.

[23] Ibid.

[24] Ibid.

Senators Arlen Specter, Dianne Feinstein, Orrin Hatch and Edward Kennedy introduced S. 2439 (Specter), the Human Cloning Prohibition Act of 2002, on April 30, 2002. S. 2439 would prohibit human reproductive cloning while allowing cloning for medical research purposes, including stem cell research. According to a press release from Sen. Specter's office, S. 2439 applies Federal ethical regulations on human subject research to nuclear transplantation research, such as review by an ethics board, inclusion of protections for research participants, privacy and informed consent. It would also impose a $250,000 fine for a violation of these conditions. S. 2439 would impose penalties for violations of the reproductive cloning ban of up to 10 years in prison and a minimum fine of $1 million. The bill defines human cloning as "implanting or attempting to implant the product of nuclear transplantation into a uterus or functional equivalent of a uterus."[25]

Some legal scholars believe a ban on human cloning may be unconstitutional because it would infringe upon the right to make reproductive decisions which is "protected under the constitutional right to privacy and the constitutional right to liberty."[26] Other scholars do not believe that noncoital, asexual reproduction, such as cloning, would be considered a fundamental right by the Supreme Court. A ban on human cloning research may raise other constitutional issues: scientists' right to personal liberty and free speech. In the opinion of some legal scholars, any government limits on the use of cloning in scientific inquiry or human reproduction would have to be "narrowly tailored to further a compelling state interest."[27]

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[25] The Specter press release can be found at: [http://www.senate.gov/~specter/020426.html].

[26] Andrews, L. B. Is There a Right to Clone? Constitutional Challenges to Bans on Human Cloning. *Harvard Journal of Law and Technology*, summer 1998. p. 643-680.

[27] Ibid., p. 667.

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Cloning: Chronology of Events, 1997-2002

Updated March 7, 2002

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Summary

This is a selected chronology of the events surrounding and following the cloning of a sheep from a single adult sheep cell by Scottish scientists, which was announced in February 1997. The project was cosponsored by PPL Therapeutics, Edinburgh, Scotland, which has applied for patents for the techniques used. This chronology also addresses subsequent reports of other cloning experiments, including the first one using human cells. Information on presidential actions and legislative activities related to the ethical and moral issues surrounding cloning is provided, as well as relevant Web sites.

More information on cloning and on human embryo research can be found in CRS Report RL31015, *Stem Cell Research*; CRS Report RS21044, *Background and Legal Issues Related to Stem Cell Research*; and CRS Report 97-335, *Cloning: Where Do We Go From Here?* This report will be updated as necessary.

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Cloning: Chronology of Events, 1997-2001

Chronology

1997

February 23, 1997. Dr. Ian Wilmut, a Scottish embryologist and his colleagues at the Roslin Institute, Edinburgh, Scotland, succeeded in cloning a sheep from a single adult sheep cell. *Dolly,* the sheep that was created in this manner, is genetically identical to the adult sheep from which she was cloned.

February 24, 1997. President Clinton asked the 18-member National Bioethics Advisory Commission to study the ethical and legal implications of cloning. Human cloning is not currently regulated by law in the United States.

March 2, 1997. Scientists at the Oregon Regional Primate Research Center in Beaverton, OR, reported cloning two monkeys. The monkeys, born in August 1996, were cloned from monkey embryo cells, not cells from an adult monkey. The cloned primates are not genetically identical to any adult monkey.

March 4, 1997. President Clinton issued a memorandum for the heads of executive departments and agencies entitled *Prohibition on Federal Funding for Cloning of Human Beings*. Also, the President issued remarks entitled *Remarks by the President on Cloning.*

The memorandum and remarks are available from the U.S. Government Printing Office (GPO) in the *Weekly Compilation of Presidential Documents,* March 10, 1997, S/N 769-007-00577-8, $3.

This memorandum may be accessed on the Internet at
[http://clinton6.nara.gov/1997/03/1997-03-04-directive-on-cloning.html].
The President's remarks on cloning may be accessed on the Internet at
[http://clinton6.nara.gov/1997/03/1997-03-04-remarks-by-president-on-cloning.html].

The House Committee on Science's Subcommittee on Technology held a hearing entitled "Biotechnology and the Ethics of Cloning: How Far Should We Go?"

March 12, 1997. A hearing entitled "Scientific Discoveries in Cloning: Challenges for Public Policy" was held by the Senate Labor and Human Resources Committee's Subcommittee on Public Health and Safety.

June 9, 1997. The National Bioethics Advisory Commission presented its report, *Cloning Human Beings*, to President Clinton. The report may be ordered at the Web

site [http://www.ntis.gov/search.htm]. At this site, search using the term "cloning;" then click on "bioethics;" and the order information for the report will appear.

President Clinton's remarks, entitled *Remarks by the President at Announcement of Cloning Legislation*, are available from GPO in the *Weekly Compilation of Presidential Documents,* June 16, 1997, S/N 760-007-00577-8, $3.

The President's remarks at the announcement of cloning legislation may be accessed on the Internet at
[http://clinton3.nara.gov/New/Remarks/Mon/19970609-15472.html].

June 17, 1997. The Senate Labor and Human Resources Committee's Subcommittee on Public Health and Safety held a hearing entitled "Ethics and Theology: A Continuation of the National Discussion on Human Cloning."

July 22, 1997. The House Committee on Science's Subcommittee on Technology held a hearing entitled "Legislative Hearing on the Prohibition of Federal Funding for Human Cloning Research."

August 7, 1997. Researchers at ABS Global, Inc., DeForest, WI, announced that they had succeeded in cloning a Holstein bull from fetal stem cells. Stem cells are "blank slate" cells that have not yet specialized their function, such as a liver or muscle cell. The stem cell has the potential to be any part of the mature animal. *Gene,* the bull, was created in this manner. *Dolly*, the sheep, was cloned from the genetic material of an adult cell.

December 18, 1997. Roslin Institute scientists reported data showing the production of the world's first lambs that carry a human gene (transgenic lambs) created by nuclear transfer. To produce the lambs, they first exposed skin cells (fibroblast) to DNA that included a human gene and a marker gene. Then they took the cells that contained both the marker gene and the human gene and followed the same cloning technique they used to make Dolly. Both lambs contain the transgenic gene in their cells.

1998

January 7, 1998. Dr. Richard Seed, a physicist from Riverside, IL, on National Public Radio discussed his plans to open a clinic to clone humans before Congress outlawed the procedure. He stated he has already assembled a team of doctors, and four couples volunteered to participate. His objective is to provide childless couples with children. He first announced his intention on December 5, 1997, at a symposium on reproductive technologies in Chicago.

January 10, 1998. President Clinton, speaking in his weekly radio address, urged swift action by Congress to ban the cloning of humans. He reiterated his support for related areas of cloning research which might lead to medical breakthroughs.

This radio address by the President may be accessed at the following Web site: [http://clinton6.nara.gov/1998/01/1998-01-10-radio-address-on-science-and-techn

ology.html]. The remarks are in the *Weekly Compilation of Presidential Documents,* January 19, 1998, available from GPO, S/N 769-007-00577-8, $3.

January 20, 1998. Michael A. Friedman, Acting Commissioner of the Food and Drug Administration (FDA), stated that the FDA has the authority under the Food, Drug, and Cosmetic Act to regulate human cloning, since it is a form of cellular or genetic therapy. Since such therapies require prior approval by FDA reviewers, anyone planning to legally attempt human cloning would have to file a formal application with the agency, which would then undertake a lengthy review of the proposal. Friedman also said the FDA would initiate legal action against anyone who fails to file such an application.

July 22, 1998. Researchers at the University of Hawaii announced that they had created dozens of mice by cloning, using a new technique in the most commonly-used laboratory animal. A paper detailing their method was published in the July 23 issue of the science journal *Nature.* The researchers were able to reprogram nuclei from cells taken from ovaries of adult mice. Known as cumulus cells, these differentiated cells surround the eggs of mice, as well as humans, and are shed with eggs during ovulation. For the cloning experiment, nuclei from cumulus cells were inserted directly into egg cells whose nuclei had been removed. The combination was then activated with chemicals prompting the eggs to start dividing and form embryos. The embryos were transferred to the wombs of surrogate mice, and some resulted in the birth of mice clones (identical to mice from which the cumulus cells were taken). This is the first published documentation that adult animals can be cloned since researchers in Scotland announced the birth of a cloned sheep named Dolly in February 1997. Some scientists had questioned the validity of that study. In the same issue of *Nature,* two other papers were published where researchers in England documented that Dolly is indeed a clone.

August 19, 1998. Scientists at the Ruakura Research Center in Hamilton, New Zealand, announced the cloning of the lone survivor of a rare breed of cow. The cloned cow is the last member of a herd which had lived in isolation on Enderby Island, a barren, subantarctic section of the Auckland Islands. From the cow's ovaries, the scientists took several granulosa cells, which nourish egg cells in the ovaries. The granulosa cells are similar to the cumulus cells that Hawaiian researchers used to clone mice. The nuclei from the granulosa cells were inserted directly into egg cells from which the nuclei had been removed. This combination was then activated with electrical shocks. The resulting fused cells divided and developed into embryos, which were transferred into the wombs of surrogate Angus cows. On July 31, 1998, the first clone was born, with slightly different markings than the adult cloned cow. However, the results of a DNA fingerprinting test proved that the clone and the cloned cow are genetically identical.

December 11, 1998. Japanese scientists published data in *Science* reporting the cloning of eight calves from an adult cow's oviduct and cumulus cells. The success rate was higher than that of any other group that cloned large mammals. Ten embryos, derived from differentiated (oviduct and cumulus) cells of one adult cow, resulted in the birth of eight calves; however, four calves died at or soon after birth.

1999

April 26, 1999. An announcement was made that a collaboration of industry and academic researchers had successfully produced the world's first transgenic goats through cloning. The three goats are genetically identical copies of a goat embryo whose genetic material was modified to produce milk containing the human anticlotting protein known as antithrombin III (ATIII).

May 27, 1999. A study was published indicating that Dolly, the cloned sheep, may be susceptible to premature aging. Researchers in Scotland found that three-year-old Dolly, who was cloned from a six-year-old ewe, has cells that appear to be at least nine years old.

June 1, 1999. University of Hawaii researchers reported the first documented cloning of an adult male animal. Fibrio, a mouse, was cloned from cells clipped from the tip of a male mouse's tail. This was a different method than was used to produce Gene, the bull who was cloned from fetal stem cells. Up to now, all animals cloned from adult cells had been female.

June 14, 1999. It was reported that two companies, Geron Corporation (Menlo Park, CA) and Advanced Cell Therapeutics (Worcester, MA) had started programs to grow their own embryos (human clones or human-cow hybrids) by cloning. The clones would be used as sources of embryonic stem cells, which may have the potential to treat a number of human conditions, including Parkinson's disease and diabetes.

2000

January 12, 2000. Dr. Gerald Schatten and his colleagues at the Oregon Regional Primate Center, Beaverton, OR, announced the first successful example of the cloning of a monkey called Tetra by using a technique called "embryo splitting." This technique splits an eight-cell embryo into four identical two-cell clones and then implants them in surrogate mothers. Clones made from split embryos are genetically identical.

This technique is different than the one used to clone Dolly the sheep, the first clone of an adult animal. In that case, the clone was created by taking an adult animal's cell nucleus and implanting it in an unfertilized egg cell from which the original nucleus had been removed.

Some scientists hope that embryo splitting can be used to develop genetically identical laboratory animals better suited for testing therapies that may eventually be used to treat humans.

March 5, 2000. Researchers at the Blacksburg, VA, facility of PPL Therapeutics announced the production of the first cloned pigs—Millie, Christa, Alexis, Carrel, and Dotcom. The Scotland-based company, which also has a research facility in New Zealand, is the same firm that cloned the sheep Dolly. Basically, the pigs were created with the same technique used to create Dolly; but the researchers have not yet

disclosed the "additional inventive steps" they say were used to create the pigs. Researchers hope that cloned pigs can eventually become a source of organ and cell transplants for humans.

July 21, 2000. Alexander Kind and his colleagues at PPL Therapeutics, the Edinburgh-based company that helped create Dolly, announced that they had successfully cloned Cupid, Diana, and a third unnamed transgenic lamb. The lambs are the first transgenic livestock to carry specifically chosen modifications in their genes.

The lambs were created using the same method applied for Dolly in 1997. DNA was taken from another sheep and transferred into unfertilized eggs. This time, however, the team picked a specific point on one of the sheep's chromosomes and inserted a new DNA gene sequence into it. This technique is called "gene targeting" and had previously only been possible in laboratory mice.

The inserted gene allows the sheep to produce the human protein alpha 1-antitrypsin in their milk. This protein may someday be used to treat a variety of lung diseases, including cystic fibrosis, but the true significance of the feat lies in the wider application of gene-altering technology. Another potential application of this technology is the development of animals that could supply organs for human patients.

2001

April 13, 2001. PPL Therapeutics PLC of Scotland announced the creation of the world's first five genetically modified cloned pigs, a critical milestone towards producing spare part transplant organs for human patients. Inserted into the genetic make-up of the five clones is a marker gene, which was taken from a jellyfish and is fluorescent. Tissue removed from the clones glowed under ultraviolet light, showing that the marker gene had been successfully integrated into their genetic blueprints.

Dr. Alan Colman of PPL Therapeutics stated that the same technique could allow scientists to create pigs whose organs would not be rejected by human patients' immune systems, since pigs have a gene which causes humans to reject their organs. The birth of the piglets suggests that the gene can be altered.

July 16, 2001. H.R. 2505, Human Cloning Prohibition Act of 2001, a bill to amend Title 18 of the *United States Code* to prohibit human cloning, was introduced. This bill was passed in the House of Representatives by a 256-162 vote (roll call no. 303) on July 31, 2001. On August 1, 2001, it was received in the Senate.

November 25, 2001. Scientists at Advanced Cell Technology (ACT), a private company in Worcester, MA, announced that they had cloned the first human embryos. They said their aim is not to produce cloned human beings, but to create genetically matched stem cells to treat a wide range of diseases. However, the cloned embryos that they produced stopped developing after dividing into just a few cells — not enough to yield medically useful stem cells.

ACT used two techniques to produce human embryos—cloning and a second process called parthenogenesis.

In cloning, the researchers obtained egg cells from seven female volunteers. They stripped the DNA from 19 egg cells and replaced it with genetic material from another person of unspecified gender. The new genetic material came from a skin cell or from ovarian material called a cumulus cell. Seven of the eggs began to divide and grow. These early embryos were clones, or offspring that carried genes from only one adult (the person who had donated the skin or cumulus cell). Two embryos divided into four cells each, and one embryo divided into six cells before the growth stopped. The growth occurred over a 3-day period.

In parthenogenesis, an egg cell is treated with chemicals that cause it to start dividing into an embryo without being fertilized by sperm. ACT exposed 22 human eggs to those chemicals. After 5 days, six eggs had matured into larger masses of cells. Scientists believe embryos created this way could mature long enough to be useful in medical treatment but would be unable to grow to term.

Both the cloned and parthenogenetically produced embryos had significant shortcomings. None developed stem cells, which can grow into any type of body cell or tissue.

November 28, 2001. President Bush issued Executive Order 13237, establishing the President's Council on Bioethics. The Council will advise the President on bioethical issues that may emerge as a consequence of advances in biomedical science and technology.

The executive order establishing the Council may be accessed on the Internet at [http://www.whitehouse.gov/news/releases/2001/11/20011128-13.html].

The following legislation to prohibit cloning of humans in some manner was introduced in 2001 during the first session of the 107th Congress: H.Res. 214, H.R. 1260, H.R. 1372, H.R. 1608, H.R. 1644, H.R. 2172, H.R. 2608, H.R. 3495, H.Amdt. 284 to H.R. 2505, S. 704, S. 790, S. 1758, and S. 1893. No action has yet been taken on these measures.

2002

January 3, 2002. PPL Therapeutics PLC of Scotland, the company that cloned Dolly the sheep, announced that it had cloned another five genetically modified pigs—Noel, Angel, Star, Joy, and Mary. The pigs were born on Christmas Day 2001 at the firm's research facility in Blacksburg, VA. As a step toward producing pigs with organs and cells that could be safely transplanted into humans, the cloned pigs (all female) have a gene that has been inactivated, or "knocked out." This is the pig gene that attaches sugar molecules to the surfaces of organs. When organs are transplanted into humans, the human immune system attaches to those sugars, recognizes the transplanted organs as foreign and rejects them. Several other genetic modifications, including the addition of up to three human genes, will be needed to avoid rejection of the pig parts. The work is being funded by a $2 million grant from the National Institute of Standards and Technology.

January 24, 2002. The Senate Appropriations Committee's Subcommittee on Labor, Health and Human Services, Education, and Related Agencies held a hearing on human cloning. At this time, no hearing transcript is available.

January 24, 2002. S. 2893, Human Cloning Ban and Stem Cell Research Protection Act of 2002, a bill to ban human cloning while protecting stem sell research, was introduced. This bill was referred to the Senate Health, Education, Labor, and Pensions Committee

January 28, 2002. S. 1899, Human Cloning Prohibition Act of 2001, a bill to amend Title 18 of the *United States Code* to prohibit human cloning, was introduced. This bill was referred to the Senate Judiciary Committee.

January 30, 2002. Researchers at Advanced Cell Technology in Worcester, MA, announced that they have used cells derived from cloned cow embryos to grow functioning kidney-like organs that are not rejected when implanted into adult cows, marking the first use of cloning technology to grow personalized, genetically matched organs for transplantation.

This is the first time that cells taken from a cloned embryo have been used to grow an organ which, like kidneys, removes toxins from the body and produces urine. Researchers are still checking to see if it carries out all the functions of a kidney. For this work to be replicated in humans, the kidney would have to be created by using cloned human embryos. Cells taken from the human patient would be used to produce a cloned human embryo genetically identical to the patient. The theoretical procedure would then harvest cells from the embryo to grow the organs needed for transplant, which would not be rejected by the patient because they would be genetically identical.

Information on this work has not been published in a scientific journal, nor has the work been confirmed by others.

February 15, 2002. Researchers at Texas A&M's College of Veterinary Medicine announced that they had created the first cloned cat, a shorthaired calico named CC (short for "carbon copy" and "copy cat"). It was cloned with cells from a cat named Rainbow. Delivered by cesarean section on December 22, 2001, in a university laboratory, CC is the first household pet to be cloned.

Working first with an adult male cat, the researchers harvested cells from the animal's mouth and then fused them with cat donor eggs that had been emptied of genetic material. This created 82 cloned embryos that were transferred into the wombs of seven cats. The process yielded only a single fetal clone, and it died in utero.

In a second attempt, researchers used cumulus cells from the ovaries of a female cat named Rainbow and created five cloned embryos. They were implanted in Allie, another female cat. This time, an embryo took hold and grew. Sixty-six days later, CC arrived.

The kitten is anything but an exact copy of Rainbow. Although tests indicate that CC is a genetic duplicate of the cat that donated the original ovary cell, CC's markings

are quite different from those of Rainbow. Calico markings such as those possessed by CC are the result of random molecular changes that occur during fetal development.

Mark Westhusin, the project's lead scientist, stated, "This is reproduction, not resurrection." He warned pet owners that cloning will never return their old pets, although the clones will probably resemble their predecessors in looks and temperament.

The work was funded by Arizona millionaire John Sperling, who gave Texas A&M about $3.7 million to develop technology to clone his pet dog Missy, an aging border collie-Siberian husky mix. Although several pregnancies have been achieved by using cells from Missy, none of the clones have survived to term. Parallel work on cats went faster, Westhusin said, in part because cat eggs grow and mature in culture dishes better than dog eggs.

To commercialize the work, Sperling 2 years ago created a Texas company called Genetic Savings and Clone, which holds the licensing rights to any proprietary pet cloning techniques developed by Texas A&M's "Missyplicity Project."

Supplementary Information

President Clinton established the National Bioethics Advisory Commission (NBAC) by Executive Order 12975 on October 3, 1995. This executive order is in the *Federal Register,* October 5, 1995, p. 52063, and may be accessed at the Web site [http://clinton5.nara.gov/textonly/WH/EOP/OSTP/Science/html/nbac.html].

Information on the NBAC may be accessed at the Web site [http://bioethics.georgetown.edu/nbac/]. The NBAC charter expired on October 3, 2001.

Information on the Roslin Institute may be accessed at [http://www.roslin.ac.uk]. The institute can also be contacted at: Roslin Institute, Roslin, Midlothian, Edinburgh EH25 9PS, U.K. Telephone: 011-440131 527 4200 (switchboard). Fax: 011-440131 440 0434.

PPL Therapeutics may be contacted at: PPL Therapeutics, Roslin, Midlothian, Edinburgh EH25 9PP Scotland. Telephone: 011-440131 440 4777. Fax: 011-440131 440 4888. Contact Person: Andy Carver.

Information on the Oregon Regional Primate Research Center may be accessed at [http://www.ohsu.edu/orprc/]. The center can also be contacted at: Oregon Regional Primate Research Center, 505 N.W. 185th Avenue, Beaverton, OR 97006-3499. Mail code: L584. Telephone: (503) 645-1141. Fax: (503) 690-5532.

Information on ABS Global, Inc. may be accessed at this Web site: [http://www.absglobal.com/]. The company can also be contacted at: ABS Global, Inc., 6908 River Road, DeForest, WI 53532. Telephone: (608) 846-6346.

Information on Advanced Cell Technology may be accessed at this Web site: [http://www.advancedcell.com/]. The company can also be contacted at: Advanced Cell Technology, One Innovation Drive, Biotech Three, Worcester, MA 01605. Telephone: (508) 756-1212. Fax: (508) 756-4468.

For constituents without access to the Internet, copies of the *Federal Register,* the *Weekly Compilation of Presidential Documents,* and congressional documents may be available for use at the nearest government depository library. Addresses of the closest depository libraries can often be obtained through a local library or from the office of Depository Services of the U.S. Government Printing Office, (202) 512-1119. Those with access to the Internet may prefer to get addresses from the GPO Access Web site's Locate Federal Depository Libraries page, which can be searched by state or area code. It is available at [http://www.gpo.gov/libraries]

Agence France Presse
August 7, 2002 Wednesday 1:08 AM Eastern Time

Australian doctors admit using aborted fetuses for stem cell research

DATELINE: SYDNEY, Aug 7

A team of Australian researchers under fire for using aborted fetuses for stem cell research admitted unapologetically Wednesday that they had been using them successfully for 20 years. Professor Bernie Tuch, director of the pancreas transplant unit at Sydney's Prince of Wales Hospital, also rejected criticism by Australia's conservative Deputy Prime Minister John Anderson that such research was "the slippery slope of utilitarianism."

"I believe society needs to set the boundaries here, not the scientists," Anderson told ABC radio. "There are still too many people who don't understand the parameters of this difficult debate." Tuch responded by comparing objections to the use for research of aborted fetuses to similar criticisms to the first use of insulin for diabetics 80 years ago and to the in-vitro fertilization process in the late 70s.

Anderson's criticism has revived controversy which has raged here and internationally over the ethics of harvesting stem cells, despite their potential to repair damaged organs and cure neurological illnesses.

The problem is that the process requires the destruction of fertilized eggs that can grow into humans.

It remains the subject of vigorous debate in Australia, although Prime Minister John Howard in April outlined a framework allowing research into stem cells derived from human embryos, despite strong opposition from some religious quarters.

Anderson expressed his concern after after Monash University professor Alan Trounson said this week that he would consider using fetal tissue for the culture layer.

British scientists last month received the go-ahead to clone human embryos for stem-cell research.

But in the United States, the Senate is due to debate a bill backed by the powerful religious right and already passed by the House of Representatives that would ban all forms of cloning and prohibit US scientists from using stem cells.

Tuch said the use of human fetal tissue by his team and other researchers in Australia had been occurring for the past 20 years.

"It's been used for diagnostic purposes, it's been used for developmental purposes, it's been used for basic research and in the 80s was used for therapeutic purposes," he said. "The use of such tissue for the growing of embryonic stem cells is simply just one further benefit of such tissue."

He said people who used the utilitarianism argument should look at their history. "When in-vitro fertilization came into being in the late 70s, early 80s, we were given exactly the same comments," he said. "I don't think today most people would support that point of view. In the 1920s, let's go back even further, when insulin was discovered ... there were people who said exactly the same thing, that we shouldn't be using it. This is not the edge of the slippery slope. It is utilization of scientific knowledge in a constructive, positive sense for the benefit of humanity."

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Sydney Morning Herald
August 5, 2002 Monday
SECTION: News And Features; Pg. 1

Abortions Set To Fuel Stem Cell Research

BYLINE: Julie Robotham And Deborah Smith

Tissue from aborted human fetuses will be used in the culture of embryonic stem cells for the first time in Australia if the creation of new stem-cell lines is approved, the country's leading scientist in the field has revealed. The disclosure by Alan Trounson, director of the institute of reproduction and development at Monash University, is certain to inflame the debate around the issue.

The Catholic Church has already branded the research based on cells from days-old embryos as morally unacceptable and is likely to see any use of tissue from fetuses aborted in early pregnancy as compounding the offence. Professor Trounson was speaking after a Singaporean team with which he is associated demonstrated for the first time the growth of human embryonic stem cells on human tissue cultures.

Previously, all human embryonic stem cells had been grown on cultures made from the skin cells of fetal mice. These cells are useful for basic research, but scientists would be reluctant to try to use them to cure human diseases because of the possibility of infection by mouse viruses. Professor Trounson said: "If we're able to [create new embryonic stem cell colonies] ourselves we would look at a broad range of [culture] cell types. We have candidate cells in mind."

The Monash group would test tissue from adults as the culture layer, including tissue from the reproductive tract, but Professor Trounson said he would also want to test the use of aborted fetal tissue as a culture medium, to establish which tissue type worked best.

People who opposed such research on moral grounds needed to appreciate that doctors had always been allowed to use tissue from aborted

fetuses, with the parents' consent, "for experimentation and even transplantation".

"Here in Australia we would be allowed to use it. There would be no impediment to that."

About 90,000 abortions are performed in Australia each year. The relative abundance of fetal tissue available was one attraction to scientists, he said.

As well, Australia would gain an important advantage in the biotechnology industry if local scientists were able to create new embryonic stem-cell lines using cultures derived from humans.

This was because of the recent moratorium by the United States Government on further taxpayer-funded grants for the creation of new embryonic stem-cell lines.

The National University of Singapore team, led by Dr Ariff Bongso, reported that the embryonic stem cells had grown just as well, if not better, than those on mouse cells. But the researchers were aware that the use of fetal tissue would be controversial. "We are in the process of evaluating other commercially available adult human [cultures] because of ethical concerns regarding the derivation of fetal cells from human abortions." They had also experimented with tissue from the fallopian tubes of women undergoing hysterectomy.

The research is reported today in the journal Nature Biotechnology.

Human embryonic stem cells, which scientists believe have the potential to treat many conditions, including diabetes, Parkinson's disease and motor neurone disease, tend to turn unpredictably into different types of tissue in the laboratory dish. To keep them growing in an unchanged state, scientists have had to nurture them carefully with special solutions and culture tissue. Some researchers have grown them on specially coated plastic beds, but they had to use mouse cells in the nourishing solution.

The Singaporean cell colony is the first to be grown in mouse-free conditions.

The Australian
August 8, 2002, Thursday
SECTION: LOCAL; Pg. 3

Aborted fetus tissue to be commercial export

BYLINE: Deborah Hope * Biotechnology writer

TISSUE from aborted fetuses could be used in the commercial production of embryonic stem cells for export early next year.

Melbourne firm ES Cell International will use tissue from aborted fetuses if it is proven to be the best medium for growing human embryonic stem cells in bulk quantities.

ES Cell chief executive Robert Klupacs said yesterday that he was unaware of any legal impediment to using human fetal tissue as a so-called feeder layer for growing the cells. Mr Klupacs said it was more likely ES Cell would use adult tissue to grow the cells, but he would not rule out using fetal tissue if it was established as the most effective medium.

"Our goal is to treat people with really nasty diseases. If the only way we can do it is by using fetal tissue, we will," he said, adding that the firm did not have a view on abortion.

ES Cell, a commercial partner in Alan Trounson's National Centre for Stem Cell Engineering, funded research in Singapore resulting in the world's first solely human embryonic stem-cell line.

The research, carried out by Ariff Bongso at the National University of Singapore, was a breakthrough because all other embryonic stem-cell lines in existence had been grown on mouse feeder cells. These cannot be used in human treatments because of the risk of spreading animal retro-viruses.

Controversy has arisen over the research because Professor Bongso tested tissue from a 14-week-old aborted fetus as a feeder layer, as well as adult fallopian tissue as a growing medium. He is yet to compare the two.

Professor Bongso said he had since grown human embryonic stem cells on feeder layers of adult skin tissue from both the foreskin and the abdomen. He hopes to publish the new research within three months to allay ethical fears over the use of aborted fetal tissue.

Mr Klupacs hopes to begin producing human embryonic stem cells from new "clean" lines in six to nine months at ES Cell's newly opened laboratory at Melbourne's Baker Heart Research Institute.

The result could be the first for-profit Australian use of tissue from aborted fetuses, taking the debate beyond the use of fetal tissue for research by scientists at Sydney's Prince of Wales Hospital.

With as many as 10 million cells likely to be involved in a single treatment of a patient, ES Cell is aiming to scale up its production into the billions. To do this, according to Mr Klupacs, new processes will have to be developed that will allow the cells to multiply in fermentation tanks and without the use of feeders.

ES Cell already is exporting human embryonic stem cells grown on mouse feeder layers to researchers around the world for $11,000 per delivery.

The company is now waiting for new clean lines of human ES cells to be developed, probably by research collaborators in Israel or Singapore. These will be imported and put into commercial production in the Melbourne facility, possibly by as early as February.

CLONING FACT OF THE DAY: June 3, 2002

"Cloned fetus provides new tissues"

Several news organizations are today reporting on a study published in the June issue of *Nature Biotechnology* in which researchers implanted into cattle cloned cells that formed functioning kidney-like organs and working heart tissue. So what's the catch? The cloned tissue came from a six week-old cloned fetus.

As reported by AP, "In the study, researchers removed the nucleus from a cow egg and replaced it with a skin cell containing DNA from another cow. **They then implanted the cloned embryo into a surrogate cow and let the embryo grow for about six weeks before removing it**."

Today's reports make it more and more difficult for proponents of human cloning to claim that human research cloning will stop at the point of cloning embryos to be destroyed and harvested at the embryonic stage.

It is inevitable that cloned human embryos will be implanted for further development to create spare parts, or for the purpose of a live birth.

Therapeutic cloning experiments show promise in cows

By PAUL ELIAS
AP Biotechnology Writer

SAN FRANCISCO (AP) _ Cows implanted with cells taken from a cloned embryo did not experience immune rejection, showing the potential of much-debated therapeutic cloning, researchers said.

The cloning technology is controversial and opposed by some, including President Bush and Pope John Paul II, as immoral because it requires creating and destroying days-old embryos.

However, some scientists who oppose cloning humans say they believe therapeutic cloning should be pursued because it could supply healthy new tissue to fix a variety of illnesses.

``While more work needs to be done, this demonstrates the potential use of this technology,'' said Dr. Anthony Atala, director of tissue engineering at Children's Hospital Boston and a co-author of the cow study published in the June issue of Nature Biotechnology.

Using healthy cells cloned with the same DNA of a patient could make difficult organ and tissue transplants much easier.

While still far from human use, experts say the latest advance demonstrates the disease-fighting potential of the method.

``It's a very important result," said Robert Nerem, director of the Georgia Tech/Emory Center for the Engineering of Living Tissues. ``Immune rejection is a very big problem in tissue engineering."

The report comes three months after other scientists used therapeutic cloning to fix genetic illness in mice.

The cow researchers removed the nucleus from a cow egg and replaced it with a skin cell containing the full DNA set from another cow.

They then implanted the cloned embryo into a surrogate cow and let the embryo grow for about six weeks before removing it.

They removed embryonic heart, skeletal and kidney cells from the embryo, grew them further in the laboratory-- even creating mini kidneys-- and implanted the cloned cells into the cow that donated the original DNA.

All of the cells thrived, with some of the mini kidneys producing a urine-like liquid, the researchers said.

``It was pretty spectacular and beautiful," said co-author Dr. Robert Lanza of Worcester, Mass.-based Advanced Cell Technology.

Despite the results, the fact that an embryo was grown for six weeks in a surrogate concerned even some therapeutic cloning proponents.

``While the research in animal models shows that it may be possible to use cloning to generate tissues and eliminate tissue rejection, it's important for the American public to understand that the methods used in this animal experiment should not be pursued in humans," said Christopher Reeve, the actor who has become a patient advocate since being paralyzed in a horse riding accident.

``Research involving the implantation of a human embryo into a woman, even to derive lifesaving cells, crosses a very important line and we need to pass legislation that would prohibit it."

The authors of the paper said they too are opposed to recreating their cow experiment in humans.

``We think it is ethically unacceptable to implant a cloned embryo in a woman for any purpose," Lanza said.

There are three competing bills now pending in the Senate addressing the cloning issue. One would ban all

forms of cloning, while the others would outlaw cloning to create a baby but allow the technology for use in finding disease cures as long as the embryos were destroyed after a few days and never implanted in women.

``The timing of this study could not have come at a better time," said Arthur Caplan, a University of Pennsylvania bioethicist who supports therapeutic cloning.

Associated Press, 6-03-02

EXPAND STORY

Health:

Cloning Breakthrough May Aid In Treatment of Host of Diseases ---- By Antonio Regalado Staff Reporter of The Wall Street Journal

The Wall Street Journal via Dow Jones

For the U.S. Senate debate over cloning technology, this could be the mouse that roared.

Biologists in Massachusetts have for the first time used so-called therapeutic cloning to treat a sick animal with corrected copies of its own cells.

Scientists have theorized that similar technology could be used to treat a host of human diseases, including Alzheimer's, spinal-cord injury and diabetes. Opponents on Capitol Hill this week continued to argue that therapeutic cloning is dangerous and immoral.

The work, in which immune-compromised mice were partially cured, is described in a scientific paper to be released today by the journal Cell. The news was welcomed by pro-research lobbyists. "We're thrilled because it's a proof of principle," said Michael Manganiello, president of the Coalition for the Advancement of Medical Research in Washington.

Scientists at the Whitehead Institute in Cambridge, Mass., showed how a potent combination of cloning, stem cells and gene therapy was used to partly restore health to mice suffering from severe combined immune deficiency. Such technologies present an increasingly powerful toolbox for biologists, one that is allowing them to rewind, alter, and reset the DNA inside animal cells.

In the experiments, the Whitehead scientists clipped off bits of skin from tails of the sick mice. Then they fused those skin cells with mouse eggs, forming cloned embryos. The cloned embryos were converted into versatile stem cells, which have the ability to transform into many types of cells. Once a healthy stretch of DNA had been added with gene-splicing, those cells were transplanted back into the sick mice.

The treatment restored the animals' immune-system function to about 5% of normal, said George Q. Daley, a Whitehead fellow who helped spearhead the effort. In humans, it is hoped that similar approaches could help treat blood disorders like sickle-cell anemia.

Attempts to extend similar technology to humans is controversial since the process involves the production of cloned embryos. Last August, the House of Representatives voted to ban the cloning of human embryos for stem cells. The Senate is now preparing to debate a similar measure.

One surprise was that the bodies of the sick mice attacked the cloned cells as foreign. The theoretical promise of therapeutic cloning is that the carbon-copy tissues it yields won't be rejected, but that has yet to be proved. "It is much more complicated than we imagined," Dr. Daley said.

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AMERICANS TO BAN CLONING

CLONING INFORMATION

Why the "Successful" Mouse "Therapeutic" Cloning Really Didn't Work

So-called "therapeutic" cloning is proposed for producing genetically matched tissues for transplant by creating a cloned embryo of the patient to be treated, and then harvesting the embryonic stem cells from the cloned embryo. In theory the patient would not reject the cells from the cloned embryo, because the embryo is the patient's identical twin.

In the first published experiments to test this theory[1], researchers started with a mouse that had a genetic defect—an immune deficiency where they lack mature white blood cells called B cells and T cells. A cell was taken from a somatic (body) cell of the mouse (from the tail tip), and the nuclear material of the cell was injected into a mouse egg which had had its nuclear material removed (somatic cell nuclear transplant, a.k.a. cloning.) The cloned embryo was grown in culture to a stage from which embryonic stem cells could be harvested (destroying the embryo.)

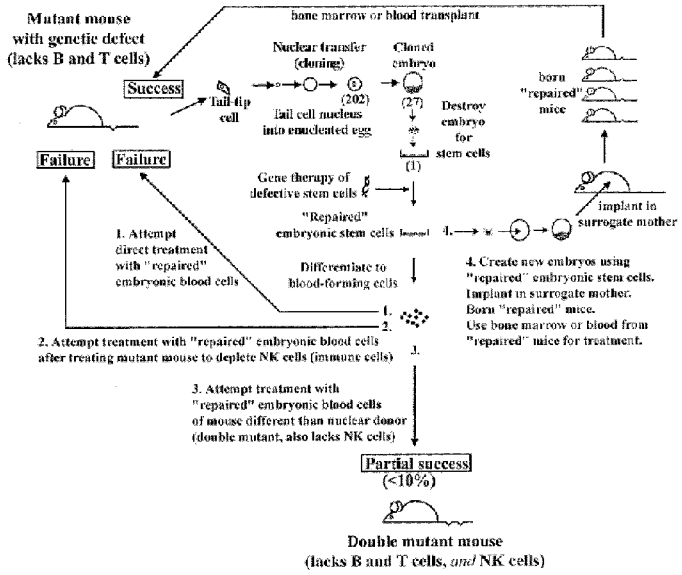
Because the mouse had a genetic defect, the embryonic stem cells still contained this defect (being from a clone of the original mouse). Gene therapy was used to "repair" the genetic defect in the cells in culture. The cultured cells were then stimulated to transform into blood cells, and these were transplanted back into the original mouse (the patient) (#1 on the figure).

The hope was that this cycle (mouse to cloned embryo to embryonic stem cells to transplant back into the mouse) would "cure" the mouse of its defect and repair its tissues. However, the experiment failed; the mouse rejected the transplanted cells. The scientists reasoned that this was because there are other immune cells, termed "NK cells", which were still present in the mouse and which attacked and destroyed the transplant. So in a second attempt (#2 in the figure), the mouse was first treated with antibodies to destroy the NK cells, then the transplant was attempted. Again, the transplant failed, possibly because the NK cells had not all been removed and still attacked and destroyed the transplanted embryonic stem cells.

In a third attempt (#3 in the figure), the scientists transplanted the embryonic cells not into the original mouse, but rather into a *different mouse*, one which had an additional genetic defect, causing it to lack both B and T cells as in the original mouse, as well as lacking any NK cells which might attack the transplant. However, this resulted in less than 10% success in treating the genetic disease in the mouse and restoring its B and T cells.

In a fourth experiment (#4 in the figure), the genetically "repaired" embryonic stem cells were used to create new cloned embryos, and these embryos were implanted in a surrogate mother and brought to birth. From these born, genetically "repaired" mice, bone marrow or blood was harvested and used to transplant back into the original, genetically defective mouse. The transplants of these "adult" stem cells successfully corrected the genetic problem of the original mouse (the patient.)

What does it all mean? "Therapeutic" cloning is supposed to produce matched embryonic stem cells that can be transplanted back into the original patient and not be rejected. Yet the original "patient" in these experiments still rejected the supposedly matched cells from its cloned embryo. Even transplantation into a different "patient" who should not have rejected the cells was still largely unsuccessful. The scientists in their paper note: "Our results raise the provocative possibility that even genetically matched cells derived by therapeutic cloning may still face barriers to effective transplantation for some disorders." In other words, **therapeutic cloning may not always produce matched tissues**. In contrast, "adult" stem cells from the born cloned mice were successful in matching the original patient and correcting the problem. This indicates that the only successful therapy using cloned embryos would be through "reproductive" cloning, to produce born clones who can serve as tissue donors for patients.



Reference:
1. W.M. Rideout et al., "Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy," *Cell Immediate Early Publication*, published online March 8, 2002; DOI:10.1016/S0092867402006815

FOR IMMEDIATE RELEASE
March 8, 2002

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"THERAPEUTIC" CLONING LAGS BEHIND ADULT STEM CELL SUCCESS

A report today in the journal *Cell*, announced by the Associated Press, purports to use "therapeutic" cloning to partially correct a genetic based immune system defect in mice.

However, this report comes years after "remedied" *adult* stem cells -- not embryonic stem cells - were used to cure *human* infants of severe combined immunodeficiency syndrome, in the first successful clinical trials in human gene therapy.

In the cloning experiments, performed by researchers at the Whitehead Institute (W.M. Rideout *et al.*, "Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy," *Cell* Immediate Early Publication, published online March 8, 2002) mice with an immune defect causing some white blood cells to be missing were cloned, and the cloned mouse embryos were destroyed for their stem cells. Since the embryonic stem cells were genetically identical to the mice (supposedly to prevent transplant rejection), they carried the same genetic defect. The researchers used gene therapy to fix the defective gene in the embryonic stem cells.

Several different attempts were then made to correct the immune defect in the mice using these stem cells.

In one experiment, the "repaired" embryonic stem cells were differentiated in culture into blood-forming cells and these were transplanted into the defective mice. The authors note that this showed little to no success (though the data are not shown in the paper).

Next they tried reducing the number of those cells in the recipient mice that were blocking successful transplant. Again, this approach was essentially negative (again, the data are not shown in the paper).

Finally, the researchers transplanted the "repaired" blood-forming cells into a *different* mutant mouse that had the same genetic defect, but also lacked the cells that had been destroying the transplanted cells. This situation resulted in a modest restoration of the missing blood cells, but at less than one-tenth the amounts in normal mice.

However, the researchers *were* able to restore normal levels of the missing blood cells by first using the "repaired" embryonic stem cells to grow *born* mice, then using the bone marrow stem cells or blood stem cells (similar to umbilical cord blood) of those born mice for the transplant. **In other words, the researchers were most successful when they resorted to using *adult stem cells.***

-more-

The published scientific paper actually shows that the "repaired" embryonic stem cells from cloned embryos were *unsuccessful* in treating the gene defect in the mice that provided the donor cells for cloning. **The authors note: "Our results raise the provocative possibility that even genetically matched cells derived by therapeutic cloning may still face barriers to effective transplantation for some disorders."**

This study also bears out the enormous global risk to women's health entailed in the speculative idea of "therapeutic cloning" to treat diseases in humans. Only 1 embryonic stem cell line was successfully cultured, starting with 202 cloning attempts. Even if the experiment had been successful, the number of human eggs needed for such treatments would translate to 303 million human eggs needed to treat the 1.5 million Parkinson's patients in the U.S., and over 3.2 billion human eggs needed to treat the 16 million diabetes patients in the U.S.

Far from being a step forward, this report shows that cloning is years *behind* the far more successful advances using adult stem cells, including their use to reverse immune deficiencies in humans.

As reported in April 2000 in the journal *Science*, French scientists restored the immune systems of 3 infants with severe combined immunodeficiency (the "bubble boy syndrome") using gene therapy with *the patients' own bone marrow stem cells*. Researchers removed stem cells from the infants' bone marrow, added a working copy of the gene to the cells' DNA, and injected the repaired stem cells back into the infants. Since the procedure used the patients' own cells, there was no problem of transplant rejection. After treatment, the numbers and function of the patients' immune cells were restored to *normal levels*, and the children were living at home and developing normally with no further treatment (M. Cavazzana-Calvo, *et al.*, "Gene Therapy of Human Severe Combined Immunodeficiency (SCID)-X1 Disease," *Science* 288, 669-672, April 28, 2000).

Far from showing the supposedly superior benefits of stem cells from cloned embryos, the new study shows that this approach continues to lag behind adult stem cell advances – even in mice, where embryonic stem cell research has been pursued for over twenty years. Adult stem cells are successfully treating real human children with serious diseases.

For more information on current and potential uses of adult stem cells, please visit www.stemcellresearch.org

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May 7, 2002 Tuesday, NORTH SPORTS FINAL EDITION

SECTION: News; Pg. 1; ZONE: N

LENGTH: 1109 words

HEADLINE: Cloning backers bank on science;
New research is timed to sway political debate

BYLINE: By Jeremy Manier, Tribune staff reporter.

BODY:
As the U.S. Senate nears a debate on competing bills to ban human cloning, supporters and opponents are marshaling arguments about a science that some see as a pathway to cures for ravaging diseases and others find unethical under any circumstances.

In a move timed to inject new science into the debate, a leading medical journal released several papers Monday defending the use of cloning technology for research. The papers range from scientific justifications for research cloning to an account of how some European countries permit such work. The main reason for the publication is widespread misunderstanding about why scientists want to pursue research using early-stage cloned human embryos, said Dr. Irving Weissman, author of one of the papers in the New England Journal of Medicine and a stem cell researcher at Stanford University.

The issues are especially difficult because research cloning is a new field. While scientists have found only the first signs of the technique's benefits in research on animals, some believe the work could yield basic insights into diseases ranging from diabetes to cancer.

Both Senate bills would ban reproductive cloning designed to create human babies. But the bills differ on whether to allow cloning of embryos that would not be implanted in a woman's womb to make a child. One bill, sponsored by Sen. Sam Brownback (R-Kan.), would ban all human cloning, while the other, introduced last week by Sens. Edward Kennedy (D-Mass.) and Dianne Feinstein (D-Calif.), would permit cloning for research.

Critics of using cloning technology for research include President Bush, who said last month that it could lead to "embryo farms"--creating cloned embryos for the purpose of studying and destroying them. But scientists say recent work suggests research cloning offers ways to study the development of cancer and other ailments that are not possible using other methods.

"As far as I'm concerned this technology is as important to opening the field as recombinant DNA was in the late '70s," said Weissman, a professor of cancer biology at Stanford and chair of a recent National Academy of Sciences cloning panel.

The brewing debate has come to resemble an all-out political campaign. A group called Americans to Ban Cloning has churned out a regular "Cloning Fact of the Day," while supporters of research cloning have

recruited advertising characters--Harry and Louise--used previously to help defeat former President Bill Clinton's plans for federal health insurance. Kennedy and Feinstein claimed a victory last week when conservative Sens. Orrin Hatch (R-Utah) and Strom Thurmond (R-S.C.) threw their support behind the less restrictive cloning bill.

Emotions vs. facts

So far, some advocates on both sides have appealed more to emotion rather than relying on facts, said Dr. Leon Kass, chairman of Bush's Council on Bioethics who is on leave as an ethicist from the University of Chicago.

"I don't think it's been wonderful," said Kass, who opposed research cloning in articles written before he was named to the panel. "People on both sides feel they have something vital to defend. But the anti-cloning groups do not do the discussion a service by talking as if scientists are mad and irresponsible, and scientists do not do the discussion a service by claiming that opposition on the other side stems either from opposition to science or religious bigotry."

Some scientists fear that misconceptions about research cloning could lead to it being banned before experts understand its potential applications.

In the last two years, scientists have realized that embryonic **clones** might be an especially useful source of embryonic stem cells, which are prized for their ability to become virtually any type of tissue in the body. Last year Bush permitted federal funding of some embryonic stem cell research, in hopes it could lead to replacement tissue to treat Parkinson's disease and other conditions.

Although critics have worried that such work could lead to the creation of cloned human babies, that would be virtually impossible in some of the newest research, which uses cloning techniques to study cancer.

The most recent studies, still unpublished, involve making cloned embryos from cancerous cells. Researchers then extract stem cells from the embryos and use them to grow new tissue, which could offer unique insights into how various genes contribute to the development of cancer. Weissman said his team at Stanford has begun such work on leukemia cells in mice.

Experts say the work shows why the term "therapeutic cloning," often used to describe the technique, can be misleading. Such basic research leads to no immediate therapies; at the same time, what it produces may not fit most definitions of a **clone.**

That's because cancer cells typically contain numerous genetic flaws that accumulate over time, making them noticeably distorted and different from a patient's normal cells. An embryo produced from such cells would not be a **clone** of the patient but of the patient's tumor, Weissman said.

"For every cancer there are on the order of four to five genetic mutations--in some cases there could be many more," Weissman said.

Such research also could not be easily used to make cloned babies, because cancerous cells typically contain numerous genetic flaws that would hinder embryonic development, experts say.

Debating terms

Although some scientists argue that such work is so different from reproductive cloning that the very term

"cloning" is inaccurate, supporters of a complete cloning ban say that's nonsense. Conservative commentator William Kristol recently wrote that such attempts to change the terminology amount to "Orwellian" tactics.

Addressing some common objections to research cloning, bioethicist George Annas of Boston University outlined some possible points for compromise in Monday's online edition of the New England Journal.

Annas proposed tight regulations that could prevent development of the "embryo farms" that the president fears. Such a system would "outlaw the freezing and storing of research embryos, [and] permit their use by only a limited number of qualified researchers," Annas wrote. To ensure that no embryonic **clones** are implanted in a woman's womb, Annas also suggested disqualifying anyone who does work on in vitro fertilization or other infertility treatments from participating in research cloning.

Annas wrote: "If a compromise cannot be reached, no law will pass, and unscrupulous persons in the United States will continue their efforts to create a cloned child, a result no member of Congress supports."

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Clone Profit? Unlikely

The technology's commercial viability faces many hurdles.

By DENISE GELLENE
TIMES STAFF WRITER

May 10 2002

Forty Nobel laureates and patient-advocacy groups have lobbied senators to allow human cloning for medical research.

Thomas Okarma, too, has met with senators to advocate cloning, but not because he sees any business potential in it. As chief executive of Geron Corp., a cell therapy company, he has no interest in using cloned embryos to produce customized treatments for disease. The odds favoring success "are vanishingly small," he said, and the costs are daunting.

Okarma said it would take "thousands of [human] eggs on an assembly line" to produce a custom therapy for a single person. "The process is a nonstarter, commercially," he said. The battle over a government ban on human cloning soon will reach the Senate floor. Advocates of a limited ban argue cloning research is needed to develop tailored stem cell treatments for Parkinson's, diabetes and other debilitating diseases.

Lost in the debate is the limited commercial promise of therapeutic cloning. Few companies believe it will produce affordable medications. The economic and regulatory hurdles are high, and the likely fallout is even more controversy.

"Where do you source that many eggs? Sourcing human eggs is a contentious issue in itself," said Alan Robins, chief scientific officer of BresaGen Ltd., a cell therapy company in Australia and Athens, Ga. "It is not something we want to get involved in."

Cloning involves stripping DNA from an egg cell and replacing it with genetic material from a patient's cell, such as a skin cell. The result is an embryo with the same genetic profile as the patient.

In theory, this embryo could be implanted in a woman's womb and become a child. But some scientists want to use cloned embryos as a source for stem cells. These stem cells could be grown into replacement tissues, such as nerve cells and heart cells. Because they would have the same genetic makeup as the patient, the cells might be accepted by the patient's body and avoid problems with immune rejection.

But the method is controversial because it involves the creation and destruction of embryos, or what some people consider the earliest stage of human life.

Geron and BresaGen study stem cells derived from embryos donated by fertility clinics, which is also controversial. Executives at those companies are not opposed to therapeutic cloning on ethical grounds. They believe there are more-efficient ways to deal with immune rejection, which is a drawback of embryonic stem cells, valued by scientists because they can turn into any of the 300 cell types in the body.

One alternative is immunosuppressant drugs, which are now administered to organ transplant recipients. Another possibility is a two-step therapy under development at Geron that involves pre-treating patients with stem cells to build their immune tolerance. The technique would allow Geron, based in Menlo Park, to treat large numbers of patients with its cells.

Therapeutic cloning, on the other hand, is a form of individualized medicine.

"We don't think it makes sense as a business model, producing cell therapies for a patient population of one," BresaGen's Robins said of therapeutic cloning. "But we don't support a ban on it."

Biotechnology Industry Organization, a trade group that represents the industry, favors a partial cloning ban. The group supports a bill by Sens. Dianne Feinstein (D-Calif.) and Edward M. Kennedy (D-Mass.) that would permit human cloning to develop new medicines but would outlaw reproductive cloning to produce children.

The bill competes with one sponsored by Sens. Sam Brownback (R-Kan.) and Mary Landrieu (D-La.) that would ban cloning for any purpose. The House has passed a similar anti-cloning measure.

Carl B. Feldman, president of the trade group, said in a statement last week that therapeutic cloning was "key to ... responsible development" of embryonic stem cell research. He said human cloning could spur development of treatments for Alzheimer's, spinal cord injuries and other degenerative diseases.

The trade group represents academic institutions as well as about 1,000 biotechnology companies.

The cloning furor picked up steam in November, when Advanced Cell Technology Inc. claimed to have cloned seven embryos from donated eggs. All died and none grew beyond six cells--too small to produce stem cells.

The Worcester, Mass., company advocates therapeutic cloning, which is a critical part of its strategy for entering the pharmaceutical business. Most of its operating revenue comes from cloning farm animals. Advanced Cell's Web site urges visitors to lobby President Bush, his Cabinet and members of Congress.

Robert Lanza, vice president for medical and scientific research at Advanced Cell, acknowledged that cloning is in the "experimental stage."

But he predicted that it would produce affordable therapies, at least when compared with organ transplants. A heart transplant, for example, costs upward of $100,000.

Lanza said the company would not be in the business of procuring eggs. Rather, he said, an egg cell would be donated by a relative of the patient--the mother of a diabetic child, for example. The egg would be stripped of its genetic material and merged with DNA extracted from one of the child's cells. Stem cells from the resulting embryo would then be transformed into insulin-producing islet cells, he said.

Advanced Cell is not close to offering such a treatment. But Lanza said such therapies, now theoretical,

could cost $10,000 or less, becoming profitable to the company and sparing patients "a lifetime of going blind and kidney failure."

However, Advanced Cell would have to spend millions of dollars to develop its cloning technology to the point at which it can be marketed, competitors said. Geron's Okarma said that with today's technology, it takes "100 eggs if you're lucky" to produce an embryo large enough from which to extract stem cells.

Okarma said the process of extracting stem cells also is inefficient. One "very prominent researcher" in Britain went through 1,000 embryos before obtaining useful cells, he said. (The embryos were donated by fertility clinics.)

Any resulting stem cell therapy can't be compared with an organ transplant in terms of price or effectiveness, said BresaGen's Robins. Cells would be placed in the body to generate repair tissue, such as patching damaged heart muscle, he said.

"We are not talking about growing new hearts here," Robins said. "We are using cells for repair, and I don't think they will be able to repair all damaged hearts, and therefore it is not an alternative to an organ."

Robins said cell therapies would be useful in "a small fraction of organ failures."

Quality control presents another hurdle, said Lutz Giebel, CEO of CyThera, a cell therapy company in San Diego. The Food and Drug Administration is set up to sample drugs produced in large commercial lots, not individual cell therapies, he said.

"It is not commercially viable," Giebel said. "Quality control is difficult; the FDA can't regulate it, [and] no one can afford the treatment."

Giebel called therapeutic cloning a "research tool only." A complete ban on human cloning would have "a limited impact on corporate product development," he said.

Cloning might make sense as a tool for developing ethnically diverse stem cell lines, Robins said. Because most cell lines were derived from embryos donated by fertility clinics, the cells have the genetic characteristics of white middle-class Americans--the typical clinic client, said Robins.

Through cloning, Robins said, companies could create additional stem cell lines that reflect a more diverse population. It would then be possible to "match" cells to patients based on genetics--just as donated organs and bone marrows are matched to patients. The process would reduce problems with immune rejection.

But such an undertaking would require many egg cells and probably would reopen further controversy.

"We've done some theoretical calculations," Robins said. To provide matches for the world's population, he said, "it would take 500 to 600 cell lines." That is 10 times the number of existing cell lines approved for government research.

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Poll: Public overwhelmingly opposes cloning; fewer support federal funding of stem cell research

By The Associated Press

The public overwhelmingly opposes scientific experimentation on the cloning of human beings, says a new poll that also suggests public opinion is mixed on stem cell research.

Nearly 4 out of 5 people opposed cloning, while one-third of those polled were against federal funding of stem cell research, according to the poll by the Pew Research Center for the People & the Press.

Stem cells are the basic building blocks of the body from which other organs and other cells develop. Public attitudes toward stem cell research can be difficult to measure because the questions often don't distinguish between a range of complex issues, such as whether the stem cells are taken from cloned embryos or from adults.

The poll of 2,002 adults was taken Feb. 25-March 10 and has an error margin of plus or minus 2.5 percentage points.

The poll found:

- People asked whether they favor or oppose scientific experimentation on cloning human beings oppose it by a margin of 77 percent to 17 percent. Most said they oppose it because it is morally wrong.
- They leaned toward supporting federal funding of stem cell research by a 43-35 margin, though that has dropped from a 55-29 margin in August.
- Two-thirds of opponents of stem cell research said they can't imagine changing their minds on the issue, while those who support it were less certain.
- Those who support federal funding were most influenced by media reports, while those opposed were most influenced by their religious beliefs.

Associated Press, 4-09-02

Pew Research Center for the People & the Press
Survey Reports

Public Makes Distinctions on Genetic Research
Conducted in association with the Pew Forum on Religion and Public Life

Released: April 9, 2002

Introduction and Summary

The public draws clear lines in assessing complex issues raised by genetic technologies. Americans are united in opposition to human cloning by more than four-to-one (77%-17%), they reject scientific experimentation in this area. There is far less agreement on the question of stem cell research. Half of those who have been paying at least some attention to the issue favor government funding for stem cell research, but a substantial minority (35%) are opposed. By a narrower margin (47%-39%), those who have been paying attention say conducting stem cell research is more important than not destroying the potential life of embryos involved in such research.

The nationwide survey of 2,002 adults by the Pew Research Center and the Pew Forum on Religion and Public Life finds that support for federal funding of stem cell research has eroded somewhat since last August. Among all respondents, regardless of whether they have heard anything about the issue, 43% back federal funding for this research, compared with 55% who expressed that view in a Gallup poll from last August.

Two Views on Genetic Research

	March 2002
Scientific experiments on human cloning	%
Favor	17
Oppose	77
Don't know	6
	100
*Govt funding for stem cell research**	
Should fund	50
Should not	35
Depends (Vol)	5
Don't know	10
	100
*Which is more important**	
Conducting research toward medical cures	47
Not destroying human embryos	39
Don't know	14
	100

*Based on those who have heard at least a little about this issue.

Federal Funding for Stem Cell Research

	Should	Should not	Depends/ DK/Ref
	%	%	%
All following issue*	50	35	15=100
White (Total)	50	35	15=100
White Evangelical	33	47	20=100
High**	**19**	**58**	**23=100**
Low**	49	35	16=100
White Mainline	59	27	14=100
High	51	29	20=100
Low	65	26	9=100
White Catholic	51	33	16=100
High	44	36	20=100
Low	57	32	11=100
Black (Total)	48	37	15=100
High	**39**	**48**	**13=100**

Equally important, there are key differences in the strength of opinion, with the stem cell opponents holding a decided edge. Nearly half (46%) of those who believe it is more important to conduct stem cell research, despite its potential for destroying embryos, say they could imagine changing their minds on this issue. By contrast, stem cell opponents largely driven by their deep religious beliefs are more committed to their positions. Fewer than a quarter (23%) say they could see themselves changing their minds and taking the view that medical cures arising from stem cell research are more important than the potential life of human embryos.

Low	61	22	17=100
Hispanic (Total)	49	39	12=100
High	40	44	16=100
Low	62	32	6=100
Secular***	64	23	13=100

*Analysis based on those who have heard at least a little about the stem cell debate in Washington.

**Groups are divided into "high" and "low" levels of religious commitment based on how often individuals pray, attend religious services, and the importance of religion in their lives.

***Seculars include atheists, agnostics and those with no religious preference who rarely, if ever, attend religious services.

Religious commitment is the most important factor influencing attitudes of opponents of stem cell research. While white evangelical Protestants stand out as the group most opposed to federal funding for stem cell research, this opposition is largely limited to highly-committed white evangelical Protestants, who oppose federally-funded stem cell research by three-to-one (58%-19%). [1]

In contrast to the divisions over stem cell research, more than seven-in-ten in every religious group oppose experimentation into human cloning. Moreover, the opposition largely arises from moral objections, not concerns over the safety of cloning. While white evangelical Protestants are more likely than others to cite moral concerns, majorities in every group base their opposition to cloning on the belief that it is morally wrong. Even seculars, who oppose research on the cloning of human beings by 56%-33%, are more influenced by moral beliefs than by safety concerns.

College Grads Favor Stem Cell Research

People with high levels of religious commitment are less supportive of federal funding for stem cell research than are those with weaker religious commitment. Aside from white evangelical Protestants, this pattern is most striking among African-Americans. Blacks in general support federal funding in this area, but highly-committed religious African-Americans are opposed (48%-39%).

College Grads Strongly Back Stem Cell Funding

	Should	Should not	Depends/ DK/Ref
	%	%	%
Total	50	35	15=100
College grad	64	25	11=100
Some college	51	33	16=100
H.S. grad	41	43	16=100
Less than H.S.	35	46	19=100
Conservative	38	45	17=100
Moderate	55	31	14=100
Liberal	69	22	9=100

Analysis based on those who have heard at least a little about the stem cell debate in Washington.

Aside from religion, political conservatives and those with the least formal education are most likely to oppose stem cell research. Nearly two-thirds of college graduates think the government should fund stem cell research, while just a quarter disagree. But among people who did not complete high school, just 35% favor government funding for stem cell research, while 46% are opposed.

And while 69% of liberals favor government funding for stem cell research, just 38% of political conservatives agree. Despite the overwhelming ideological differences on the issue, however, there is only a modest partisan gap. Republicans are divided on stem cell funding (45% in favor vs. 41% opposed). Democrats are slightly more supportive (55%-31%).

Supporters Cite Media, Education

The vast majority of those who support government funding of stem cell research are influenced by what they have seen in the media (42%) or their education (28%). Religion plays a relatively minor role in shaping the views of supporters just 5% cite it as having the biggest influence on their thinking.

By contrast, 37% of those who think the government should not fund stem cell research cite religious beliefs as their biggest influence. This is particularly the case among white evangelical Protestants, fully 55% of whom explain their opposition to stem cell research in terms of their religious beliefs. Just 31% and 27% of white mainline Protestants and white Catholics, respectively, cite religious beliefs in explaining their opposition to stem cell funding.

Religion Behind Opposition, Education Behind Support

		Government funding for stem cell research	
Biggest influence on attitudes	Total	Favor	Oppose
	%	%	%
Seen/Read in media	36	42	29
Education	21	28	12
Religious beliefs	19	5	37
Personal experience	8	10	4
Friends and family	3	4	3
Something else	11	10	12
Don't know	2	1	3
	100	100	100

Analysis based on those who have heard at least a little about the stem cell debate in Washington.

Unmovable Opposition

Though almost evenly divided overall, there is a significant disparity in how firmly Americans favor or oppose stem cell research. Overall, 43% say that conducting stem cell research that might result in new medical cures is more important than protecting human embryos involved with this research. However, nearly half (46%) of those who feel this way also say they can imagine themselves placing a higher priority on not destroying the potential life of human embryos.

Among the 38% who already believe that protecting the potential life of human embryos is more important than medical research on stem cells, fully two-thirds say they cannot imagine changing their minds on this issue, and just 23% say they could see themselves ever thinking that discovering medical cures from stem cell research is more important.

Research Opponents Won't Change Minds

	Which is more important?	
Imagine thinking differently?	Conducting research	Protecting embryos
	%	%
Can	46	23
Can't	47	69
Don't know	7	8
	100	100
Number of cases	(777)	(637)

Analysis based on those who have heard at least a little about the stem cell debate in Washington.

No to Cloning Research

The majority of people oppose research on human cloning on moral grounds. Overall, 55% of Americans oppose cloning research because they see it as morally wrong, compared with just 15% who frame their objections in terms of the science not being safe enough. Put in other terms, nearly three-quarters of those who oppose cloning research object on moral grounds.

White evangelical Protestants, 88% of whom oppose cloning experimentation, are the most

Widespread Moral Opposition to Cloning

White Black

likely to explain their opposition in moral terms. Moral opposition is also highest among women, older Americans, and those with no more than a high school diploma.

	Total	Evang.	Mainline	Catholic	Protest.	Secular
	%	%	%	%	%	%
Favor	17	8	15	18	13	33
Oppose	77	88	79	75	81	56
Science not safe	15	9	18	14	14	18
Morally wrong	55	71	53	54	63	32
Don't know	7	8	8	7	4	6
Don't know	6	4	6	7	6	11
	100	100	100	100	100	100

Endnotes

1. "Evangelical" Protestants are those who think of themselves as born again or evangelical Christians. "Mainline" Protestants are those who do not think of themselves in these terms.

EXPAND STORY **Opposition to Stop Creation of Human Cloned Embryos for Research Grows**

By Lisa M. Krieger, San Jose Mercury News, Calif. Knight Ridder/Tribune Business News

Mar. 20--A wide array of influential liberal political groups have joined religious conservatives in calling for a moratorium on the creation of human cloned embryos for research, saying more oversight is needed before scientists move forward on the contentious issue.

Joining conservatives in opposition to so-called "therapeutic cloning," an Oakland-based group called the Center for Genetics and Society released a letter on Tuesday asking the U.S. Senate to call a halt, at least temporarily, to research.

The letter is signed by 100 leaders of environmental, health, disability rights and bioethics groups. Among them are such notables as former University of California-San Francisco chancellor Dr. Philip R. Lee, Sierra Club board member Michael Dorsey, and Abortion Access Project director Susan Yanow.

Their efforts disrupt the political dividing line between left and right that marked the abortion debate, creating an unusual political amalgam.

But unlike the right-to-lifers, the opposition is not due to concern for the welfare of pre-embryos. Rather, they worry about genetic modification, enhancement of humans and the "commercial eugenics" that the new technologies threaten to unleash.

"These technologies are being developed at a frenzied pace. The general public has had little real opportunity to understand and consider their full implications. There are few significant controls," according to the letter.

"These conditions leave us vulnerable to being pushed into a new era of eugenic engineering, one in which people quite literally become manufactured artifacts," it states.

Many members of the scientific community, along with disease advocacy groups, have rejected any efforts that they feel will impede the progress of medicine. Others, saying that there is still much to be learned in animal research, don't mind a delay.

Responding to Tuesday's letter, stem cell biologist Arthur Lander, chair of the Department of Developmental and Cell Biology at the University of California-Irvine, said, "I don't know of any responsible member of the scientific community that intends to go off in that direction. It is not such a bad thing to slow down, but let's slow down for the right reasons -- because this research is too important to do in rush."

The new coalition urges a moratorium on research cloning as the middle ground between the two positions of an immediate permanent ban and an unconstrained green light. A moratorium would allow time for further scientific study, public review and the creation of some system of legislative oversight.

A bill proposed by Sen. Sam Brownback (R -- TN) would create a permanent ban; one proposed by Sens. Dianne Feinstein (D-CA) and Ted Kennedy (D-MA) would permit research. A vote is expected in April.

The debate is not over making cloned babies, which is almost universally opposed.

Rather, the debate is over therapeutic cloning, which creates -- and destroys -- cloned human embryos for research. The stem cells that are inside these embryos hold therapeutic promise for diseases such as Parkinson's, Alzheimers and others.

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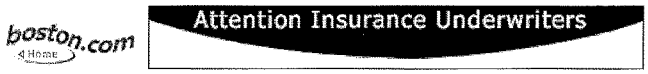

THIS STORY HAS BEEN FORMATTED FOR EASY PRINTING

Coalition urges a ban on all human cloning

By Mary Leonard, Globe Staff, 3/22/2002

WASHINGTON - Congress is facing mounting calls from some unexpected quarters to halt medical research involving human cloning.

Since the US House approved a ban on both reproductive and therapeutic cloning last summer, the dynamic in the nation's capital has changed from one that pitted religious conservatives and antiabortion groups against scientists, biotechnology firms, and patient advocates. Now some environmentalists, feminists, and other activists are joining social conservatives in calling on lawmakers to put the laboratory work on hold.

A broad coalition of biologists, ethicists, public-health advocates, abortion proponents, and human-rights activists signed a letter to leaders of the US Senate this week, urging a total ban on cloning to make babies and an indefinite moratorium on the creation of cloned embryos for use in medical research.

"Human cloning could be a gateway to a frightening new kind of eugenics, where discrimination and inequality are permanently written into our genetic code," said Marcy Darnovsky, a spokeswoman for the Center for Genetics and Society, a group based in Oakland, Calif., that organized the 100 signers and produced the letter.

In the Senate, lobbying is intense on the cloning issue. Senate majority leader Thomas A. Daschle, Democrat of South Dakota, has indicated that he will schedule a debate on cloning legislation in April or May.

One bill - sponsored by Senator Sam Brownback, Republican of Kansas - would ban and criminalize all human cloning. Senators Edward M. Kennedy, Democrat of Massachusetts, and Dianne Feinstein, Democrat of California, have introduced a separate measure banning reproductive cloning but allowing biomedical research with cloned embryos.

None of the cloning bills pending in the Senate would impose a moratorium on research. But both the Biotechnology Industry Organization, which represents 1,100 companies and research institutions, and the Coalition for the Advancement of Medical Research, made up of disease-research foundations and universities, are working feverishly to prevent the idea from catching fire.

Before research proceeds, the health risks posed to women in producing and harvesting the many eggs required for embryonic cloning needs to be addressed, perhaps through federal regulation, Judy Norsigian, founder of the Boston Women's Health Book Collective, told a

Senate committee recently.

Norsigian and more than 100 women's health advocates have signed a statement calling for a ban on reproductive cloning and a five-year moratorium on embryonic cloning for medical research.

"This has nothing to do with the moral status of the embryo," said Norsigian, asserting that she is not aligned with antiabortion groups or the Roman Catholic Church, which condemn therapeutic cloning as the destruction of human life. "I don't believe we have enough good data to go forward with the large-scale participation of women in harvesting eggs for stem-cell research."

In November, Advanced Cell Technology of Worcester said it had created the first cloned human embryo by inserting adult DNA into a donated, hollowed-out egg. Medical researchers hope to harvest stem cells from these early embryos and produce healthy tissue to treat a variety of medical conditions, such as Parkinson's disease and juvenile diabetes.

The announcement by the Worcester firm alarmed some groups and individuals who suddenly saw human cloning as a here-and-now technology with the potential for genetic engineering of human beings.

"The problem with therapeutic cloning is that it introduces commercial eugenics from the get-go," said Jeremy Rifkin, a frequent critic of the biotechnology industry who heads the Foundation on Economic Trends in Washington.

"These new companies aim to control human reproduction from conception to birth, and that raises tremendous social issues about who holds the patent on life, who owns life," said Rifkin, who supports the Brownback bill to ban all cloning.

Leaders of several environmental groups, including Friends of the Earth, Greenpeace, and the Sierra Club signed the letter backing a moratorium on research cloning.

So has the president of the American Association of People with Disabilities, the executive director of Physicians for Human Rights, and the head of both the National Latina Health Organization and the California Black Women's Health Project.

"Dangling cures for a host of diseases, [Advanced Cell Technology] and others who will surely follow in their wake seek to throw open a Pandora's box of technologies that could easily do more harm than good," said Brent Blackwelder, president of Friends of the Earth.

"We have to have some regard for the consequences of our actions before we carry them out," he said.

Almost all senators are expected to support a ban on reproductive cloning.

But more than 20 senators remain undecided on the therapeutic-cloning issue, according to Daniel Perry, executive director of the Alliance for Aging Research.

"No senator wants to have the blood on their hands of saying `no' to medical research," Perry said. "So this idea of a moratorium is a back door way to say we aren't going to criminalize

research cloning, but we are going to put it on hold indefinitely. From the point of view of a girl with diabetes, it is really unacceptable to ask her to wait 5 or 10 years for research to proceed."

Brownback, Kennedy, and Feinstein have rejected the idea of a research moratorium.

President Bush had said he wants a human-cloning ban but is awaiting a report on the medical and moral implications from his bioethics council this summer.

Michael Werner, vice president for bioethics at the Biotechnology Industry Organization, said the industry organization will probably begin running ads to "put a human face on this research and its potential."

Werner said his organizatoin could support a ban on reproductive cloning but not on research.

"A moratorium on research is a ban on research, and that it is not a compromise to us," he said.

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Los Angeles Times latimes.com.

http://www.latimes.com/news/nationworld/nation/la-030502clone.story

COLUMN ONE

Clones, Free Love and UFOs

Medical researchers fear the group that says space aliens have instructed them to start cloning humans will cause lawmakers to ban the technique.

By AARON ZITNER
Times Staff Writer

March 5 2002

VALCOURT, Canada -- In the course of 29 years, Claude Vorilhon built a small yet international religious group by preaching that scientists from another planet created all life on Earth. But in 1998, Vorilhon had an especially big pronouncement for his 5,000 or so followers: The creators would soon board their flying saucers and return. It was time to prepare.

And so Vorilhon called for beautiful young women in his group to step forward as hostesses for the arriving aliens. Members of the elite Order of the Angels were to devote themselves fully--and in some cases sexually--to the creators and their prophet on Earth, Vorilhon. According to former members, well more than 100 women volunteered.

It is an unusual tale, but the strangest part may be this: Today, Vorilhon has won a prominent role in one of the most sober policy decisions before Congress--whether to outlaw human cloning, even as a research tool that might help cure disease.

At the direction of the aliens, Vorilhon says, his group is working to create the world's first cloned child. Some of the Angels have agreed to act as the egg donors and surrogate mothers that the process requires.

Cloning "is the key to eternal life; that's the goal," Vorilhon said at his Quebec headquarters, called UFOland, which features a large model of a UFO he says he boarded in 1973 to meet an alien scientist. "Everyone who enjoys life would like to live forever. Don't you?"

Now, with Congress engaged in an emotional battle over whether to ban human cloning, lawmakers are also debating whether to take the French-born religious leader seriously. Is he truly a rogue cloner, an example of why regulation might be needed? Or is he merely a charlatan, riding the public's unease over cloning to gain publicity for his religion?

It is impossible to determine, yet lawmakers have made Vorilhon part of their debate. And that has some

medical researchers hugely frustrated. They say Vorilhon, who calls himself the Prophet Rael and testified before Congress last year in a futuristic white jumpsuit, has made cloning look unduly creepy. His cloning claims, they say, are pushing lawmakers to ban the technique not only as a way to produce children, but as a potential method for growing new cells for Alzheimer's patients, heart attack victims and other people whose own tissues have gone awry.

"For those of us who want a reasoned debate, it's been a disaster to have him come out of the woodwork," complained Michael West, chief executive of Advanced Cell Technology Inc., a Massachusetts company that aims to create cloned human embryos for disease research. "This is absurd. It's a circus. Why is Congress debating this by talking to someone who says he flies around in flying saucers?"

And yet, some biologists say that if it is possible to create a baby through cloning, Vorilhon and his Raelian Movement might well be the first to do it.

Scientists have successfully cloned cows, pigs and several other species, most recently cats. But each birth has followed scores of failed or aborted pregnancies, and cloned offspring are often unhealthy. Given the risks, what woman would help create or carry a cloned embryo?

It would take someone with a strong commitment--maybe the commitment of an Angel. "This cadre of women gives them an advantage over everyone else in contention," said Dr. Lee Silver, a professor of molecular biology and public affairs at Princeton University. "For anyone to be successful, it will take a lot of eggs, a lot of wombs, and a lot of guts now. The Raelians seem to have a hold on all three."

For some lawmakers, that means no one should be permitted to produce a cloned embryo for any purpose, whether for reproduction or medical research. "Once you have these embryos around, and if groups like the Raelians had access, I don't think it would be difficult for them to succeed," said Rep. Dave Weldon (R-Fla.), a physician. The House has already voted to bar the creation of cloned human embryos for any purpose, and a Senate vote is expected within weeks. President Bush supports the House bill.

Who is Claude Vorilhon, and what is his true goal? A close look at the Raelians shows a long history of publicity stunts, and the cloning effort may be one more. No cloning expert has ever publicly acknowledged working with them.

On the other hand, the Raelians did open a secret laboratory in West Virginia, which they closed last year after the location was discovered. Last month, Vorilhon claimed he had begun work at a new lab to clone a terminally ill man, who has no family and wants to be "reborn like a blank tape."

And some people who know the Raelians intimately say they are very committed to their cause.

"These women, they are not told that this is dangerous," said Dominique Saint-Hilaire, a 14-year Raelian from Bordeaux, France, until she quit in 2000. "They are acting for the Great Cause. They are hoping to be the first mother of a clone. They want to be the most important Raelian on the planet."

Every summer, Vorilhon's followers drive 90 minutes northwest of Montreal, past cows and cornfields, tractors and silos. In the small farming community of Valcourt, they gather at an odd, tear-shaped building for two weeks of meetings and meditation.

This is UFOland, part office complex, part museum of the Raelian religion. The tourists who trickle in are guided through Vorilhon's life and vision--the story of how, in 1973, he was hiking in the French woods when a UFO landed, and an alien explained to him the true origins of mankind.

Vorilhon was 27, the editor of a small auto racing magazine. He had also achieved minor success as a singer. The alien gave him a new mission: to pave the way for a second coming of the creators from space.

Vorilhon's task was to teach people to accept the aliens as their true fathers. He was also to preach the alien philosophy: peace, tolerance, a love of science and sexual freedom.

"When I first heard all this, it was like a philosophical orgasm," said Michel Beluet, the UFOland director and a Raelian since 1976. "You can say we're crazy and on an acid trip, but some people vibrate to it, and they join."

Today, the Raelians claim 55,000 members in 84 countries, though Vorilhon says only 10% are active. Others put the membership at about 3,000, with the biggest groups in French-speaking Europe and Canada.

Building a religion takes skill and sensitivity. "The leader of a new religion has to make followers feel special, like they're the chosen ones," said Susan Palmer, a Montreal sociologist and author of "Alien Apocalypse," a forthcoming book about the Raelians. "Otherwise there's no point in being there, and people drift away."

To keep members engaged, Vorilhon, now 55, has long courted the press. Media attention makes the Raelians feel important, Palmer said. It also allows them to spread their message about the alien creators.

The media, in turn, have found the Raelian talk of sex, science and UFOs to be irresistible. To protest a 1992 decision barring condom machines at certain Quebec high schools, Raelians passed out condoms from a van adorned with large spaceships. They bought billboard space in Toronto to welcome the extraterrestrials. When stories on their activities appear in print, the Raelians take it as confirmation that the world is coming to understand their religion and their work is having an effect.

Vorilhon uses another technique to hold the interest of his followers, say people who study the group. On regular occasions, he makes apocalyptic pronouncements, asserting that a world-shattering event is imminent and that only Raelians are in the know.

Most of his statements have been sufficiently vague or aimed at future events so that his credibility does not come under direct challenge.

In 1998, for example, Vorilhon announced that he had received a telepathic message from the aliens with dramatic news: The creators would soon return.

"Which Christian would not like to serve Jesus personally?" the aliens asked, according to a purported transcript. "Which Jew, Moses? . . . That's why, for those who would like to, we ask our last prophet Rael to found a religious order."

Any pious woman could join the new Order of the Angels and help prepare for the alien arrival. But the

creators expressed a special fondness for beautiful women. Moreover, some women could join an elect group within the Angels by agreeing to sleep only with the aliens and their prophets, including Vorilhon.

In an interview at UFOland, Vorilhon said the Angels came under no pressure to have sexual relations with him. His group believes in sexual freedom, not coercion, he said.

But Angels must be highly committed--willing even to sacrifice their lives. "When people are ready to die to protect somebody they love from aggression, I think it's beautiful," he said.

Now the devoted Angels, the apocalyptic announcements and the drive for media attention have become intertwined with cloning.

After Dolly the sheep was born in 1996, Vorilhon quickly capitalized on the media frenzy. He said he had created a company, Clonaid, that would use cloning to help any gay or infertile couple have children, for a $200,000 fee.

Today, however, Vorilhon says that Clonaid was little more than a post office box in the Bahamas. "For a minimal investment, it got us media coverage worth more than $15 million," he wrote last year in a book, "Yes to Human Cloning." "I am still laughing."

Vorilhon says things turned more serious in the summer of 2000, when a follower named Brigitte Boisselier told him that she had found an American investor willing to put up $500,000 to clone his 10-month-old son, who had died during heart surgery.

Clonaid announced its new cloning effort at a Montreal news conference. Boisselier, who holds two doctorates in chemistry, became the company's scientific director.

Clonaid refused to say where the cloning would take place, or to name any scientists on its team. But as a sign of its credibility, it introduced several of the 50 Raelian women who had agreed to act as egg donors and surrogate mothers. Most but not all of them are Angels, Vorilhon said.

Florence Laudoyer, one of the volunteers, said she saw no health risk to carrying a cloned child. "The surrogate mother will be followed more than any other pregnant woman on Earth," she said in an interview at UFOland. "If there is any problem, there will be an abortion at an early stage. So there is nothing to fear."

The Clonaid announcement had an important effect within the Raelian Movement, said Saint-Hilaire, the former member from France.

"Cloning came just in time, because a lot of people had started getting bored and quitting," she said. "It generates a lot of excitement."

In Washington, Rep. James C. Greenwood (R-Pa.), watched the media coverage of Clonaid. As chairman of a House Energy and Commerce subcommittee, he was planning a hearing on human cloning, with an eye toward proposing a ban on cloning to produce children.

Greenwood invited the Raelians to testify last spring, and Vorilhon appeared in his white jumpsuit, his hair tied atop his head in a knot. He told the lawmakers that people one day would clone themselves and then download their personalities into the clones, achieving a kind of eternal life.

The testimony, Greenwood later said, convinced lawmakers that "even kooks may have the capacity to make human beings through cloning, and we better get serious about legislating here."

When the House voted last summer, it chose to bar human cloning for reproduction and research. That would stop scientists from trying to produce cloned human embryos for their stem cells, which in turn might be grown into replacement tissues for patients with a variety of ailments. Some people said Vorilhon was a big factor in the vote. "The House invited Rael down to show that cloning was kooky and dangerous and imminent, then they acted in terror at the image they created," said Arthur Caplan, a University of Pennsylvania bioethicist. "And Rael allowed himself to become the poster boy for the anti-cloning forces in order to gain publicity."

Vorilhon agreed he was used by cloning opponents. "But, we are winners in any case, even if cloning is banned," he said. "We are winners because our organization had worldwide media coverage."

Caplan isn't laughing. "If I was a patient," he said, "I'd be angry at the media and at the politicians."

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One night in April, Greg Casto woke at 4 a.m. and had trouble returning to sleep. He flipped on CNN, and there was Boisselier, talking about human cloning.

Casto had seen the woman before--right there in the small city of Nitro, W.Va., at the community center, which Casto manages.

Casto realized he knew something that nobody else knew: The Raelians really did have a cloning lab. A lawyer, Mark Hunt, had rented a room at the center and had been stocking it with lab equipment. He had to be the Raelians' secret financier.

Hunt had lost his 10-month-old son during heart surgery two years earlier. "What he said was that he wanted to study DNA to cure disease and get patents," Casto recalled.

When Casto realized Hunt's real intent, he called the authorities, and Hunt was asked to leave.

Even though the Raelians had set up a lab, there were signs that it was no more a real attempt at cloning than was Vorilhon's post office box in the Bahamas.

There was little equipment, Casto said, and there was little activity. "It was very, very minimal," he said. "There was nothing going on in there."

Hunt eventually broke with the Raelians, saying Boisselier seemed more interested in publicity for the religion than in cloning.

Hunt declined interview requests for this story, but he explained his involvement to his hometown newspaper and to ABC television. He said he had hoped, through cloning, to reclaim something of his son. But Boisselier, he complained, had become a "press hog."

Today, Vorilhon says he has a team working to clone the terminally ill man, whom he will not name, at a secret location outside the United States. It is impossible to verify his claim.

In the Senate, there is widespread support for outlawing cloning to produce children. But senators are divided over whether to join the House in barring it in disease research. A vote could come as soon as this month.

Vorilhon claims that 3,000 people have signed up for Clonaid's service, and that the Americans among them would file a lawsuit if Congress bars cloning. Clonaid wants to operate in the United States, "which is really the only country in the world where individual freedom is guaranteed by your wonderful Constitution," he said.

He predicted the Supreme Court would strike down any cloning ban and rule that Clonaid's clients have a right to reproduce as they choose.

Lawmakers are still unsure what to make of the Raelians. "If you want me to put my nickel on the table, I think they're serious," said Weldon, the lawmaker and physician. "But if you came back in two years and said they're a hoax, I wouldn't be surprised."

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HEADLINE: Mortal enemies unite against cloning

BYLINE: By Steve Skutnik, Iowa State Daily

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BODY:
These are strange times in Washington. After all, you know something's amiss when the force of the Christian Right merges with feminists of the uber-left to spearhead the same side of an issue. The "issue" in question now is one of human cloning: President Bush expressed his desire on an outright ban of all forms of human cloning last week, to the cheers of support from both the followers of Pat Robertson and Patricia Ireland.

Huh? Aren't these folks mortal enemies? Apparently, as they say, "politics makes strange bedfellows." No stranger indeed than polar opposites of the political spectrum joining hands along with the President to press the Senate into finishing what the House had already done: to pass a total ban on human cloning.

Note the lack of modifier there -- as in, a ban on all cloning, including "therapeutic" cloning, under which a blastocyst is created for the purpose of using its stem cells.

Naturally, the two sides have their own reasons for pursuing the ban -- conservatives on the vaunted principles of the "protection of human life in all forms" and feminists on their cherished mantles of

"exploitation of a woman's body." Yet with regard to an outright ban on cloning, including therapeutic cloning, each of these positions comes with its own logical contortions.

For instance, while the opposition of conservatives to human cloning is at least somewhat understandable given their leanings on the topic of abortion, what of the millions who will suffer and die due to diseases that could be treated by the stem cells in question -- aren't their lives valuable too? Further, it should be noted that none of this grim scenario about cloning humans for stem cells would have even come about had they not exerted such enormous pressure upon the president in August to render his "Solomonian" decision to limit federal funding to research on existing stem cell colonies.

Rather, had they relented and allowed research to occur on discarded fetuses from fertility and abortion clinics, the need for

"therapeutic cloning" would be outright marginal at best. Perhaps thinking out the alternatives would have served conservatives better right now.

Feminists and other members of the left are hardly better off, though. For one, where are feminists with regard to one of their most celebrated mantles, "the woman's right to do what she wishes with her own body"?

Namely, why exactly are feminists now telling women that they cannot implant and give birth to a **clone** if that is their wish? Furthermore, it is somewhat ironic that the same folks who declare the fact that a blastocyst is not a person with the same moral status or legal rights as you or me (and can simply be disposed of at will) are suddenly so quick to prevent such a "non-entity" from being used for the good of humankind?

Yet the majority of the blame rests only with President Bush, who now rather ironically is seeking to close any possible gaps open in August for medical science to operate in. Did the president honestly believe that limiting the available supply of stem cell colonies for research would simply close all other avenues of research with it? Or did he simply not think this far ahead in time?

Most of this, however, has simply been an issue of therapeutic cloning, somewhat removed from the more dicey issue of "reproductive cloning," the type of cloning most people are more familiar with.

Feminists and ultra-conservatives alike have been painting a grim scenario of secret laboratories carrying out eugenics experiments on an unsuspecting populace, of "X-Files"-like scenarios in which unsuspecting women are kidnapped, their ova stolen and their wombs used for some dark government experiment. Yet all of this ignores much larger issues at hand -- namely the rights of parents who, for one reason or another, simply wish to use cloning as another avenue of carrying on their genetic lineage.

For instance, what of an infertile couple who, having other options fail, decide to simply create a **clone** of one parent to finally be able to have a child who bears a blood connection? Where, pray tell, is the "exploitation of a woman's body" or the rampant disregard to human life occurring here? What compelling interest does the state have in this particular case if under precedents such as Roe v. Wade it has none?

The only remaining argument to be made in this case is the ethical question -- namely that the technology does not exist yet to safely **clone** human beings with any reasonable consistency.

Why then, should the government be so quick to head off the issue before the ethical questions of cloning are even relevant?

Senate Majority Leader Tom Daschle (D-S.D.) said Wednesday, "There is resolute, determined, universal opposition to cloning for creation of human beings."

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Free to Be Me: Would-Be Cloners Pushing the Debate

By Rick Weiss
Washington Post Staff Writer
Sunday, May 12, 2002; Page A01

Liz Catalan lives in a nice house in Miami. She does marketing for a cruise line. She's been married to a wonderful guy for five years. She is, in short, an ordinary woman of 41.

Except that Catalan, who suffers from an untreatable form of infertility, has an extraordinary craving to be cloned.

"I'm not crazy," says Catalan, whose ovaries went into premature failure years ago. "I just want to have a child of my own." Not a child made from a donor egg provided by someone she doesn't know. Not one adopted from halfway around the globe. She wants a baby genetically related to her. And if that means one who's genetically identical, then so be it.

Catalan is part of a small but serious cadre of would-be clonees, people who have studied the science, considered the issues and concluded that their pursuit of happiness might best be fulfilled by having themselves or a loved one cloned.

Their perspective is not countenanced on Capitol Hill, where Congress -- though vigorously debating whether to allow the cloning of human embryos for research -- is unified in its opposition to the creation of cloned babies. Nor is human cloning widely favored by the public. In a poll of Americans conducted last summer, almost 90 percent said scientists should not be allowed to use cloning to try to create children for infertile couples.

Yet many of those who wish to be cloned are not easily dismissed as kooks or cranks. And by bucking the majority view, they are pushing policymakers and the public to contemplate human futures unthinkable even a few years ago.

In fact, say ethicists and constitutional scholars, the cloning debate is important not because it will settle the question of whether cloning is "right" or "wrong" -- it will not -- but because it is forcing people to think more deeply about who we are and what we want to become, as individuals and as a species. In our reflexive dismissal of human cloning, these experts say, there may be a missed opportunity to clarify what the issues really are and why they carry such emotional power.

Such soul-searching is one of the unanticipated but more immediate byproducts of a genetic revolution that is rewriting the rules of biology and society. It's an incremental revolution, without clear milestones that might make it easier to comprehend. And it is still largely confined to the laboratory. Yet it is being shaped not only by scientists but also by the basic longings that define the lives of ordinary people -- people like Liz Catalan -- who claim nothing less than a democratic right to be pioneers on the biomedical frontier.

"I'm willing and ready for whatever it takes," she said.

'No Need for Men'

Human reproductive rights were far from Ian Wilmut's mind when he and his colleagues in Scotland took

a skin cell from a 6-year-old ewe's udder, placed it in a laboratory dish, and -- with a tiny bolt of electricity -- fused it to an egg cell whose own genetic material had been removed. The result of that fusion was an embryo, which the Scottish team transferred to the womb of a surrogate mother sheep that, five months later, gave birth to a lamb named Dolly.

Dolly offered the first living proof that mammals could be created from a single cell and without any contribution from a father. Centuries of scientific thinking collapsed in a heartbeat, and the social implications left people reeling. The day after Dolly's birth was announced, in February 1997, Washington University biologist Ursula Goodenough said pointedly that with human cloning, "there'd be no need for men."

President Bill Clinton responded immediately, ordering the National Bioethics Advisory Commission to study the topic and report back to him within 90 days. The commission's 120-page report, which remains the definitive critique of the technology, concluded that there was a lot to worry about.

Among the commission's concerns was that a clone might find it oppressive to know that his or her genetic life had already been lived, and feel robbed of the "open-ended future" that human rights advocates generally agree should be the birthright of every child. Moreover, a clone's "parent" might have onerous expectations as to how the clone should behave. Why else would someone be cloned, except to get a known quantity? "Cloning is a kind of Rorschach test for some of the worst excesses of parental hyper-expectations," said Thomas Murray, president of the Hastings Center, a bioethics think tank in Garrison, N.Y., who served on Clinton's bioethics commission.

The commission also warned that cloning could "undermine important social values by opening the door to a form of eugenics," genetic engineering. Sen. Sam Brownback (R-Kan.), chief sponsor of a Senate bill to ban all cloning, echoes that thought. "Efforts to create human beings by cloning mark a new and decisive step toward turning human reproduction into a manufacturing process in which children are made in laboratories to preordained specifications," he said in February.

But perhaps more than anything, what disturbs some ethicists is the literal self-promotionalism of it all. Cloning, after all, is about the ascendancy of the individual, the chance to propel one's genetic self into the future undiluted by another. Such "blatant narcissism," Murray said, can only undermine society.

Of course, some people want to clone others rather than themselves, most commonly a loved one, such as a child who met an untimely death. But ethicists foresee problems there, too. "This encourages all of us to view children as interchangeable commodities," said George Annas, a professor of health law at Boston University. "The death of a child thus need no longer be a singular human tragedy, but rather an opportunity to try to duplicate the no longer priceless deceased child."

Despite these and other concerns, Clinton's commission was not convinced that cloning posed unique or insurmountable social harms. It did recommend that Congress impose a moratorium on human cloning, but not on ethical or moral grounds. Rather, the commission was concerned about safety. And recognizing that research would likely overcome the miscarriages and deformities of early attempts, the commission recommended that any congressional ban automatically expire in five years.

Now five years have elapsed and, although the House has passed a ban, a divided Senate is only now considering similar bills. In the meantime, animal cloners have become increasingly adept. And a small number of doctors are compiling waiting lists of people who want to be cloned. Liz Catalan is on one of them.

'Happens All the Time'

She was a legal secretary for 15 years, during which she became well informed about a lot in medicine. She has thought about the possible problems, including the idea that clones might feel that their lives were already being lived, or had been lived, by another.

"I really, honestly think that clones could feel unique, depending on how you bring them up," Catalan said. "It happens all the time with identical twins."

Catalan's observation reflects a truth often overlooked in the age of the genome. With discoveries of genetic links to disease and personality announced every week, one could easily misbelieve that identity is written in the language of DNA. It is not. Our physical, cultural and social environments all influence what we become. Even Wilmut, who strongly opposes human cloning, has said he can easily tell his cloned sheep apart by their individual quirks, though all are genetic replicas.

"Having the same genome as another individual is no threat to the fact of human uniqueness or individuality," Brown University philosopher Dan Brock wrote in the April 12 issue of Science, "because the full identity, individuality or self of a person is determined by much more than the person's genome."

In fact, some have noted, clones might be expected to have less difficulty defining their own identities than twins typically have. Twins generally have to share both their genes and their environment. By contrast, a clone would likely be a generation younger than his or her parental twin.

As for the safety issues, Catalan and other cloning advocates cite the precedent of in-vitro fertilization, or IVF. Study after study has confirmed that babies conceived through IVF have significantly heightened odds of being born with medical and developmental problems (mostly due to IVF's higher prevalence of twins and triplets), yet no one demanded those data before the practice became widespread. And parents today are given the freedom to assess those risks and take them if they choose.

Similarly, some Jewish couples have 25 percent odds of giving birth to a baby with Tay-Sachs disease, a genetic condition that typically kills its victims by age 5. The federal government has not tried to stop them from having children. Why, advocates ask, is human cloning different?

Using safety concerns to set legal criteria for reproduction could have unintended consequences, said University of Alabama philosopher Gregory Pence. "If cloning one day becomes safer than sexual reproduction, will cloning then be the only [legal] way to have children -- based on the good of future children?" Pence asked at a House subcommittee hearing last year. "To me, the essential moral question is whether human cloning is intrinsically wrong. But how can a new way of creating a family be intrinsically wrong?"

A family is all Liz Catalan wants. "I know it's not right for everyone," she said. "But I do personally believe that it should be up to each person. And if the only way a person can have a child of their own is to do this, and if they are willing to take a chance, then they should be able to."

At least a few doctors and scientists agree, and Catalan has been communicating with one of them: Kentucky fertility researcher Panos Zavos, who announced a year ago his intention to collaborate in an offshore human cloning effort. Catalan is one of more than 2,200 adults Zavos says are on his waiting list.

Zavos, who has been invited to testify before a House subcommittee on Wednesday, isn't the only one

claiming to have begun a cloning effort. Italian fertility doctor Severino Antinori has said he intends to produce a human clone as soon as he can. Last Wednesday he claimed to have three pregnancies underway, but others in the field were skeptical.

Meanwhile, leaders of the obscure Raelian religion, who believe that cloning can bring people closer to enlightenment and who say they've heard from 3,000 volunteers, announced in London earlier this year that they had begun a project to clone a terminally ill man. According to the Raelians, the unidentified man plans to stop taking his medications if the effort succeeds and die peacefully in the knowledge that he -- or a reasonable facsimile of himself -- may enjoy a second chance at life.

The Raelians don't stop with the dying, either; they are willing to clone the dead. Unlike Zavos and Antinori, who have said they will offer cloning only to infertile couples, the Raelians are offering their services to grieving relatives who want to see their loved ones again.

That offer could appeal to an especially motivated, distraught and vulnerable subset of potential clients, people like Kathy Gordon, whose tireless efforts to have her dead daughter cloned testify to the lengths to which some will go to heal a broken heart.

'I'd Trade Everything'

Gordon's eldest daughter, Emily, was 16 years old in 1997, when the news about Dolly the sheep came out. At the time, Gordon said, Emily spoke enthusiastically about the prospect of human cloning. Six months later she was killed by a drunk driver.

Devastated by the sudden loss, Kathy Gordon became obsessed with the idea of cloning a girl from some of Emily's cells. She spoke to the coroner soon after the accident and tried to have some tissues frozen in liquid nitrogen, but to no avail. She contacted many of the top scientists in the world of cloning, but those who replied, she said, simply "offered condolences." The few tubes of Emily's blood that remain today have been stored in refrigerators not cold enough to ensure proper preservation of her cells for cloning. But Gordon still harbors some hope that the technology will improve, allowing their use someday.

"I don't understand people who want to clone themselves," says Gordon, 42, a lab technician who lives in central Montana and has a doctorate in ethics. But cloning one's dead daughter is different, she said. "I'd trade everything I have today just to have Emily back."

Gordon rejects the idea that she would try to mold her new child into some preconceived persona.Don't *all* parents struggle with the dueling urges to shape a child and let that child become its own person? It's a struggle, Gordon said, that she'd be having with Emily if not for the accident that took her away.

And besides, she asked, since when does the government engage in the business of distinguishing between good and bad reasons for having a child? Surely, Gordon said, her freedom to reproduce is at least as compelling as a clone's right to be unique.

She has some case law on her side. The Supreme Court has recognized that "procreation" and the right to "have offspring" are fundamental rights, which means the government cannot restrict them without overwhelmingly good reason. "If the right of privacy means anything," the court said 30 years ago in *Eisenstadt v. Baird*, "it is the right of the individual . . . to be free from unwarranted governmental intrusion into matters so fundamentally affecting a person as the decision whether to bear or beget a child." Other cases offer similar language.

Of course, even cloning won't bring Gordon's daughter back, but Gordon knows that. She knows that cloning replicates nature, not nurture. But that's part of her inspiration.

Emily grew up in difficult circumstances during Gordon's previous marriage, Gordon said, declining to go into details. "But in the end, she turned out wonderfully," Gordon said. "If I could have a child with her predisposition to life, her humor, but have her grow up in this new life I've created for myself, which is much better now. I'm married to an attorney. I have all kinds of things now. . . ." Her voice trails off.

'It Wouldn't Be Me'

Any parent would want something better for his or her child. But what about people who want to better themselves -- or make better versions of themselves -- through the alchemy of cloning?

What about Jonathan Colvin?

Colvin, who is 34 and holds degrees in physics and philosophy, was a science fiction buff as a kid and remembers reading tales about human cloning long before it became scientifically plausible. Now he's a technical writer for a computer company in Vancouver.

He was born with cystic fibrosis, an inherited lung disease that could easily kill him within the next decade. There is no cure, but by adding a healthy version of the gene that's defective in CF, scientists have been able to "cure" individual cells taken from patients with the disease. Now Colvin wants scientists to do just that, and a little bit more: Take one of the trillions of cells in his body, fix the tiny molecular mutation that causes the disease, and then clone that single repaired cell to grow a new and literally improved copy of himself -- a newborn Jonathan Colvin who would be free of the disease.

"In some respect, it would give me a second chance at life without CF," Colvin said. "It wouldn't be me, but it would be very similar to me."

To opponents, of course, Colvin's vision just feeds their worst fears that cloning will lead to a new eugenics. "Human nature itself lies on the operating table, ready for alteration," the University of Chicago's Leon Kass warned in the New Republic last spring. "We can see all too clearly where the train is headed, and we do not like the destination," wrote Kass, who is now chief of President Bush's Bioethics Council.

But Colvin does not see his situation in that light. He's not interested in building a superior human.

He doesn't want a kid with Michael Jordan's jumping genes or Georgia O'Keeffe's artistic vision. He just wants to make a normal, healthy boy.

Colvin is not the only one who sees the specter of eugenics as an argument for, rather than against, *laissez-faire* human cloning. Think about the Nazi era, when the state "knew" what was best, said Nick Bostrom, a philosopher at Yale University. Think about Scandinavia through the 1970s, when mentally handicapped people were "encouraged" to be sterilized.

In Bostrom's view, eugenics movements of decades past were problematic precisely because governments got involved in decisions about reproduction. "The best way to avoid these scenarios," he said, "is for people to make their own reproductive choices."

Recently Colvin has been getting some legal advice as to whether he might have a good case under the Canadian constitution favoring his right to clone a healthy version of himself. "Most of the objections I've heard so far are for religious reasons, which I believe should not be imposed on me, or because people are just plain scared," Colvin says. "They're afraid of science fiction, like 'The Attack of the Clones.' "

What Colvin fears is the possibility that his offspring would suffer as he has. Does the government really feel compelled to stop him from having a child with healthy, pink lungs? A child who need not think about every breath? "If anything," he says, "it would be socially irresponsible for me to clone myself and *not* knock out the CF."

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THE NATION

Cloning Advocates, Foes Battle for Senators' Votes

Medicine: Both sides, desperate to pass a bill, are modifying their positions to sway undecided lawmakers.

By AARON ZITNER
TIMES STAFF WRITER

April 17 2002

WASHINGTON -- With an upcoming Senate vote on the issue too close to call, both sides in the dispute over the use of human cloning in disease research are exploring ways to modify their competing bills to win support from the 10 or so undecided lawmakers.

The discussions show how the tight nature of the battle may wind up changing the final shape of anti-cloning legislation. The issue is one of the most emotional and politically volatile before Congress this year.

Lobbyists who support cloning for medical research are talking up a requirement that no cloning take place in or near fertility clinics. In addition, they may propose that researchers be barred from preserving cloned embryos in frozen storage, according to people familiar with the discussions.Reproductive Cloning Concerns Senators

These rules would be aimed at answering critics, including President Bush, who say that embryos created for research will inevitably be misappropriated and placed into women as part of attempts to create children.

The new regulations might make research cloning more palatable to some senators, allowing them to argue that safeguards are in place to prevent abuse, said one aide to an undecided lawmaker. Like others familiar with legislative maneuvering, he did not want to be identified because of the sensitive nature of the discussions.

Among opponents of cloning in medical research there is discussion of dropping a provision from their bill that would impose hefty fines and jail time on anyone who imported a medical treatment from another country that had been created through cloning.

No such treatments now exist. But some senators have said they are wary of hindering patients from seeking cures for diseases.

Cloning involves using a cell from a person to create an embryo, which has the same genetic makeup as the person who donated the cell.

There is broad support in Congress for banning anyone from creating embryos this way and then implanting them in women to produce children.

But the Senate is divided on whether scientists should be able to create embryos for research. Among other things, researchers want to dissect the embryos for their stem cells, the cells that have drawn intense interest for their potential to lead to cures for disease.

The House of Representatives and Bush favor a ban on human cloning for any purpose, and about 40 to 45 senators agree. An equal number of senators are believed to support a measure that would ban cloning for reproduction but preserve it as a tool of medical research.

The dispute raises the possibility that no ban on cloning will become law, and that the issue will become prominent in the fall campaigns for control of the closely divided Senate.

Supporters of a total ban say it is immoral to create human embryos only to destroy them. They also say that a partial ban is unworkable.

"Cloned human embryos created for research would be widely available in laboratories and embryo farms," Bush asserted in a speech last week. "Once cloned embryos were available, implantation would take place. Even the tightest regulations and strict policing would not prevent or detect the birth of cloned babies."

Bush also said cloning would create a "massive national market" for the human eggs that the process requires, leading to the exploitation of women.

In discussions with undecided senators, advocates of cloning in medical research have tentatively suggested several ways to address the criticisms.

Research teams might be required to offer psychological tests or other screening to women who offer their eggs for cloning research.

Other rules would seek to ensure that cloned embryos are kept away from fertility clinics, where non-cloned embryos are routinely created and transferred to women as part of high-tech methods for conceiving children.

Researchers could also be required to register with the Food and Drug Administration before undertaking cloning. And the federal officials might be required to report violations of the cloning rules to state licensing officials, who could revoke the right to practice if the violator is a doctor or other licensed professional.

Frist Opposes Importation Ban

The proposed regulations have not been approved by Sens. Dianne Feinstein (D-Calif.) or Edward M. Kennedy (D-Mass.), lead sponsors of the legislation that would bar cloning only for reproduction, people familiar with events said.

Sen. Sam Brownback (R-Kan.), sponsor of the measure that would ban all human cloning, has not agreed to drop the provision that would bar the importation of medical treatments derived from cloned embryos, said his spokesman, Erik Hotmire.

But Bill Kristol, a conservative activist and founder of an anti-cloning group, said recently, "There's some unhappiness about the importation ban, and there's been indications that Brownback might remove that himself."

The importation ban is opposed by Sen. Bill Frist (R-Tenn.), who nonetheless supports Brownback's legislation. As the Senate's only physician, Frist's opinions on health matters are closely watched by his colleagues.

If you want other stories on this topic, search the Archives at latimes.com/archives. For information about reprinting this article, go to www.lats.com/rights.

The Age (Melbourne)
July 29, 2002 Monday
SECTION: News; Pg. 2

Stem-cell Cloning Not Needed, Says Scientist

BYLINE: Tom Noble Health Editor

Leading stem-cell researcher Alan Trounson has abandoned his call for therapeutic cloning, saying scientific breakthroughs mean there is now no need for the controversial technique.

In April, Prime Minister John Howard announced a three-year moratorium on therapeutic cloning, despite strong lobbying from scientists including Professor Trounson, who described the technique as very important.

Professor Trounson told The Age that the pace of change was so rapid in stem-cell technology that therapeutic cloning was now unnecessary. "My view is there are at least three or four other alternatives that are more attractive already," he said.

Therapeutic cloning involves removing DNA from a human egg and replacing it with a donor's DNA.

The egg grows to an embryo several days old - an exact copy of its donor - before it is destroyed for its stem cells. In theory, these stem cells can be grown into, say, nerve cells and returned to the donor's body to repair nerve damage, with little chance of rejection. Supporters say stem cells can be grown into any human cell and could cure a range of illnesses.

Opponents of the technology - in which "spare" IVF embryos have been destroyed to harvest embryonic stem cells - question the "hype" of stem cells. They say therapeutic cloning is especially distasteful because embryos are created specifically to be destroyed.

Professor Trounson said therapeutic cloning faced logistical problems,

including the difficulty of obtaining large numbers of donor eggs and the fact the stem cells would be useful only to the donor, making the process time-consuming and expensive. New techniques, including those being developed in Australia, Britain and Japan, offered better options.

"We know that the egg can reprogram a skin cell, for example," Professor Trounson said.

"We also know embryonic stem cells will do it, so why wouldn't we just use embryonic stem cells to reprogram our skin cells, rather than an egg? You don't have to actually form an embryo that way.

"I can't see why, then, you would argue for therapeutic cloning in the long term because it is so difficult to get eggs and you've got this issue of (destroying) embryos as well."

Last year, Professor Trounson did an about-face on the need for new embryonic stem-cell lines. After having said there was no need to destroy any more embryos because cell lines imported from Singapore were adequate for research, he changed his mind.

The Singapore stem cells were grown on mouse "feeder tissue". The cells had grown perfectly well, but the thought of injecting mouse-grown tissue into humans raised many questions, not least the risk of an animal virus moving across species. The issues raised by mouse-grown tissue also threatened the acceptance of any tests using those cells ahead of human trials. Professor Trounson said he wanted to grow the first Australian embryonic stem-cell lines - without mouse tissue - once the Federal Parliament passed the legislation.

Despite opposition from a range of MPs, including cabinet ministers, laws that allow limited use of "spare" IVF embryos to grow stem cells are expected to be approved in the next session of parliament.

Professor Trounson, who was awarded $44.5 million in May to set up a national stem-cell research institute, said he hoped Victoria would amend its laws once the federal law passed, so stem-cell lines could be legally grown.

"We would prefer to do it here than anywhere else," Professor Trounson said.

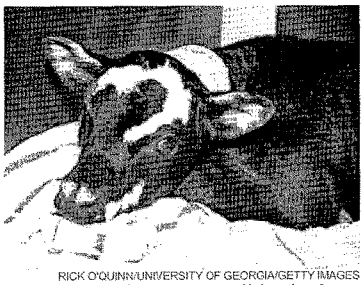
TIME.com
June 24, 2002

Science

The Fatal Promise of Cloning

Advocates say they will never create human fetuses. Can we believe them?

BY CHARLES KRAUTHAMMER



RICK O'QUINN/UNIVERSITY OF GEORGIA/GETTY IMAGES
The first calf ever cloned rests at the University of Georgia April 25, 2002

Monday, Jun. 17, 2002

As the cloning debate rages in Washington, there is news from the scientific frontier. It involves cows, but tomorrow it could easily involve humans.

Scientists at Advanced Cell Technology in Worcester, Mass., took a skin cell from Cow A, cloned it (by injecting the nucleus into a cow egg whose nucleus had been removed), then implanted the embryo in the uterus of Cow B. That embryo clone grew into a fetus, which, had it been born, would have been Cow C. But it was not born. The fetus was removed from the uterus and harvested for its tissues. These tissues from the clone were then put back into the original Cow A. Lo and behold, it worked. These cells from the clone were not rejected by Cow A and even organized themselves into functioning tissue (such as a kidney).

An amazing success. This is precisely what the advocates of research cloning are promising. Clone, grow it and then use the cloned tissue to create near identical replacement parts for the original animal and thus presumably put us on the road to curing such human scourges as Alzheimer's disease, Parkinson's, spinal-cord injuries and the like.

Do this in humans, and we might have thousands cured, millions relieved of suffering. Who could possibly stand in the way of this research?

We do, say cloning advocates. We would never countenance such work in humans, they say. Cows, yes, but we would never implant a cloned human embryo in the uterus of a woman and grow it to the stage of a fetus. We solemnly promise to grow human clones only to the blastocyst stage, a tiny 8-day-old cell mass no larger than the period at the end of this sentence, so that we can extract stem cells and cure diseases that way. Nothing more. No fetuses. No implantation. No brave new world of fetal farming.

This is all very nice. But curing with stem cells is extremely complicated. First, you have to tease out the stem cells from the blastocyst. Then you have to keep the stem cells alive, growing one generation after another while retaining their pluripotentiality (their ability to develop into all different kinds of cells). Then you have to take those stem cells and chemically tweak them in complex ways to make them grow into specialized tissue cells — say, neurons for a spinal-cord injury. Then you inject the neurons into the patient and get your cure.

The Advanced Cell Technology cow experiment suggests the obvious short circuit that circumvents this entire Rube Goldberg process: let the cloned embryo grow into a fetus. Nature will then create within the fetus the needed neurons, kidney cells, liver cells, etc., in far more usable, more perfect and more easily available form.

Tempting? No way, the cloning advocates assure us. We will never break that moral barrier. It is one thing to grow a cloned embryo, a tiny mass of cells not yet implanted. It is another thing to grow a cloned human fetus, with recognizable human features and carried in the womb of a woman.

I am skeptical of these assurances. Why? Because just a year or two ago, research advocates were assuring us that they only wanted to do stem-cell research on discarded embryos from fertility clinics but would not create a

human embryo in the laboratory just for the purpose of taking it apart for its stem cells.

Well, that was then. Today these very same advocates are campaigning hard to permit research cloning — that is, the creation of human embryos for the purpose of taking them apart for their stem cells. They justify this reversal of position by invoking the suffering of millions. And they heap scorn on opponents for letting old promises and arbitrary moral barriers stand in the way of human betterment.

Well, the cow experiment shows the way to even more human betterment. Fetal tissue offers a far simpler and more promising way to produce replacement tissues — it skips all the complications of stem-cell biology and gives you tissue that you can implant right into the human patient. Millions are suffering, are they not?

Millions are suffering. This is precisely the argument that research-cloning advocates are deploying today to allow them to break the moral barrier of creating, for the first time, human embryos solely for their exploitation. What is to prevent "millions are suffering" from allowing them to break the next barrier tomorrow, growing cloned embryos into fetuses?

We will never go there, the research-cloning advocates assure us. Promise. Cross my heart and hope to die. But what are such promises worth? At some point, we need to muster the courage to say no. At some point, we need to say: We too care about human suffering, but we also care about what this research is doing to our humanity.

We need to say that today, before it is too late. The time to stop human cloning is now.

From the June 24, 2002 issue of TIME magazine

THE AGE
theage.com.au

Beware: human cloning risks creating monsters

By Alasdair Palmer
April 9 2002

'It is simply a matter of determination, and we are determined," declared Panos Zavos six months ago when asked whether it was possible that he and colleague Severino Antinori could clone a human. If the announcement in Abu Dhabi last week is to be believed, their "determination" has paid off - the doctors have implanted a cloned human embryo inside a woman's womb.

While the announcement has been met with scepticism, it is not impossible that Antinori and Zavos have done what they claimed. The techniques for "single nuclear transfer" are now fairly well understood, and have been used in a host of species since Dolly the sheep nearly six years ago became the first cloned animal to be born.

Antinori and Zavos do not have the expertise to implant a cloned human embryo themselves, but they could hire scientists who do. They have the money: the desire to have a child can be so strong that it can overcome even the visceral revulsion that cloning a human generates in most people.

That explains why there is no shortage of childless couples willing to pay exorbitant fees for the chance to be experimented on by Antinori and Zavos. They say that they have almost 5000 volunteers. The woman chosen to implant the embryo is said to be the wife of a Saudi billionaire willing to commit unlimited resources to the project.

No surprises there, then.

But implanting an embryo is a long way from producing a healthy cloned baby. The great majority of cloned animals die as the foetus develops. The success rate is less than one in 200. To produce Dolly, it took 277 embryo implants before there was a successful pregnancy. Other projects to clone animals since Dolly was born have experienced the same appallingly high rate of attrition.

Furthermore, if they do not die prematurely, cloned animals are born with serious defects, or develop them. Problems with the immune system, the lungs, the heart and the brain are very common.

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No one knows quite why. One theory is that when the experimenters manipulate the cells to be cloned, they scrape off some surrounding molecules. Those molecules may play an important role in ensuring that genes are "switched on" in the right sequence, ensuring that each organ is in its proper location (so that, for instance, your brain cells end up in your head rather than in your stomach). By interfering with them, the experimenters may ensure that the developmental process cannot proceed properly.

All that is certain is that serious developmental problems have emerged in practically every case. Dolly is exceptional in her rude health - and even she has arthritis, although that may just be the result of too much gambolling during photo shoots.

Antinori and Zavos have insisted that "we won't create monsters - we have made the technique safe". The animal experiments that have produced the defective animals have been "poorly designed and carried out", they say - adding that "humans are different". Their claims are fraudulent.

The only relevant way in which cloning humans is different from cloning animals is that developmental defects are more likely, not less.

"There is no method for screening defects in clones," says Dr Harry Griffin, of the Roslin Institute, which cloned Dolly. "Antinori and Zavos are operating completely in the dark. That is why it is so appallingly irresponsible to try this procedure with people."

It is doubtful if Antinori and Zavos would have quite so many women willing to pay to be implanted with cloned embryos if they told the truth about the likely consequences: aborted foetuses, dead babies, or, if they are lucky, severely handicapped children who die early.

Antinori and Zavos will not have told them, possibly because the people who they deceive most completely are themselves - they seem actually to believe their own publicity.

But then neither Antinori nor Zavos have much knowledge of the molecular biology of reproduction. Antinori's claim to fame rests on delivering IVF to a woman, 62. Zavos made a small splash when he was fired from an Alabama hospital for "unethical and illegal behaviour", including keeping the money for a procedure which he had no part in performing, and charging $US1400 when it should have cost $US60.

Panned in part by Antinori and Zavos, whose antics only help to spread the vision of clones as chemically created Frankensteins, there is now considerable opposition to any cloning technology. President George Bush has banned it in the US and the European Parliament wants to ban it.

Yet properly developed, cloning holds the hope of a medical revolution. Using cloned cells to produce clusters of cells rather than whole people, it may be possible to "grow" parts of the body that have been destroyed or ceased to function properly.

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If Antinori and Zavos turn out to have a long-term legacy, it will be one that blights the future by retarding beneficial cloning research.

Alasdair Palmer is a columnist with ***The Sunday Telegraph****, London, where this article FIrst appeared.*

This story was found at:
http://www.theage.com.au/articles/2002/04/08/1017206310093.html

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The Australian

April 29, 2002, Monday

SECTION: LOCAL; Pg. 3

LENGTH: 398 words

HEADLINE: All clones defective, says Dolly creator

SOURCE: MATP

BYLINE: Jonathan Leake

BODY:
A REVIEW of all the world's cloned animals suggests every one of them is genetically and physically defective.

Ian Wilmut, co-creator of Dolly the sheep, the first mammal to be cloned from an adult cell, published his findings this weekend and suggested cloned humans could be vulnerable to genetic defects.

This was a clear warning that "nobody should be attempting to clone a child". In Italy, Severino Antinori has claimed three women are pregnant with cloned babies, and in the US , Panayiotis Zavos has said he will achieve such a pregnancy within two years.

The new study surveys **cloning** efforts worldwide. "The widespread problems associated with clones has led to questions as to whether any clone was entirely normal," Professor Wilmut says.

Dolly, the sheep cloned by Professor Wilmut five years ago at the Roslin research centre in Scotland, has already shown defects.

Earlier this year, Dolly was found to be developing arthritis at a far younger age than is normal in sheep.

Professor Wilmut lists defects occurring regularly in other cloned animals, including gigantism (excessive size) in cloned sheep and cattle, placentas up to four times the normal size in mice and heart defects in pigs.

Despite being given normal amounts of food, many cloned mice also become grotesquely fat, while many cloned cows, sheep and pigs have developmental difficulties, lung problems and malfunctioning immune systems.

Cloned animals have also shown a variety of individual defects. A calf cloned in France appeared to be thriving but suddenly died at 51 days old after a failure in its ability to produce white blood cells.

Scientists at Roslin had to put down a cloned lamb at 12 days old because the muscles around its lungs were so abnormally thick that it could hardly breathe.

Professor Wilmut believes DNA is formatted radically differently in the **cloning** process and this is why the genes of cloned animals seem to behave in unpredictable ways.

He concludes: "There is abundant evidence that **cloning** can and does go wrong and no justification for believing that this will not happen with humans."

The researchers behind the human **cloning** programs said they could overcome such problems. Dr Zavos claims to have two laboratories perfecting their techniques on animals before attempting to reproduce a human in the "near future".

The Sunday Times

LOAD-DATE: April 28, 2002

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DAILY MAIL (London)

April 29, 2002

LENGTH: 578 words

HEADLINE: HEALTH DANGERS OF THE HUMAN CLONES

BYLINE: Tim Utton

BODY:
THE dangers of human **cloning** were dramatically underlined yesterday.

A review of all the world's cloned animals found clear evidence that they are at risk of a catalogue of abnormalities.

The study by Professor Ian Wilmut, leader of the team that cloned Dolly the Sheep, suggests the animals are all genetically or physically abnormal, even if they appear healthy. Problems that have already emerged include organ deformity, premature ageing, massive obesity and damaged immune systems. There is also a high abortion rate for cloned foetuses.

Professor Wilmut said: 'There is abundant evidence that **cloning** can and does go wrong, and no justification for believing this will not happen with humans.'

The report will strengthen calls for a worldwide ban on **cloning** that is aimed at producing a human baby.

Professor Wilmut says the ban already in operation in Europe and the U.S. should be extended everywhere. There is already deep concern that projects to clone humans may be under way.

Earlier this month controversial Italian doctor Professor Severino Antinori said he had succeeded in implanting a cloned embryo into a woman, although he has produced no evidence to back the claim.

Unlike British and American scientists, who are working to produce cloned embryos as a source of 'spare-part' cells to treat disease, Professor Antinori sees no ethical bar to creating a cloned baby.

He claims 5,000 couples, including 'three or four' from Britain, have volunteered to take part in his work.

But Professor Wilmut, whose study was published at the weekend, said it was a clear warning that nobody should be trying to clone a child.

He said: 'The widespread problems associated with clones have led to questions as to whether any clone is entirely normal.'

Dolly, who was cloned at the Roslin Institute in 1996, has developed arthritis earlier than might have

been expected. Scientists believe she may be ageing prematurely because she was cloned from a six-year-old adult.

Professor Wilmut's study highlighted other unpredictable defects suffered by cloned animals.

A calf cloned in France did well for several weeks but died suddenly at 51 days after its ability to produce white blood cells failed.

Scientists at Roslin had to put down a 12-day-old cloned lamb because the muscles around its lungs had grown so thick that it had great difficulty breathing. Currently, almost 99 per cent of animal **cloning** procedures end in failure. Only just over 1 per cent result in living, apparently healthy offspring.

The rest of the embryos are so badly damaged they tend to be aborted, stillborn or born with chronic deformities affecting key organs including the heart, lungs and kidneys.

The problems involved in **cloning** animals are thought to be due to inadequate or inappropriate 'reprogramming' of genes during the process, which involves injecting DNA from the original into a hollowed-out donor egg.

Some scientists believe that the **cloning** process can turn any gene on or off at random, with unpredictable and potentially devastating impact on the health and even behaviour of a human clone.

If Professor Antinori's claim is true, the cloned embryo he said has been implanted in a woman will currently be at about 11 weeks gestation.

But some scientists are sceptical about his assertions. He has claimed to have created the first cloned monkeys - but never produced any evidence.

t.utton@dailymail.co.uk

LOAD-DATE: April 28, 2002

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The Independent (London)

July 6, 2001, Friday

SECTION: TITLE PAGE; Pg. 1

LENGTH: 592 words

HEADLINE: HUMAN CLONING 'WILL NEVER BE SAFE'

BYLINE: Steve Connor Science Editor

BODY:

SCIENTISTS HAVE found potentially definitive evidence that cloning is far too unsafe to be used in human reproduction, should it ever be viewed as ethically acceptable in the future.

Hidden genetic defects were found in otherwise healthy cloned animals in a study that could fatally undermine the arguments for loosening controls on the most controversial area of reproductive technology.

The research could explain why a huge proportion of cloned animals are either stillborn or suffer from congenital defects, and points to the presence of an underlying genetic flaw in all **clones.** Professor Ian Wilmut, the British scientist who cloned Dolly the sheep, said last night that the research represented a serious blow to people such as Sevorino Antinori, the Italian doctor who has said that he wants to **clone** a baby. "It surely adds yet more evidence that there should be a moratorium against copying people. How can anybody take the risk of cloning a baby when the outcome is unpredictable?" Professor Wilmut said.

The study was done by scientists drawn from two leading laboratories in America. They found that cloned mice that were healthy in all outward respects carried a high "burden" of genetic abnormalities, which could shorten their lives.

The cloning process has also been shown to cause a higher-than-normal incidence of birth defects. Other lambs cloned with Dolly, for example, either died in the womb or were born with serious imperfections.

Now, a team led by Rudolf Jaenisch of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, has found that healthy, cloned mice possess a hidden "instability" of their genes, which is not present in normal mice. The instability causes some genes to work, or to be "expressed", at abnormal levels, probably as a result of the cloning process bypassing the normal way that chromosomes from two parents work together when a sexually produced embryo is created by the fusion of sperm and egg.

Despite this instability, many of the cloned embryos survived to adulthood suggesting that mice and other mammals - including humans - are surprisingly tolerant of such genetic aberrations.

"This suggests that even apparently normal **clones** may have subtle aberrations of gene expression that are not easily detected in the cloned animal," Professor Jaenisch said.

The study, published in the journal Science, suggests that reproductive cloning causes unavoidable fundamental flaws, a finding that has surprised the researchers themselves, who included Ryuzo Yanagimachi of the University of Hawaii, the first person to **clone** adult mice.

David Humpherys, a member of the research team, said that by tagging certain genes, the scientists found that cloning appeared to upset a phenomenon known as "genomic imprinting", where the genes on the chromosomes from one of the parents are switched on or off.

"The big concern is that there would be some underlying problem that you can't see at birth or that there are other problems you can't even assess in mice, such as cognitive problems," Mr Humpherys said. "It seems very unwise to attempt this sort of cloning on humans."

Dr Yanagimachi was hailed in 1998 when he led a team of American, Japanese, Italian and British scientists who succeeded in producing a colony of 22 cloned mice.

The achievement, which some scientists believed was a biological impossibility, was expected to lead to new cancer therapies, improvements in agriculture and in the production of pharmaceutical drugs.

LOAD-DATE: July 6, 2001

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DAILY MAIL (London)

July 6, 2001

SECTION: Pg. 37

LENGTH: 622 words

HEADLINE: 'It's very scary to contemplate';
Scientists warn over fatal f laws in cloning

BYLINE: James Chapman

BODY:

SCIENTISTS today issue a chilling warning about the dangers of using cloning technology to produce a baby.

They have found the first evidence that normal-looking **clones** can harbour serious genetic abnormalities.

The experts are warning that their findings may mean that reproductive cloning is fundamentally unsafe. They say that the cloning process can turn any gene in the body on and off at random, with unpredictable and potentially devastating impact on the health and even behaviour of a human **clone.**

Last night the British scientist who produced the world's first cloned mammal, Dolly the sheep, called for an international ban on cloning a human baby because of the prospect of horrific effects.

Professor Ian Wilmut, of the Roslin Institute in Edinburgh, insisted: 'There should be a universal moratorium against copying people.

'How can anybody take the risk of cloning a baby when the outcome is unpredictable?'

American scientists examined the genetic structure of cloned mice and found that many genes were not working as they should.

The researchers, at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, and University of Hawaii, whose findings are published in the journal Science, say they confirm the previous suspicion that reproductive cloning is not only inefficient, but may actually be unsafe.

David Humpherys, one of the scientists who carried out tests on 38 mouse **clones,** warned last night: 'It's like Russian roulette.

'It seems that the way the cloning process changes the way genes express themselves in the body is random.

'Even a baby that was born and appeared outwardly normal could have serious genetic flaws.

'It could affect health in later life, it could affect cognitive development.

It's not at all unreasonable to suspect it could affect behaviour.

'It is very scary to be contemplating this in humans.' Several groups around the world have signalled their intent to try t o produce the first cloned human baby.

The most credible, led by fertility experts Professor Severino Antinori, an Italian, and American Panayiotis Zavos, announced earlier this month that they would press ahead with their cloning plans despite an international outcry.

Professor Antinori says hundreds of childless couples, including several from Britain, have volunteered to take part in his project.

'Cloning creates ordinary children, ' he insisted.

Brigitte Boisselier, a French biochemist who belongs to a cult called the Raelians, says that her company Clonaid plans to produce a cloned child within a year, though her claims are being treated sceptically by mainstream scientists.

She said that cloning will allow infertile or homosexual couples the chance to have children, adding: 'We are doing nothing wrong. We are trying to help mankind. And we are not going to be stopped, even if I have to take a bullet.'

But the American experts say that their discovery of random 'slips' in the genetic makeup of **clones** should sound a warning to the scientists who want to use the technology in humans.

They said the discovery shows why cloned animals often develop life-threatening diseases and flaws.

Cloned cows, sheep and pigs have been observed to have developmental problems, heart defects, lung problems and malfunctioning immune systems.

Dr Patrick Dixon, author of The Genetic Revolution, said: 'Even if scientists succeed in producing a healthy cloned baby for the cameras, it may be 20 or 30 years before we know the truth about silent gene damage.

'For the first time, we're seeing science that exposes the stark truth about the inherent dangers in the cloning process.' j.chapman@dailymail.co.uk

GRAPHIC: BRAVE NEW WORLD: DOLLY THE SHEEP, THE FIRST CLONED ANIMAL

LOAD-DATE: July 7, 2001

Copyright 2001 Guardian Newspapers Limited
The Guardian (London)

July 6, 2001

SECTION: Guardian Home Pages, Pg. 7

LENGTH: 319 words

HEADLINE: Scientists warn of hidden defects in 'healthy' **clones**

BYLINE: James Meek Science correspondent

BODY:

The controversial new science of animal cloning receives a setback today with a warning by researchers that even apparently healthy **clones**, such as Dolly the sheep, could have hidden genetic defects.

The study by US scientists suggests that attempts to **clone** a human being, already being discussed publicly and privately by fertility specialists, would be even more dangerous than was thought.

Scientists have successfully cloned sheep, cattle, pigs, goats and mice, but only at a massive cost in squandered eggs, miscarriages and still births. In today's issue of the jour nal Science, researchers from the Massachusetts Institute of Technology and Hawaii University describe how a number of critical genes in mice they cloned behaved abnormally.

In normal reproduction, animals inherit two sets of almost identical genes, one from the mother, one from the father. But of these tens of thousands of genes, about a hundred are "imprinted" according to whether they come from the father or mother. Many of these genes are to do with growth. The female tends to "silence" her legacy of growth genes, the male to "switch on" his.

There has been speculation that a reason for the high failure rate of cloning is that this imprinting process goes hay wire. Many **clones** which do make it to birth are abnormally large, or have abnormally large organs.

The new research, which looked at what a small number of these imprinted genes were doing, backs this up- and suggests that even cloned animals which seem to be fine are messed up inside.

Alan Coleman, research director of the British firm PPL Therapeutics, which worked with the Roslin Institute on the cloning of Dolly, complained that the US team had cloned mice with a different type of cell, embryonic stem cells. The kind of cells used to **clone** Dolly, he said - mature cells from an adult ewe - were genetically more stable.

LOAD-DATE: July 6, 2001

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Los Angeles Times

July 6, 2001 Friday Home Edition

SECTION: Part A; Part 1; Page 1; Metro Desk

LENGTH: 1337 words

HEADLINE:
More Doubt Cast on Cloning Safety;
Science: Researchers find unpredictable genetic flaws that can cause premature death or abnormalities.

BYLINE: ROBERT LEE HOTZ, TIMES SCIENCE WRITER

BODY:
Strengthening the scientific case against human cloning, researchers have discovered that even apparently healthy **clones** may harbor unpredictable genetic abnormalities.

In experiments with laboratory animals, scientists at the Whitehead Institute at the Massachusetts Institute of Technology and the University of Hawaii discovered that **clones** created with embryonic stem cells develop apparently capricious errors in when and how their genes become active. Those errors can lead to premature death or serious abnormality in the resulting animals, the researchers said. The research also found that stem cells themselves are surprisingly unstable.

The findings bolster misgivings about the basic biology of cloning. Developmental biologist Brigid Hogan of Vanderbilt University and the Howard Hughes Medical Institute called the research "a technical tour de force. This certainly is raising a flag."

The report, published today in Science, comes as federal investigators have targeted a U.S. laboratory where members of a religious sect allegedly were experimenting with ways to **clone** a human being. The group is led by a man who claims that he witnessed a UFO landing in 1973 and that humans must create new life through cloning because aliens created humanity. Members told a congressional committee in March that they had hired several researchers to work on cloning.

Two fertility experts also have recently announced their intent to try to **clone** a human being.

The new research also could influence the debate over a separate use of embryonic stem cells to create tissues for research on diseases and their treatments. The Bush administration is expected to decide soon whether researchers who take government money should be allowed to work on tissues derived from embryonic cells.

Medical researchers hope to use stem cells to produce perfectly matched tissues to replace or repair organs that have stopped functioning, thus treating diseases--including diabetes, heart problems and Parkinson's--and perhaps allowing the replacement of body parts. The work is controversial because obtaining the stem cells requires the destruction of embryos.

"I am concerned that this [research] may feed those who want to ban the research," said Robert Lanza,

vice president of medical and scientific development at Advanced Cell Technology, which is researching human embryonic stem cells for the treatment of several diseases.

Clones May Not Be Normal

The scientists who conducted the new research, however, said their findings should not alter the potential of stem cell technology as a source of disease therapies. The problems discovered in the new research only arose when the cloned embryos were forced to develop into a mature animal, said Rudolf Jaenisch at the Whitehead Institute, the senior scientist on the project.

Those who support human cloning say the technique could be used as a means of human reproduction for childless couples unable to conceive with more conventional medical assistance, for those seeking to regenerate a loved one, or for people wanting to copy themselves. The new research calls into serious question the safety of all those ideas, cloning experts said.

"Our findings clearly argue against reproductive cloning," said Jaenisch. "Even apparently normal **clones** may not be normal. We have the hard evidence now."

The research suggests that there can be errors in a cloned embryo that even a conscientious infertility specialist could not detect in a screening procedure. That may be an insurmountable safety problem for reproductive cloning, said Alexander M. Capron, an expert on biomedical ethics at the USC Law School who is a member of a national bioethics commission.

"It undermines the claims of those who say that they will be able to select out good cloned embryos from those with abnormalities," Capron said. "This is a false hope."

Since 1997, when the first adult mammal was cloned, researchers around the world have successfully cloned sheep, cattle, mice, goats and pigs. A Korean team even reported cloning a human embryo. But researchers have been unable to **clone** many species, such as rabbits, rats, cats and dogs.

In all species, success rates are low.

To better understand why so many cloned animals either die or are abnormal, Jaenisch and David Humphreys at the Whitehead Institute and their colleagues cloned generations of mice to study the behavior of six genes responsible for normal fetal growth and development. The activity of these genes normally varies depending on which parent they come from.

The researchers looked at embryonic stem cells, which can give rise on their own to all the tissues an organism requires, because they more readily produce **clones** that survive pregnancy and birth and live into adulthood.

To create genetically identical animals by cloning, researchers transfer the nucleus of an adult or embryonic cell into an unfertilized egg from which the nucleus has been removed. The newly constructed embryo cell contains a full set of chromosomes--much as a normal embryo would--but must revert to a more primal state in which it can recover the embryo's ability to develop into a new organism.

As part of the cloning process, within a few hours of the new cell's creation, its biological clock must be reset. That affects when and how genes turn on and off at critical moments of development.

Chemical Cues Went Awry

In the research reported today, the scientists discovered that the genes themselves were normal enough in the cloned animals. But the chemical cues that orchestrate when the genes turn on and off went awry in a variety of almost random ways. The activity of the genes varied significantly in the placentas and kidney, heart and liver of cloned mice, compared to normal mice and mice created by in vitro fertilization.

The problems also cropped up when the mice were grown directly from the embryonic stem cells, without the extra step of cloning. The embryonic cells, themselves, seemed extremely unstable when grown in the laboratory, with even sister stem cells showing wide variations in when genes were active, the researchers reported.

The cloning process also appeared to be at fault.

"You don't see these huge missing chromosomes or a chunk of DNA missing or a mutation," said cloning expert Mark Westhusin at Texas A&M University. "What you see is abnormal gene expression, and there is no way to predict it."

"They are almost like environmental effects, where the environment is the cloning process itself," Westhusin said.

Despite the genetic problems, many of the cloned mouse embryos survived into adulthood. That suggests that mammalian development is surprisingly tolerant of genetic mistakes, the researchers said.

The researchers studied **clones** made from embryonic stem cells, so their work does not directly address whether similar flaws may occur in **clones** made from more specialized stem cells that exist in adults or from adult cells from skin or other mature tissue. The use of adult cells to create a **clone** is the most common technique when duplicating genetically engineered livestock, but the practice has had an extremely high failure rate.

Even in the most experienced hands, barely one in 100 cloned embryos survives, published data show. Many cloned animals die late in pregnancy or soon after birth. The placentas that nourish them in the womb often are abnormal. Even those that survive into adulthood frequently are larger than normal.

"So little is known about why cloning of mammals is so inefficient from a purely biological point of view," Hogan said. "No one knows why the large majority of the **clones** don't develop normally."

Added Capron of USC: "It would certainly seem to me that the problem seen here needs a good deal more basic science exploration in animals before moving on to human beings."

*

MORE INSIDE

Research limits: Germany's dark past has heightened its debate about genetic engineering. A5

LOAD-DATE: July 6, 2001

LexisNexis

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The Irish Times

July 7, 2001

SECTION: CITY EDITION; WORLD NEWS; Pg. 13

LENGTH: 359 words

HEADLINE: Research finds cloned animals likely to have hidden genetic flaws

BYLINE: (PA)

BODY:
Shortly after a statement in the US that the first cloned human would be produced "very soon", scientists have issued a new warning about the effect of creating cloned babies.

Researchers found evidence that even healthy, normal looking animal **clones** are likely to have hidden genetic flaws and therefore the cloning of duplicate individuals may be intrinsically unsafe, the findings suggest.

The scientists were investigating why so many cloned animals failed to survive or grew to a grossly distorted size. They found that cloning affected the way certain important developmental genes were switched on or off by chemical "tags". The workings of these genes varied significantly in the placentas and kidney, heart and liver of cloned mice, compared with normal mice and those born as a result of in-vitro fertilisation.

The genetic instability also showed up in the embryonic stem cell lines used to create the **clones,** the researchers reported in the journal Science.

Stem cells, precursor cells with the ability to become different kinds of tissue, are currently being investigated for possible therapeutic uses.

"Therapeutic cloning" of stem cells aimed at developing replacement tissue treatments has been given the go-ahead in Britain, while reproductive cloning is banned. Creating **clones** such as Dolly the Sheep involves removing the nucleus of an egg and replacing it with the nucleus from an adult cell, or embryonic stem cell.

The US team found that even **clones** made from sister stem cells had differences in their gene expression. Yet many embryos survived to adulthood, suggesting that developing mammals were surprisingly tolerant to faulty gene regulation.

"This suggests that even apparently normal **clones** may have subtle aberrations of gene expression that are not easily detected in the cloned animal," said Mr Rudolf Jaenisch from the Massachusetts Institute of Technology in Cambridge, USA.

In an interview with the USA today newspaper, Ms Brigitte Boisselier, a director of the Clonaid company which is engaged in a human clonding project, said that the first cloned human would be

produced "very soon".

LOAD-DATE: July 7, 2001

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The Weekend Australian

July 7, 2001, Saturday

SECTION: LOCAL; Pg. 6

LENGTH: 234 words

HEADLINE: Study shows danger of cloning

BYLINE: Stephen Brook * Science writer

BODY:
STEM cell **clones** have been found to have hidden abnormalities, confirming the dangers of reproductive cloning.

The research has implications for therapeutic cloning, which scientists hope will help to treat diseases. The evidence shows reproductive cloning using stem cells -- immature cells which can develop into any cell type -- may produce serious abnormalities within normal-looking **clones** of mice.

A report in Science by US scientists from the Whitehead Institute and the University of Hawaii says the abnormalities are difficult to detect until after the **clone** is born, as the abnormalities affect genes that respond to the environment, not developmental genes.

"They are saying there are these changes in **clones** that might not develop in parent individuals," said Simon Walker, principal scientist with the South Australian Research and Development Institute.

"The significance of the changes are yet to be determined. They are saying beware, be careful," Dr Walker said.

But professor of biochemistry at the University of Adelaide Peter Rathjen said he doubted the research would make any difference to therapeutic cloning.

The research was released as federal Health Minister Michael Wooldridge responded favourably to a compromise plan under consideration by a parliamentary committee.

The plan would make available discarded IVF embryos to stem cell researchers.

LOAD-DATE: November 27, 2001

LexisNexis™

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Omaha World-Herald

July 7, 2001, Saturday SUNRISE EDITION

SECTION: EDITORIAL; Pg. 6;

LENGTH: 489 words

HEADLINE: More Red Flags on Cloning

BYLINE: 5

BODY:
There's embryonic stem-cell research, and then there's embryonic stem-cell research. New findings in this area brought out in the journal Science add significant weight to the idea that human cloning is currently, and possibly forever, a bad idea.

It was previously demonstrated that cloning experiments in animals encounter problems. Most cloned cells show problems in the fetal stage as pregnancy progresses. One out of perhaps dozens will be normal. Also, even those that are born and grow to adulthood sometimes develop abnormalities such as extreme obesity. Those who think animal cloning is a good idea have no problem with aborting fetal lambs or fetal mice until they get a "good" one. But how can that attitude be carried over into human cloning? The idea is so Frankensteinian, so inherently evil, that contemplating it will make any thoughtful person shudder.

With the latest research comes a second approach, one that on the face of it would have seemed to show promise. In this method, researchers stripped the DNA out of a normal mouse egg, then inserted DNA from embryonic stem cells of the mouse they sought to **clone.**

Given embryonic stem cells' now well-known versatility, what the scientists were doing appeared to make sense. But then they found troubling evidence that during embryonic and fetal development, the genes didn't function properly. As they explained it, the biological "blueprint" was just fine, but for unknown reasons those instructions weren't properly read and interpreted. The researchers fear this could result in abnormal organs and tissues. That carries troubling implications for such human attributes as personality and intelligence.

Rudolf Jaenisch, senior author of the new study and a researcher at the Massachusetts Institute of Technology, explained that the concerns found in these experiments don't automatically carry over to efforts to use embryonic stem cells for treating health disorders.

He pointed out that in using cells for therapeutic purposes, researchers would be able to sort out and inject into patients only normal cells. But in cloning, he said, no such selection is possible. An embryo must use the DNA provided - genetically, it has been dealt just one hand and it must play it for better or worse.

This argues that if scientists progress to the point of using embryonic stem cells for curative purposes, they'll have to exercise rigorous control over which cells are used and which ones are culled out. But that

level of precision seems to be within the reach of existing technology. Cloning via use of these cells, by contrast, doesn't seem anywhere close. It may, in fact, be a scientific dead end.

It's important that the difference be understood - especially by those in the Bush administration who are wrestling with the question of federal funding for embryonic stem-cell research.

LOAD-DATE: July 7, 2001

NewScientist.com

Cloned animals meet early deaths

19:00 10 February 02
Philip Cohen

Cloned animals may indeed die young suggests the first direct study of their lifespan, carried out by Japanese researchers on mice.

Cloning involves removing the nucleus from an egg and replacing it with the nucleus of a donor cell. Many of these "nuclear transfer" embryos never develop or miscarry. Even after birth some clones die. But many cloning scientists argue that the few survivors can be perfectly normal.

Atsuo Ogura of the National Institute of Infectious Diseases in Tokyo says his team's work suggests that some effects of cloning are not apparent in the days, weeks or even years after birth. "It is very probable that, at least for some populations of clones, some unpredictable defects will appear in the long run," he says.

The debate over the health of clones and how they age has swung one way and then the other. In November 2001, US biotech company Advanced Cell Technology reported the cloning of two dozen apparently healthy cloned cows. But in January, the first mammal cloned from an adult cell, Dolly the sheep, was reported to have prematurely developed arthritis.

Rudolf Jaenisch, a mouse cloner at Massachusetts Institute of Technology in Boston says the new work "shows that to look at animals at one point in time and say they are healthy and normal is really wishful thinking."

Immune system defect

Ogura's team cloned 12 male mice and these were compared with seven males from natural matings and six others produced using in vitro fertilisation. The clones appeared active and healthy, gained weight normally and matched the control animals in 14 of 16 physiological measurements.

But the first cloned animal died after only 311 days and, by day 800, 10 (83 per cent) of the animals were dead. In contrast, only three (23 per cent) of the controls died during the same period.

The dead clones showed high rates of pneumonia, liver disease, cancer and a lower level of antibody production, suggesting they had an immune system defect. Ogura's team is now trying to pinpoint the precise cause of death and repeat the experiment with more animals.

ACT's Tony Perry points out that it remains unclear if clones from other species such as cows or pigs die early. And even if clones in general do prove to have a shortened lifespan, he does not think that undermines data from ACT and others that clones can be healthy.

All the researchers agree that the work should be an additional warning to would-be human cloners.

Journal reference: *Nature Genetics* (DOI: 10.1038/ng841)

19:00 10 February 02

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The World's No.1 Science & Technology News Service

Cloned monkey embryos are a "gallery of horrors"

19:00 12 December 01
Sylvia Pagán Westphal, Boston

A high percentage of cloned monkey embryos that look healthy are really a "gallery of horrors" deep within, says a researcher at Advanced Cell Technology, the company that last month published the first paper on cloned human embryos.

Photo: Magnum

This could mean that there is something unique about primate eggs that will make cloning monkeys or people far more difficult than cloning other animals. At the very least, the experiments show that there's a lot to learn before primates can be cloned.

Tanja Dominko, who presented the results last week at a conference in Washington DC, did the work before joining ACT, while she was working for the reproductive biologist Gerald Schatten at the Oregon Regional Primate Research Center in Beaverton.

Several groups have been trying for years to clone monkeys, but while the embryos look normal, no one has ever got them to develop further.

Uneven scatter

To try and figure out what was going wrong, Dominko looked at 265 cloned rhesus macaque embryos created by nuclear transfer - plucking out an egg's nucleus and then adding a nucleus from a donor cell. She followed development of the embryos through several divisions, from the two-cell stage until the 32-cell stage.

Though they appeared superficially healthy, the cells in the vast majority of Dominko's embryos did not form distinct nuclei containing all the chromosomes. Instead, the chromosomes were scattered unevenly throughout the cells.

"The surprising thing is that these cells keep dividing," says Dominko. Some embryos developed to the stage known as a blastocyst, but by day six or seven they had started to look abnormal.

The cloned human embryos created by ACT didn't even get this far. Only one reached the six-cell stage.

Trauma of removal

Dominko says that the trauma of removing the nucleus from the egg might be what triggers the defects. Eggs whose nuclei are removed and then put back inside show the same abnormalities, as well as evidence of programmed cell suicide. "This is not to say that normal embryos can't be made, but not on a regular basis," says Dominko.

Ian Wilmut, who cloned Dolly the sheep, told the conference that Dominko's results were not surprising in the light of experience of nuclear transfer in mice and cows. Even in these animals the success rates are not high, so the phenomena observed by Dominko probably occur in them as well - it's just that everyone focuses on the few successes, he says.

Even so, researchers hoping to publish work on nuclear transfer in humans may now have to come up with better evidence that embryos are healthy. William Haseltine, editor of the journal in which ACT

published details of its cloned human embryos, now agrees that pictures alone aren't enough.

19:00 12 December 01

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The Advertiser
May 16, 2002, Thursday
SECTION: FOREIGN; Pg. 35

Gene find casts doubt on cloning

CHICAGO: US scientists have identified a gene which they say helps explain the low survival rate in animal cloning, a finding that illustrates how vastly problematic it would be to clone a human. The study casts real doubt on prospects for reproductive cloning.

The gene, called Oct4, switches on early in embryonic development and must function with exquisite precision for life to continue, University of Pennsylvania researchers say.

If Oct4 is missing or not working normally, the fate of the clone is sealed, even though the embryo may appear to be normal, survive birth and even grow to adulthood.

Posted on Sun, Feb. 10, 2002

Cloned Mice Die Young, Japanese Team Finds

BY MAGGIE FOX, HEALTH AND SCIENCE CORRESPONDENT

WASHINGTON - (Reuters) - Japanese researchers who cloned a dozen mice reported on Sunday that virtually all of the animals died early, a report that casts more doubts on the safety of cloning.

The report, sure to be taken as more evidence that cloning people should be banned, also suggested that the technique used to clone an animal can have an impact on its ability to live a normal life span, cloning experts said.

``The possible negative long-term effects of cloning, as well as the high incidence of spontaneous abortion and abnormal birth of cloned animals, give cause for concern about attempts to clone humans for reproductive purposes,'' Atsuo Ogura and his colleagues at the National Institute of Infectious Diseases in Tokyo reported in the Feb. 11 issue of the journal Nature Genetics.

The U.S. Congress is currently considering several bills aimed at banning human cloning. Two would allow research to continue so long as no baby was created using the technology, and a third would ban the use of all cloning technology to make a human embryo.

Experts at the National Academy of Sciences, which advises the government, have also said cloning is far too uncertain to try to use as a method right now for making babies, although the report leaves open the possibility of doing so in the future, if the technique is perfected.

Labs that have cloned animals have reported that the cattle, sheep and goats that make it to adulthood are normal in every way that can be measured.

One big glitch has been in Dolly, the sheep that was the first mammal cloned from an adult in 1997. She has developed early arthritis, which her creators say could be bad luck or could be some result of the cloning process.

Ogura's team reported on 12 male mice they cloned that looked normal at birth, although certain liver enzymes, used to monitor liver activity, were abnormal.

``The cloned mice started to die 311 days after birth, and 10 of the 12 cloned mice died before 800 days,'' they wrote.

Mice born through natural mating and conceived using artificial fertilization lived much longer.

DAMAGED LUNGS AND LIVERS

The mice had abnormal livers, lungs and perhaps some immune system anomalies, Ogura's team reported.

Two of the clones are still alive and might live normal lives. It might be that the genetic makeup of the clone's "parent" is key to healthy survival, they said.

They also noted that clones may be born ``old." Some clones have shortened telomeres, which are a kind of cap on the chromosome, the structures that carry the genes. Each time a cell replicates, this telomere cap frays a little and this process is believed to be associated with aging.

Technique could also be important, said Tony Perry of Advanced Cell Technology in Worcester, Massachusetts, one of the groups trying to use cloning technology to make human embryos for medical uses.

Perry, who was part of the first group to clone mice, said the method used to make cloned mice is different from the method used to make larger animals such as Dolly.

Dolly was made using electrofusion. One sheep's egg had the nucleus taken out, and a cell from the mammary gland of another adult sheep was fused to it using a burst of electricity. The second cell's nucleus and its genetic material replaced the missing nucleus, and the egg grew and divided as if it had been fertilized by a sperm.

To make mice, the Japanese team micro-injected the nucleus from the second cell into the egg. ``This method is rather different," Perry said in a telephone interview.

One method might somehow damage the tiny embryo, Perry and colleague Teruhiko Wakayama said in a commentary on the study.

Or it could be the cytoplasm, the part of the cell outside the nucleus, carries key factors for survival that are transferred with the electrofusion method.

Perry also noted that not all adult cloned animals are normal and that most clones die at or before birth.

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TIME europe

Tuesday, April 16, 2002

But She's So Young

Even Ian Wilmut, the scientist who cloned her, can't say if Dolly's premature arthritis is a legacy of her unorthodox birth

BY AISHA LABI

As the genetic carbon copy of another creature, Dolly the sheep --- the world's first cloned mammal --- doesn't really have parents in the normal sense. But Ian Wilmut, 57, the embryologist who led the experimental team that produced her in 1997, could be considered something of a father figure to the famous ewe. And since one ambition of Wilmut and his colleagues at the University of Edinburgh's Roslin Institute has been to strengthen the bond between humans and animals, his disclosure last week that Dolly is afflicted with premature arthritis was more than just the dry clinical announcement of a scientific development.

Despite his concern for his subjects' welfare, Wilmut's goal as a cloning pioneer is to genetically alter animals so they can eventually be used as a source for organ transplants and other potentially life-saving therapies for humans. "For exactly the kinds of things that have just been achieved with the pigs," he says, referring to two separate cloning experiments announced last week that produced pigs lacking a gene that prompts organ rejection in humans. PPL Therapeutics, a company affiliated with the Roslin Institute, delivered five such piglets on Dec. 25; the next day, rival Immerge BioTherapeutics said four similar miniature pigs had been born in September.

The early onset of arthritis in Dolly's knee and hip could have vast implications for cloning. "We'll never really be sure," says Wilmut. "But if the arthritis is due to cloning, it's one more piece of information about cloning's impact on animals. We already knew it's an inefficient process, with only a small proportion of the embryos becoming live offspring and some of those dying soon after birth. This may be another symptom."

Potentially lethal uncertainties like these have prompted some animal-rights activists to call for a halt to all cloning activity. Wilmut is undeterred. He says he is an agnostic, "though not hostile toward religion," and notes that his wife is a Church of Scotland elder. "We have laudable, reasonable objectives," he says. "But we do owe it to the animals to be particularly thoughtful about

them and the way we use them."

Wilmut has enjoyed working with animals since his childhood in Yorkshire, where both his parents were schoolteachers. The sort of animal husbandry he now practices may not be what he had in mind when he set out to study agriculture at Nottingham University, but it's probably more lucrative. Despite last week's fall in the company's stock price in reaction to its competitors' pig cloning advances, Wilmut's 50,000 shares in Geron Corporation, a biopharmaceutical firm that is one of the Roslin Institute's partners, are still worth nearly half a million dollars.< A NAME="QA">

Q&A

TIME: This news has prompted some animal welfare groups to call for a halt to cloning experimentation. Should we heed them?
WILMUT: No. We should do two things. There should be detailed monitoring of all the clones that we have, and then complete openness about what people are finding. We have suspicions that not everybody is being open.

TIME: Since your field is genetics, is there any special significance to the fact that one of your three children is adopted?
WILMUT: Before we were married we decided that we would probably choose to have only two children. Both were daughters and we liked the idea of having a son, so we adopted a boy. Once they get past infancy, there are a number of children who aren't adopted and are left in homes. We became attached to this lad who was three when we adopted him and is now 26.

TIME: Do you think you'll see animals used routinely as organ-transplant sources in your lifetime?
WILMUT: Yes. Give me 15 years, until I'm 72. During that period, I believe programs various labs have to genetically change pigs to make them suitable as organ donors will come through to clinical practice. I also believe the production of cells, from animals or from humans, for the treatment of degenerative diseases will come into routine practice. I also think that improvement to the technique will continue for much longer than 15 years.

TIME: If you needed a transplant and the technique were still experimental, would you use it?
WILMUT: That makes me sound like a hero. If your choice is you die or you take a chance by having an organ from an animal, I don't think that's difficult. You take the organ and you are grateful.

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Earth Island Journal

June 22, 2002

SECTION: No. 2, Vol. 17; Pg. 15; ISSN: 1041-0406

IAC-ACC-NO: 84867028

LENGTH: 118 words

HEADLINE: Time to stop cloning around; Asia; premature death of cloned mice; Brief Article

BODY:
JAPAN -- Research at Tokyo's National Institute of Infectious Diseases (NIID) revealed that cloned mice have something in common -- premature death. Or, as The Guardian (London) put it: "a **clone's** life is wheezy, liverish and short." According to findings published in the journal Nature Genetics, NIID's 12 cloned mice began dying within a year of birth and the survivors barely lived longer than two years. Autopsies revealed that the **clones** all had severe pneumonia and seriously damaged livers. The scientists concluded that the "possible negative tong-term effects of cloning, as welt as the high incidence of spontaneous abortion and abnormal birth of cloned animals, give cause for concern."

IAC-CREATE-DATE: May 2, 2002

LOAD-DATE: May 03, 2002

University of Tennessee's second cloned cow dies of stomach disorder

KNOXVILLE, Tenn. (AP) _ The University of Tennessee's second cloned cow has died after complications from a stomach disorder, the university said Monday.

Emma, a heifer born Aug. 30, was euthanized April 15. Millie, the first cow university researchers successfully cloned from an adult cell, died in June from a bacterial infection at 9 months.

``Both of them died at a fairly young age from completely different conditions, and from conditions that are not unusual," said Jack Britt, vice president of the university's Institute of Agriculture. ``It could be the luck of the draw."

Emma was created to be a twin of a Jersey cow with a history of mastitis, an inflammation of the mammary gland that can reduce the quantity and quality of milk. By studying Emma, researchers hoped to find a cure.

Britt said the university's cow cloning effort will continue despite the setbacks.

On the Net:
University of Tennessee: http://www.tennessee.edu

Associated Press, 4-22-02

Genetic abnormalities found in cloned animals

The Cincinnati Post, 05/27/02

Researchers working with clones of a Holstein cow say genetic programming errors may explain why so many cloned animals of all types die, either as fetuses or newborns.

In cloning, the DNA of an adult animal is inserted into a donor egg emptied of its own DNA. For that cell to develop, genes that may have been turned off in the adult animal that was being cloned must be turned onagain to guide the egg to form a new, genetically identical individual.

In females, the embryo receives two X chromosomes, each containing several hundred genes. In natural reproduction, the genes on the two X's are active in female embryos; one of the X's is later inactivated to match the male complement of one X and one Y chromosome.

However, female clones receive an active X and an already inactive X; the latter, and all its genes, must be reprogrammed and then, later in development, inactivated again.

Scientists at the University of Connecticut studying how the normal patterns of X chromosome inactivation are erased and then re- established during cloning found abnormalities in nine of 10 genes they examined on the X chromosome.

The scientists found the genes had been incompletely reprogrammed in five dead cow clones and one aborted fetus. Looking at four live clones, as well as control animals conceived naturally, the scientists found the same genes were normal.

"Our study demonstrates that in clones, even though they can develop to full term, many abnormalities in gene expression exist, which may be partially responsible for the developmental abnormalities frequently observed, including death," said Xiangzhong "Jerry" Yang, lead author of the study. Results appear online in the journal Nature Genetics.

AMERICANS TO BAN CLONING

CLONING INFORMATION

The Latest Cloning Numbers

With Dr. Severino Antinori claiming that a woman is 8 weeks pregnant with a human clone and his now ex-partner Panos Zavos planning to have 9-12 women pregnant with clones by August, we wanted to examine just how successful is animal cloning these days now that more than 5 years has passed since Dolly the sheep was born?

Dolly the sheep, first cloned mammal: 1 live birth out of 277 cloned embryos (0.4%)

Cloned mice: 5 live births out of 613 cloned embryos (0.8%)
5 live births out of 314 cloned embryos implanted (1.6%) (0.8%; 1 survived)
26 live births out of 312 cloned embryos implanted (8.3%) (4.2%; 13 survived)

Cloned pigs: 5 live births out of 72 cloned embryos implanted (7%)

Cloned goats: 3 live births out of 85 cloned embryos implanted (3.5%)

Cloned cattle: 30 live births out of 496 cloned embryos implanted (6%)
(4.8%; 24 survived)

Cloned cat: 1 live birth out of 188 cloned embryos (0.5%); of 87 embryos implanted (1.1%)

Cloned rabbits: 6 live births out of "hundreds" of cloned embryos
(Note: 2 of the 6 clones who made it to birth died almost immediately)

Debate on Human Cloning Turns to Patents

The New York Times

Friday May 17, 2002
Section A; Page 14, Column 4

By ANDREW POLLACK

The University of Missouri has received a patent that some lawyers say could cover human cloning, potentially violating a longstanding taboo against the patenting of humans.

The patent covers a way of turning unfertilized eggs into embryos, and the production of cloned mammals using that technique. But unlike some other patents on animal cloning, this one does not specifically exclude human from the definition of mammals; indeed, it specifically mentions the use of human eggs.

Those opposed to cloning and to patenting living things say the patent is a further sign that human life is being turned into a commodity.

"It is horrendous that we would define all of human life as biological machines that can be cloned, manufactured and patented," said Andrew Kimbrell, executive director of the International Center for Technology Assessment, a Washington group that has long opposed patenting of living things and also wants to ban all human cloning.

The patent was issued in April 2001, but attracted no attention until Mr. Kimbrell's group ran across it recently.

Senator Sam Brownback, the Kansas Republican who has been a leading opponent of human cloning, said he intended to introduce a bill to prohibit patents on human beings and human embryos, which he said were "akin to slavery."

"I think the patent office will appreciate having that clarity, given the applications that are coming into the patent office," Mr. Brownback said.

That bill would be separate from a bill the senator is already sponsoring that would prohibit all human cloning. The Senate is debating how extensively to ban human cloning, but none of the bills it is considering deal with the patent issues.

The patent also illustrates the tricky legal and ethical issues the United States Patent and Trademark Office is confronting as scientists race to develop cloning and to grow human tissues to treat disease. Mr. Kimbrell said he had found a few other patents that had been applied for but not granted that might cover human cloning.

The United States has been more liberal than most other countries in granting patents on living things, ever since a Supreme Court decision in 1980 that allowed the patenting of a microbe genetically engineered to consume oil spills. There are patents on complete animals, like a mouse genetically engineered to be prone to cancer. There are patents on human genes and human cells. The University of Wisconsin has a patent on human embryonic stem cells, which are cells taken from human embryos that have the ability to turn into any other type of tissue.

But the patent office has drawn the line on patenting of humans or human embryos themselves, saying it would not be

constitutional. Many experts say this is because such patents would violate the 13th Amendment ban on slavery. Brigid Quinn, a spokeswoman for the patent office, said the agency was not using the 13th Amendment argument anymore but was not granting
patents on humans because it had not received any guidance from Congress or the courts saying it should do so.

The result has been that many patents that conceivably could cover humans -- like on cloning animals or on genetically engineering animals to produce drugs in their milk -- specifically exclude humans.

A spokesman for the University of Missouri, Christian Basi, said it believed its patent covered human cloning because it applied to all mammals. The university has licensed the patent to BioTransplant, a Massachusetts biotechnology company that is working on creating pigs that can be used as human organ donors. But the license, Mr. Basi said, covers only the use in pigs.

"We have absolutely no interest in using this to research humans and we will not license this technology to anyone for use in humans," Mr. Basi said, suggesting that the patent could actually help stop human cloning. "This gives us control of this particular technology so we will know that this technology will not be used in humans."

Ms. Quinn said the patent office did not comment on individual patents but had not changed its policy of not issuing patents "drawn to humans."

Randall S. Prather, a professor of reproductive technology at Missouri whose work was the basis for the patent, said the mention of human eggs "was put there by the attorneys and they

wanted to cover all mammals."

Charles Cohen, who wrote the patent when he was a lawyer at a St. Louis law firm, declined to comment.

Some lawyers who have looked at the patent, No. 6,211,429, say it is not clear that it covers human cloning and that interpreting patents requires careful analysis of the patent's history. That the patent office did not appear to have problems with it could be a sign that the agency believes that the patent does not cover humans.

"You'd have to go through line by line, word by word," said Gerald P. Dodson, a lawyer with Morrison & Foerster in Palo Alto, Calif., who read the patent and said he could not reach an immediate conclusion.

Mr. Dodson and others noted that the specifications and examples of how the patent could be used dealt with pigs and cows.

Even if the patent does cover human cloning, some lawyers say, it would be a stretch to say it covers humans themselves, although the abstract of the patent says it covers the "cloned products."

But even a patent on the process of cloning humans could give the patent holder some rights over people, some lawyers said. Conceivably, for instance, the university could bar people created overseas by its cloning process from entering the country.

"It definitely is a patent for cloning a human, and under the laws we have right now, it might actually cover the human," said Richard Warburg, a patent lawyer at Foley & Lardner in San

Diego who represents Infigen, an animal cloning company.

Dr. Rochelle Seide, a New York patent lawyer who heads the biotechnology practice at the law firm of Baker & Botts, said the lack of the nonhuman disclaimer in the Missouri patent was surprising.

"Looking at it," Ms. Seide said, "I can see where people who are against cloning would have a big problem with it."

Advanced Cell Technology, a company that wants to clone human embryos to obtain stem cells for disease treatments, licensed a patent from the University of Massachusetts on its method of cloning. But the patent is on only nonhuman embryos produced by the process, though it does seem to cover human cells.

It might be difficult to draw the line on what constitutes a human. George J. Annas, professor of health law at Boston University School of Public Health, said it was unclear whether the antislavery amendment would be a basis for denying patents on human embryos because courts, in cases like those involving custody of frozen embryos, have said an embryo is not a person.

The U.S. Patent Office (PTO) Has Granted a Patent on Human Reproductive Cloning and the Embryos, Fetuses and Children That Would Be Created Through That Process

Patent Watch Also Discloses Three Pending Patents Which Would Include Cloned Human Embryos and Fetuses Watch Dog Group Calls on the PTO and Congress to Halt Patenting of All Human Life Forms and Human Cloning Processes

WASHINGTON, May 16 /PRNewswire/ -- Patent Watch, a public interest oversight group, announced today that it had uncovered a patent on human reproductive cloning and any "products" created by that process, theoretically including embryos, fetuses and children. The patent, U.S. Patent No. 6,211,429, was granted on April 3, 2001, but went unnoticed until Patent Watch discovered that the claims were applicable to human reproductive coning. The owner of the patent is the University of Missouri, but financial interest in the patent is shared by a Massachusetts biotech company Biotransplant Inc.

Patent Watch also revealed today that it had uncovered three pending patents currently before the PTO that cover cloned human embryos and fetuses.

* Patent application serial number 09/816,971, assigned to Geron Corp., which claims a "reconstituted animal embryo" described as having "its main use in ... mammalian embryos, particularly ruminant, human, or primate embryos;" * Patent application serial number 09/755,204, assigned to the Univ. of Connecticut, claiming any "animal" embryo made by a cloning process; and * Patent application serial number 09/828,876, assigned to the Univ. of Massachusetts and exclusively licensed to Advanced Cell Technology, claiming a mammalian "fetus obtained according to" a particularly specified cloning process. This patent application specifically contemplates the use of human tissues derived from cloned human embryos, fetuses, and offspring, for transplantation purposes.

Commenting on the pending patents Patent Watch Project Director Peter DiMauro stated, "In deciding on these patents the PTO will be making an historic decision on the commodification of human life. They should reject these patents as violation of public policy."

The PTO has the legal authority under both national and international law to reject patents that offend public morality or order but did not do so in the case of the Missouri patent. Nor does any current Congressional bill on human cloning halt the patenting of the process or its products. "This is not a slippery slope, rather this an ethical and legal free fall," stated Patent Watch Executive Director Andrew Kimbrell commenting on the Missouri patent.

"The Patent Office has become a ghoulish human body shop allowing researchers and corporations to patent and own human body parts, cloning processes and even human life forms," Kimbrell continued.

"The Patent Office and Congress must move quickly to halt this commodification of life and to ban all forms of human cloning," Kimbrell concluded.

Patent Watch is a project of the International Center for Technology Assessment. CTA is a non-profit, bi-partisan organization committed to providing the public with full assessments and analyses of technological impacts on society, and is devoted to fully exploring the economic, ethical, social, environmental and political impacts that can result from the applications of technology or technological systems.

/CONTACT: Andrew Kimbrell or Peter Di Mauro of Patent Watch, +1-202-547-9359/ 13:22 EDT

THE WALL STREET JOURNAL. ONLINE

May 16, 2002

HEALTH

The University of Missouri Receives Patent for Human-Cloning Method

By ANTONIO REGALADO
Staff Reporter of THE WALL STREET JOURNAL

In a bizarre twist to the cloning saga, the University of Missouri has been granted what may be the first patent on human cloning.

The U.S. Patent and Trademark Office has explicitly said it won't allow patents on cloned humans. But early last month, it granted a patent to Missouri livestock-cloning expert Randall Prather on a method for making them. It wasn't clear if the move marked a loosening of agency policy on such inventions. Brigid Quinn, a spokeswoman for the Patent Office said, "Our policy is that we do not issue patents to claims drawn to humans. Our policy has not changed."

A patent attorney familiar with the case said because Dr. Prather asked only to patent a method of making people -- and not people themselves -- that it may not have triggered the agency's concerns.

The patent is likely to renew urgent calls for a ban on human cloning. But scores of other cloning patents now await approval, a sign the technology may be outpacing legislators' ability to regulate it. Just this year, scientists have added rabbits and a

house cat to the growing list of animals they have cloned, including sheep, cattle and goats.

Experts said the Missouri patent didn't give anyone the right to clone people. It is possible to hold patents on inventions that are otherwise illegal to use, such as thermonuclear weapons.

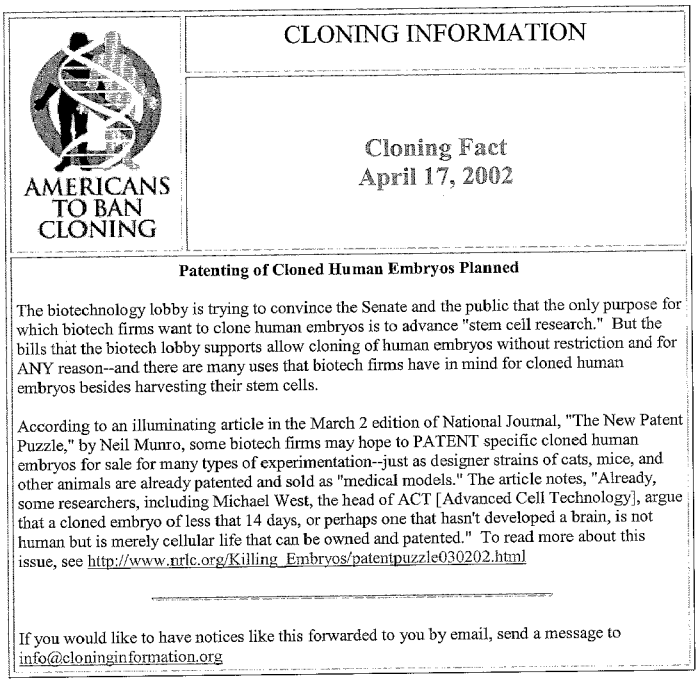
The patent, No. 6,211,429, arose from Dr. Prather's work cloning pigs, but the patent describes the technology much more generally. "The patent includes all mammals. And yes, humans are mammals," said Christian Basey, a spokesman for the university. Dr. Prather couldn't be reached for comment.

Mr. Basey said the school is opposed to human cloning and, if necessary, would use the patent to block anyone else from cloning people.

Patents on living things got rolling in 1980, when the Supreme Court gave the green light to a General Electric patent on an oil-eating bacterium. But in 1987 the Patent Office said patents on humans wouldn't be permitted, due to conflicts with the 13th Amendment's prohibition of slavery.

However, the Patent Office's thinking has been in flux, and its stance remains confusing to many legal experts. Many believe the agency lacks authority to reject patents on human beings, but has done so to avoid controversy.

Opponents of human cloning and genetic tailoring of the species see the patent as a red flag. "Once they own these processes, they will have locked up commercial eugenics. You will shop for specific traits for your offspring and pay the companies that own the methodology," predicts Jeremy Rifkin, a well-known biotechnology critic who heads the Foundation on Economic Trends in Washington, D.C.



CLONING INFORMATION

Cloning Fact
April 17, 2002

Patenting of Cloned Human Embryos Planned

The biotechnology lobby is trying to convince the Senate and the public that the only purpose for which biotech firms want to clone human embryos is to advance "stem cell research." But the bills that the biotech lobby supports allow cloning of human embryos without restriction and for ANY reason--and there are many uses that biotech firms have in mind for cloned human embryos besides harvesting their stem cells.

According to an illuminating article in the March 2 edition of National Journal, "The New Patent Puzzle," by Neil Munro, some biotech firms may hope to PATENT specific cloned human embryos for sale for many types of experimentation--just as designer strains of cats, mice, and other animals are already patented and sold as "medical models." The article notes, "Already, some researchers, including Michael West, the head of ACT [Advanced Cell Technology], argue that a cloned embryo of less that 14 days, or perhaps one that hasn't developed a brain, is not human but is merely cellular life that can be owned and patented." To read more about this issue, see http://www.nrlc.org/Killing_Embryos/patentpuzzle030202.html

If you would like to have notices like this forwarded to you by email, send a message to info@cloninginformation.org

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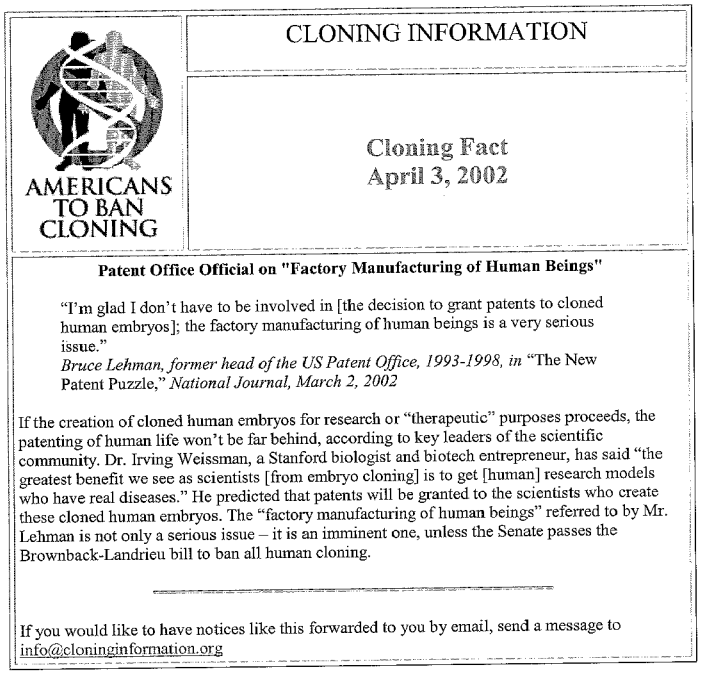

CLONING INFORMATION

Cloning Fact
April 3, 2002

Patent Office Official on "Factory Manufacturing of Human Beings"

> "I'm glad I don't have to be involved in [the decision to grant patents to cloned human embryos]; the factory manufacturing of human beings is a very serious issue."
> *Bruce Lehman, former head of the US Patent Office, 1993-1998, in* "The New Patent Puzzle," *National Journal, March 2, 2002*

If the creation of cloned human embryos for research or "therapeutic" purposes proceeds, the patenting of human life won't be far behind, according to key leaders of the scientific community. Dr. Irving Weissman, a Stanford biologist and biotech entrepreneur, has said "the greatest benefit we see as scientists [from embryo cloning] is to get [human] research models who have real diseases." He predicted that patents will be granted to the scientists who create these cloned human embryos. The "factory manufacturing of human beings" referred to by Mr. Lehman is not only a serious issue – it is an imminent one, unless the Senate passes the Brownback-Landrieu bill to ban all human cloning.

If you would like to have notices like this forwarded to you by email, send a message to info@cloninginformation.org

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The New Patent Puzzle
by Neil Munro
from National Journal
March 2, 2002

The world's first cloned cat, CC, was advertised as a prototype for the pet-cloning market by her corporate parent, Texas-based Genetic Savings & Clone. But she is also a prototype for a much larger market for "animal models," or animals created for use in medical experiments. And she is a precursor to what many researchers and biotech entrepreneurs see as an important new arena -- the cloning and use of human embryos for specific research and commercial purposes.

Cloning technologies depend on patents for their commercialization and growth. The U.S. Patent and Trademark Office has already begun awarding these valuable patents for cloning techniques for many types of "modified" animals, and for some cells grown from human stem cells. Biotech experts predict that the patent office will eventually grant patents for methods used in human-embryo cloning. But in the new biotechnology, "the boundary is quite blurred" between what is human and what is nonhuman, said Kent Cheng, a lawyer with the NewYork-based law firm of Cohen, Pontani, Lieberman & Pavane, which specializes in patent issues.

The market in animal models is already large, with one company claiming revenue of more than $500 million a year. In 2000 alone, 25,560 ordinary cats -- plus another 1.4 million animals, not counting mice, rats, and birds -- were used in medical experiments. The cats were used principally for research into AIDS, the human brain, and various viruses. Specially bred disease-free cats can be sold for up to $600.

But even that is far less than the price of designer mice -- mice that have been given human genes, or carry unusual mice genes, or have particular genes "knocked out." The price of these mice, many of which are patented, can exceed $2,000 for a breeding pair, depending on the desires of the buyer and the seller. There are more than 1,000 types of these specialty mice, said Joyce Peterson, a spokeswoman for the Jackson Laboratory in Bar Harbor, Maine. The lab develops and breeds mice and other animals for research. Indeed, these mice are so important that the National Institutes of Health is funding two groups, each of which is to develop 50 new types of mouse models each year, Peterson said. Overall, the annual U.S. market for animal models is more than $1 billion.

The technology used to clone CC allows cats to play in this specialty market. Twenty cloned cats would produce the same quality of research data that now requires 40 ordinary cats, said Duane Kraemer, a professor at Texas A&M University and a principal at Genetic Savings & Clone. And these genetically engineered cats can be patented, hindering other companies from developing them, according to Charles Long, the company's general manager. To clone CC, Genetic Savings & Clone paid to use other companies' patented cloning techniques, "but we hope to change the process so significantly that we wouldn't be bound by other patents, and we'd have our own [genetic-engineering patents] that someone might license," Long said. "That's the position you want to get yourself in -- to get others to pay."

That's where the Patent and Trademark Office enters the picture. Companies can obtain patents on new animals that are "novel" and "nonobvious," and that have substantial, credible, and significant utility. The patent office has already awarded many patents for modified mice, including mice that carry human genes, and mice designed to mimic human psoriasis, Huntington's disease, cancer, and many other ailments.

These patents can be very valuable, especially for companies that stake years of expensive research on the prospect of winning them. For example, Advanced Cell Technology Inc. in Worcester, Mass., holds patent No.5,945,577, which is for the creation, via cloning, of genetically modified nonhuman mammals. Two other companies, Geron Corp. in Menlo Park, Calif., and Infigen Inc. in DeForest, Wis., have protested, arguing that ACT's patent interferes with their patent

applications. In early February, the patent office agreed to consider the dispute, but the fight over the patenting of nonhuman mammals is only a precursor to a much more difficult debate: To what extent can human clones be patented?

Some researchers say that cloned human "embryo models" will provide the best -- and in some cases, the only -- way to study some aspects of human biology, particularly the gradual emergence of genetic diseases and traits.

The leading proponent of human research cloning is Irving Weissman, who helped found a biotech company, StemCells Inc., in Palo Alto, Calif., which is now backed by biotech giant Amgen. He argues that stem cells from human embryos produced by cloning can serve as valuable laboratory models and as the foundation for the next stage in biotech's evolution. Such models should be created and used, Weissman said, even if other researchers use stem cells from adults to repair diseases.

"Even if we could treat one disease, or two or five or 10, with adult stem cells that are around, I would not block research that would open up whole fields," Weissman said. He was speaking at a February 6 Senate Judiciary hearing chaired by Sen. Dianne Feinstein, D-Calif., who has drafted a bill that would ban the implantation of cloned embryos in women's uteruses. Feinstein's bill stands in opposition to legislation pushed by Sen. Sam Brownback, R-Kan., that would ban human cloning for any purpose. The House has already passed a comprehensive ban on human cloning.

Weissman is well-versed in patent policy. In 1997, he sold his SyStemixInc. for a reported price of $570 million, netting himself $25 million. The company's value was based on its critical patents, including a patent for one of the earliest mouse models, called a SCID-hu mouse, which incorporates a human immune system transplanted from an aborted fetus. Several competing varieties of the SCID mice are now used, along with cats and other models, to study AIDS.

According to Weissman, the patent office will be reluctant to grant a single broad patent for all research cloning of human embryos, partly because his discussion of the concept in public means it couldn't pass the "novelty" test. But Weissman predicted that the patent office will be much more likely to grant narrow patents to those who actually create cloned human embryos with particular genetic features and then use them to create millions of stem cells carrying those genetic features for study by researchers. These features could include a predisposition to breast cancer, or to Lou Gehrig's disease, for example. He asserts that it would be in the public interest to grant patents to researchers who first develop such "nuclear transfer models," because they provide the best model for the study of diseases. Weissman believes that there could be very many such patents granted, especially as scientists develop improved versions of these models. He says that an embryo itself cannot be patented, because it has no utility except as a source of valuable stem cells for researchers. At least one other researcher, however, says the embryos themselves are valuable for study.

The patent office has gone part way toward realizing Weissman's prediction. Last September, the office granted a patent to Neuralstem Inc. in Gaithersburg, Md., for brain cells grown from stem cells extracted from aborted fetuses. The brain cells are sold in batches for $990 to companies that develop and test drugs. The cells may also be used for transplantation into patients with Parkinson's disease.

But no human-embryo-based patents should be awarded, says Peter Di Mauro, a scientist and patent agent with the Washington-based International Center for Technology Assessment, which opposes human cloning. Even if the embryo-based models prove useful, he said, they violate the patent office's rules that inventions should not be "detrimental to the public interest." He also contends that the many other models can provide the information scientists need.

The Patent and Trademark Office is not eager to join the debate on granting patents for cloning human embryos. When asked for a comment, its chief spokesman, Richard Maulsby, would say only, "The U.S. Patent and Trademark Office does not issue patents drawn to human beings."

The key issue will be the patent office's interpretation of patents that involve humans and cloning, said Lila Feisee, a patent expert for the Biotechnology Industry Organization. "The patent office won't sit down and define 'human' ... but I do know that they do patent stem cells, and methods of ... deriving them from cloned embryos."

But Bruce Lehman, who served as head of the patent office from to 1993 to 1998 and now heads the Washington-based International Intellectual Property Institute, said that, on that difficult issue, "I would not have even proposed a decision myself [because it] is something that would go up to the President." Lehman said that the question lies "at the heart of the 'is an embryo a person' debate," but it does not implicate the 1973 Roe v. Wade decision legalizing abortion, principally because there is no pregnant mother involved. But supporters of President Bush and patent office director James Rogan, said Lehman, include those who believe "any human embryo ... is [human] life," so "it would be completely inconsistent for them to patent that kind of subject matter." He added, "I'm glad I don't have to be involved in that; the factory manufacturing of human beings is a very serious issue."

Already, some researchers, including Michael West, the head of ACT, argue that a cloned embryo of less than 14 days, or perhaps one that hasn't developed a brain, is not human but is merely cellular life that can be owned and patented.

Others, including some scientists, anti-abortion-rights advocates, and left-of-center opponents of biotechnology, argue that human life exists from conception. "I don't think the Supreme Court has been able to answer that question," Feisee said.

Political opposition may delay the award of a patent, Weissman said, "but in the end, a judge or some judges will decide" the legal issue. If a model is worth developing, he said, it is worth patenting.

Cloning Patent Doesn't Preclude Use on Humans, Missouri College Says

By Justin Willett, Columbia Daily Tribune, Mo.
Knight Ridder/Tribune Business News

May 23--A patent that protects cloning technology developed by University of Missouri-Columbia researchers intended for use with pigs does not preclude its use on humans.

But an MU spokeswoman says that isn't a bad thing. While unsure whether it was the original intent of the patent, MU spokeswoman Mary Jo Banken said that by leaving open the possibility of using the technology on humans, patent No. 6,211,429 allows the university to prevent others from using it for human cloning.

The patent"licensed the cloning technology, and it allows us to be able to control that technology,"Banken said."Since we have a patent on it, we would not license it to anyone who would use it do anything unacceptable."

MU's patent drew attention last week when Washington, D.C.-based International Center for Technology Assessment, a group that opposes patenting living things and wants to ban human cloning, held up its language as proof that federal lawmakers need to call for tougher laws and regulation regarding human-cloning research.

MU animal science Professor Randy Prather, Banken, Director of MU's Office of Technology and Special Projects Tom Sharpe, Interim Vice Provost for Research Rob Hall and legal counsel met on Tuesday to formulate a response to the questions raised

about the patent. Banken said they talked with an attorney from the St. Louis law firm that wrote the patent's language, who closely analyzed it at MU's request.

Charles Cohen, the St. Louis attorney who wrote the patent and now works for a different firm, has refused to comment.

Prather said the technology could theoretically be used to clone humans, but he does not advocate human cloning. Prather and fellow researcher Zoltan Machaty created the technology, which involves turning unfertilized eggs into embryos for the purpose of cloning pigs.

Their work garnered national media attention earlier this year when it was announced that he and a team of MU animal science researchers successfully cloned four piglets that lack one of the two genes that make their organs incompatible with humans. The breakthrough could lead to a process for transplanting animal organs into people.

The university has licensed the patent to BioTransplant Inc., a Charlestown, Mass., firm working to develop swine for use as organ donors for people.

Prather said the St. Louis lawyers who drafted the patent intentionally left the language open so as to get the broadest claims they could for the university.

That's what bothers Peter DiMauro, director of ICTA's subsidiary Patent Watch. He said that while MU might have good intentions, the precedent could allow others to patent other cloning techniques.

"The flaw is in the law, not in the intent of the University of Missouri," DiMauro said. "If the law is not clarified, then in

progression other types of variants on the human cloning process can go forward."

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Other Names: Lupron®, leuprorelin acetate

UPMC Health System

University of Pittsburgh Cancer Institute

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About This Drug

Leuprolide acetate is a drug that affects the production of certain hormones in your body. It is used to treat cancer and other medical conditions. This drug is given by subcutaneous injection (SQ) or intramuscular injection (IM).

Possible Side Effects

- feeling flushed ("hot flashes"). This is usually temporary.
- bone pain
- difficult or painful urination (rare)
- weakness. This is usually temporary.
- numbness, tingling, or decreased sensation in legs, feet, or toes. This is usually temporary.
- swelling of hands, ankles, or feet
- dizziness
- headache
- breast enlargement in men (rare)
- breast tenderness
- impotence in men (rare)
- loss of menstrual period in women
- nausea
- unusual sweating

Treating Side Effects

Ask your doctor or nurse about medication that is available to help prevent or lessen bone pain and nausea.

Food and Drug Interactions

There are no known interactions of leuprolide acetate and any food. Limit your salt intake to lessen swelling. This drug may interact with other medications. Tell your doctor and pharmacist all the medications that you are currently taking.

When to Call the Doctor

Call your doctor or nurse as soon as possible if you have any of the following symptoms:

- swelling of hands, ankles, or feet
- bone pain unrelieved by prescribed medication
- nausea unrelieved by prescribed medication
- numbness, tingling, or decreased sensation in fingers and toes
- difficulty in walking or changes in the way you walk
- clumsiness in buttoning clothes, opening jars, or other routine hand activities
- painful or difficult urination
- sexual problems
- uncomfortable hot flashes or recurrent sweats

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EXCERPTS FROM THE FDA WEBSITE REGARDING LUPRON (leuprolide acetate)

LUPRON DEPOT (leuprolide acetate)
[September 12, 1996: TAP Holdings]

ADVERSE REACTIONS:
Section revised to include reports from post-marketing surveillance and information regarding bone mineral density: Mood swings, including depression, have been reported as physiologic effect of decreased sex steroids. There have been very rare reports of suicidal ideation and attempt, with many, but not all, of these patients having a history of depression or other psychiatric illness. Patients should be counseled on the possibility of worsening of depression.

There have been rare reports of symptoms consistent with anaphylactoid or asthmatic process, with rash, urticaria and photosensitivity reactions also reported.

Localized reactions, including induration and abscess at the site of injection, have been reported.

Cardiovascular System: hypotension;

Hemic and Lymphatic System: decreased WBC;

Central/Peripheral Nervous System: peripheral neuropathy, spinal fracture/paralysis;

Musculoskeletal System: tenosynovitis-like symptoms;

Urogenital System: prostate pain.

See other Lupron Depot and Lupron Injection package inserts for other events reported in different patient populations.

Endometriosis: Subsection revised to indicate that in controlled study in endometriosis patients, patients tested at six or twelve months after discontinuation of therapy showed mean bone density return to within 2% of pretreatment.

LUPRON DEPOT (leuprolide acetate) for Depot Suspension 3 Month, 11.25 mg.
[September 4, 1997: TAP]

[Changes to other formulations of Lupron within past 12 months: Jan97, May97]

ADVERSE REACTIONS:

"Table 2: Adverse Events Reported to be Causally Related to Drug in > or = 5% of Patients" has been revised to correct errors found in the approved label. Contact the company for a copy of the labeling/package insert.

Postmarketing: New fourth paragraph added - "Symptoms consistent with fibromyalgia (e.g., joint and muscle pain, headaches, sleep disorders, gastrointestinal distress, and shortness of breath) have been reported individually and collectively."

Cardiovascular System: "Pulmonary embolism" added.

LUPRON DEPOT (leuprolide acetate) Depot Suspension 3.75 mg & 3 Month 11.25 mg

[April 9, 1998: TAP]

3.75 mg Dosage Form -

CLINICAL STUDIES:
Hormonal Replacement Therapy (new subsection):

"Clinical studies suggest that the addition of hormone replacement therapy (estrogen and/or progestin) to Lupron is effective in reducing loss of bone mineral density which occurs with Lupron, without compromising the efficacy of Lupron in relieving symptoms of endometriosis. The optimal drug/dose is not established."

PRECAUTIONS:
Information for Patients: Bullet #5: Text added at end of subsection -

"Clinical studies suggest that the addition of hormone replacement therapy (estrogen and/or progestin) to Lupron is effective in reducing loss of bone mineral density which occurs with Lupron, without compromising the efficacy of Lupron in relieving symptoms of endometriosis. The optimal drug/dose is not established."

ADVERSE REACTIONS:
Changes in Bone Density: Subsection revised (new text in italics) - "["Endometriosis:" deleted] a controlled study in endometriosis patients showed that vertebral bone density as measured by dual energy x-ray absorptionmetry (DEXA) decreased by an average of ["3.9%" deleted] 3.2% at six months compared with the pretreatment value. ["For those patients who were tested at six or twelve months after discontinuation of therapy, mean bone density returned to within 2% of pretreatment. Use of Lupron Depot 3.75 mg for longer than six months or in the presence of other known risk factors for decreased bone mineral content may cause additional bone loss." deleted].

"["Uterine Leiomyomata (Fibroids): In one study, vertebral trabecular bone mineral density as assessed by quantitative digital radiography (QDR) revealed a mean

decrease of 2.7% at three months compared with the pretreatment value. Six months after discontinuation of therapy a trend toward recoery was observed. Use of Lupron Depot 3.75 mg for uterine leiomyomata for longer than three months or in the presence of other known risk factors for decreased bone mineral content may cause additional bone loss and is not recommended." deleted here, revised and moved as last paragraph in section].

"In this same study, Lupron Depot 3.75 mg alone and Lupron Depot 3.75 mg plus three different hormonal add-back regimens were compared for one year. All add-back groups demonstrated mean changes in bone mineral density of < or = 1% from baseline and showed statistically significantly (P-value < 0.001) less loss of bone density than the group treated with Lpron Depot 3.75 mg alone, at all time points. Clinical studies suggest that the addition of hormone replacement therapy (estrogen and/or progestin) to Lupron is effective in reducing loss of bone mineral density which occurs with Lupron, without compromising the efficacy of Lupron in relieving symptoms of endometriosis. The optimal drug/dose is not established.

"When Lupron Depot 3.75 mg was administered for three months in uterine fibroid patients, vertebral trabecular bone mineral density as assessed by quantitative digital radiography (QDR) revealed a mean decrease of 2.7% at three months compared with the pretreatment value. Six months after discontinuation of therapy a trend toward recoery was observed. Use of Lupron Depot 3.75 mg for uterine leiomyomata for longer than three months or in the presence of other known risk factors for decreased bone mineral content may cause additional bone loss and is not recommended."

3 Month 11.25 mg Dosage Form

CLINICAL STUDIES:
Hormonal Replacement Therapy (new subsection):

"Clinical studies suggest that the addition of hormone replacement therapy (estrogen and/or progestin) to Lupron is effective in reducing loss of bone mineral density which occurs with Lupron, without compromising the efficacy of Lupron in relieving symptoms of endometriosis. The optimal drug/dose is not established."

PRECAUTIONS:
Information for Patients: Bullet #5: Text added at end of last paragraph -

"Clinical studies suggest that the addition of hormone replacement therapy (estrogen and/or progestin) to Lupron is effective in reducing loss of bone mineral density which occurs with Lupron, without compromising the efficacy of Lupron in relieving symptoms of endometriosis. The optimal drug/dose is not established."

ADVERSE REACTIONS:

Changes in Bone Density: Subsection revised (new text in italics) - "In controlled clinical studies, patients with endometriosis (six months of therapy) or uterine fibroids (three months of therapy) were treated with Lupron Depot 3.75 mg. In endometriosis patients, vertebral bone density as measured by dual energy x-ray absorptionmetry (DEXA) decreased by an average of ["3.9%" deleted] 3.2% at six months compared with the pretreatment value. ["For those patients who were tested at six or twelve months after discontinuation of therapy, mean bone density returned to within 2% of pretreatment." deleted] .

"In this same study, Lupron Depot 3.75 mg alone and Lupron Depot 3.75 mg plus three different hormonal add-back regimens were compared for one year. All add-back groups demonstrated mean changes in bone mineral density of < or = 1% from baseline and showed statistically significantly (P-value < 0.001) less loss of bone density than the group treated with Lpron Depot 3.75 mg alone, at all time points. Clinical studies suggest that the addition of hormone replacement therapy (estrogen and/or progestin) to Lupron is effective in reducing loss of bone mineral density which occurs with Lupron, without compromising the efficacy of Lupron in relieving symptoms of endometriosis. The optimal drug/dose is not established.

"When Lupron Depot 3.75 mg was administered for three months in uterine fibroid patients, vertebral trabecular bone mineral density as assessed by quantitative digital radiography (QDR) revealed a mean decrease of 2.7% at three months compared with the pretreatment value. Six months after discontinuation of therapy a trend toward recoery was observed. Use of Lupron Depot 3.75 mg for uterine leiomyomata for longer than three months or in the presence of other known risk factors for decreased bone mineral content may cause additional bone loss and is not recommended."

Side effects of LUPRON include the following:

THE FOLLOWING SIDE EFFECTS NOTED FOR LUPRON AT THE U of Pittsburgh Cancer Institute webpage: hot flashes, bone pain, difficult or painful urination, weakness, numbness, tingling, swelling of hands, dizziness, headache, breast tenderness, nausea, unusual sweating

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Taken from the webpage,
http://womenshealth.about.com/library/weekly/aa050801a.htm:

Side Effects and Lupron Depot

Side effects that have been associated with the use of Lupron Depot include hot flashes and/or night sweats in more than 5% of women; and palpitations, syncope, and tachycardia in less than 5% of the women who participated in clinical trials. Other side effects include generalized pain, headaches, vaginitis, nausea/vomiting, fluid retention, weight gain, acne, hirsutism, joint pain, decreased libido, depression, dizziness, nervousness, and breast changes that include tenderness and pain, among others. There have been no deaths directly related to therapy with Lupron Depot.

_____\

THE FOLLOWING TAKEN FROM: http://www.jennifer-o.com/Hormones/f2m/leuprolide-acetate.htmAdverse reactions ----

CNS
Anxiety. Delusions. Dizziness. Headache. Hearing disorders. Insomnia. Memory disorder. Nerve disorders. Personality disorder.

Eyes
Eye disorders.

Gastrointestinal
Anorexia. Constipation. Coughing up blood. Dry mouth. Nausea. Thirst. Vomiting.

Skin
Change of facial and body hair. Skin rash.

Other
Ankylosing spondylosis. Blood in the urine. Bone and muscle pain. Change in heart electrical activity. Congestive heart failure.
Decrease of bone density. Decreased tolerance of protein. Decreased red blood cell count. Decreased white blood cell count.

Difficulty urinating. Elevated blood pressure. Elevated LDH. Elevated phosphorus. Escape of blood into the tissues from
ruptured blood vessels. Fluid retention. Hair loss. Hot flashes. Increased heart beat rate. Increased uric acid. Increased
urination frequency or urgency. Lactation. Liver disorder. Loss of strength. Low blood pressure. Lymphadenopathy. Mild to
extreme allergic reaction. Palpitations. Pelvic fibrosis. Penile swelling. Prostate pain. Pulmonary disorders. Respiratory
disorders. Temporary increase of hormone production. Temporary suspension of respiration and circulation.

PERSONAL STORIES from the Internet

I'm 22 years old and in September of 2000 I had my one and only shot of Lupron. I didn't know much about the drug and my doctor was very reluctant to tell me anything about it. He insisted I'd only suffer hot flashes. A few hours after receiving the shot I started to get dizzy and I blacked out. I had nausea, dizziness, insomnia, anxiety, forgetfulness, lactation, I thought I was going off the deepend. My family doc told me to stop it and that was that, I went straight back to taking the pill normally.

This past summer I had to come off the pill for 3 months prior to my laser lap and I had the shock of my life. The lactation was back. Until I started back on the pill I lactated. I went through 1 and a half boxes of nursing pads. I now lactate whenever I am not on the pill. For a 22 year old woman this is very upsetting. I always find I can't be around people the day it happens as I'm very upset.

I have also noticed that since taking Lupron, my chest size has continued to increase significantly. I just found out last weekend that I am now a D cup! This isn't normal as I'm a very tiny person and have not gained any weight anywhere else. People have noticed a change in my breast size, even after not seeing me for 6 weeks.

I'm just wondering if there is anyone else who has had this happen. I feel very lost and unsure of what is going on and whether or not this is going to cause more problems for me in the future. My doctor won't listen to me when I tell her of my concerns as she insists it's just hormonal. Yes, I agree it's hormonal, but I can trace it all back to that fateful day in September 2000.

I hope that I find understanding here and I finally realise I'm not

alone.
Arianna

Date/Time: 1/1/2002 9:13:55 PM

Hello all... I was searching the net on side effects of Lupron and found this site. I had my second injection of Lupron a week ago. I had gone to my appointment prepared to not get another injection because of the side effects I had with the first dose, but i allowed my doctor to talk me into taking it. I told him off all the side effects I was having and he basically told me that most of it was "all in my head". I am so frustrated right now. So tonight I went searching for anything I could find of Lupron that my doctor hadn't told me and i am amazed at what I have found. I would like to know how a doctor can justify giving this drug to a patient and not informing them off that can happen! And when it does happen tell them it must be in thier head.

Last month I ended up with a headache that lasted 15-16 days, muscle aches, I am so sore when I get up in the mornings (stiff), I m extremely irritable and I cry at the most unexpected times. i feel like i am on an emotional rollercoaster. I am an at home mom of a 6 and 4 year old and I find that I have to really made myself crawl out of bed in the morning to even take care of my children. And once I am out of bed i have no energy. How can all of this be in my head??? I feel like i'm going to cry again now just telling about what is happening to me! These side effects are worse than the problems it is taking care of!!!

I guess I am just trying to make sure that I'm not going crazy here and are these really side effects that my doctor just doesn't want to admit to? My husband told me today that he wants to go with me to a doctor appointment and talk to the doctor too and that he does not want me to get any more shots. And also at the last appointment when I troed telling my doctor about this he tried to give me a prescription for Darvcet (spelling?) for the headaches which he says is probobly migrains and not the shots.... I had to explain to him that I am a mom who is at home with a 4 year old all day..how can I take a pain killer that I would imagine would affect me even more and still take care of my child safely? I don't want to start taking more medicine to get rid of side effects of other drugs! It makes no sense at all to me.

I'm sorry of it appears that I am just rambling here..once i started I guess it all just started coming out. If anyone has any suggestions for me I would great appreciate it! I feel like my life is falling apart and I'm only had 2 shots..how in the world would I feel if i continued with the 6 month treatment plan????? I can't even imagine it!

I understand your anger - most, if not all of us, live with the daily pain - some days worse than others. Are you new to all of this lupron stuff? Way back at the beginning, my goal was to find out what was wrong with me. I knew (still know) that this is all related. But over time, I've discovered, the best treatment that I've been able to get, is symptom-by-symptom. I do take anti-inflamatories, which helps the stiffness. I also was on Vioxx for about a year. I now take Arthrotec and that seems to be about the best one yet. Fibromyalgia is what a rheumatologist said that I have. It's probably close enough.

I have been on and off lupron for the last 10 years. I was on it in 93 for 6 months, 98 for 1 year, then in Sept of last year for 1 month and then found this site when researching the drug. I have had syptoms for the last 6 years ranging from all of the ones we have all talked about, but never new that it might be an underlying cause of my problems until I found other people had similar syptoms. I have had pain in my bones for the last year or so but nothing like I am experiencing as of late. Just yesterday I worked on my house for 2-3 hours and I woke up today and could not move my elbow it was in so much pain. This type of pain is VERY new to me cuz I can't work on a regular basis, or sleep on a regular basis. I am very scared at the moment cuz, I don't have a job now, I don't have a husband to help with money and pay for house payments, etc. I just feel like most of you that this drug has taken my life. I have been suffering with endo since I was 15 and now I am 32. I feel for all of you that have gone through the trama of the after effects of this drug. I feel like I need to do something proactive. I would like to try to start something locally to draw attention to the TAP industry about the after effects of this drug.

I am not working right now and have been watching day time TV and the Oprah Winphrey Show. This may be far fetch, but I thought about gathering some information that I have seen, read, and talk to this panel about, and write her a letter about doing a show on the after effects of Lupron on women. I know her audience is wide and she is pro woman. Maybe it is worth a try. I feel like I should do something. What do you think? Is it worth a try or do you think I would be wasting my

energy?

Anyone who has any experience to share with me, I welcome it. I thought I was just crazy until I found this site last night. My mother made me start reaching lupron, now I wish I didn't know as much as I do. My life has changed so much. I don't feel normal at all. I'm not. I have not slept in months, I cry all the time, my body hurts (but they say not from lupron), I have awlful anxiety (but they say lupron has never effected pts this way) I am very depressed, my imagination is beginning to runnaway with bad thoughts. People would tell me snap out of it, but last night when my mom and husband read messages from the site they became has scared as I have been for months. I wish I had know more before I took my injections, my side effects are nothing like what I read in the doctor's phamplet.

I am so sorry that you have been thrown into the world of "post-lupron" survival. And no, you are not crazy, and no, it is not all in your mind. What you are experiencing now is very real. It happened to me and it happened to the other people who post on this site. Life after lupron is not easy, to say the least. But at least you have found this site, just as I stumbled across it in my search for answers. It's been over a year since my last injection and I am still trying to find my former self, the "real me" again. I know she's inside me somewhere, buried deeply perhaps, underneath this other person that I am now...this person that I definitely do not like. And no, the doctors do not tell you ANYTHING about the "true" side effects. Hot flashes and maybe some achiness were the side effects that my doctor told me that I would experience. That's it! And whenever I complained to him about the HORRIBLE PAIN in my legs that made it difficult for me to even walk, the insomnia, the migraines, the depression, etc., he just kind of shrugged and made some excuse and brushed it off. A year later and I am still struggling with achiness, sleep disorders, fatigue, and weight gain. Prior to lupron, my metabolism was great. Never gained an ounce, ate whatever I wanted. Loved to exercise just for the enjoyment of it. I was into kickboxing, going to the gym, taking long walks.... now I can't walk up a flight of stairs without huffing and puffing. Everyday is a struggle, but you have to keep trying! Don't give up!

Something most definitely has happened to our bodies. Our systems have been thrown completely out of whack by a drug that was supposed to help, that only hurt us instead. There are so many questions, but so few answers. The truth is out there, somewhere. We just have to keep searching. And hoping.... Hope is a good thing. Grab hold of it and don't let go!
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DateTime: 7/26/2001 6:37:44 PM

I can understand your feelings. I felt the same way today. I got mad at my previous doctor for giving me this drug. She did not inform me of the sides. Our nightmare may be just starting. I am going to the Media. I have a name of a producer with a major network. I am not giving up. I don't want other women to suffer the way that I have. I will keep everyone posted on the outcome. My husband knows how I feel because he was by my side. He sees hairloss, weight gain, blurred vision, moaning from joint pain and nerve damage. I had a chemical body odor during the time I was taking the injections. I told the doctor she said it was my sinus. Now I understand that is a side effect of Lupron. Everthing will fall in to place for us. I love posting but action needs to be taken. I was given the drug in the year 2000 and some went before me and or still suffering.
DateTime: 4/10/2001 8:07:47 PM

Hello Everyone,

I would like to hear more about your experiences with Lupron related arthritis, arthralgia, and/or joint pain.

I am a 41 year old female, with a history of fibroid tumors, endometriosis, surgical adhesions, and infertility. Because of high risk for more adhesions, I decided to "try Lurpon" instead of an LAVH-BSO. I researched it VERY carefully, and was aware of the risks.

My Doctor and I agreed to do add-back therapy -- which to answer some questions from previous posts -- is used in VERY low doses ... the lowest doses of estrogen and progesterone possible to relieve the hot flashes, depression, mental fogginess, etc..., without further stimulating the endo. Two weeks after the first injection, the hot flashes and other symptoms began, and I started the add-back. Those symptoms all went away .. and never came back.

My abdominal pain DID improve ... my left ovary pain (which is adhered to my abdominal wall) is gone! And my uterine pain is now MUCH less painful, and more easily controlled with my pain killers (vicodin/relafen). The pain now is at the level it was after my last lap -- and that is a HUGE

improvement over what it was.

However ... the cure turned out to be worse than the disease ...

The one side effect I am experiencing, is SEVERE arthritis like joint pain. It started after my 2nd monthly Lupron injection. It lasted for about 6-8 weeks, until it subsided a bit. Then, I actually felt good for about 6 weeks with just occassional joint pains -- at the end of the day, when I was really tired. Then a week after my 5th Lupron shot, the SEVERE arthritis like pain returned. This pain is in EVERY paired joint, head to toe (not in my neck or back though).

My Doctor said this is a known side effect ... probably a "hypo-estrogenic effect" (low estrogen) -- since estrogen serves as a lubricant throughout the body ... "they" suspect it somehow affects the synovial fluid. (Similar to Rheumatoid Arthritis ... but not the same mechanism)

"Arthralgias" (meaning joint pain), and "Joint disorders" and "joint pain" are KNOWN side effects of Lupron ("officially" 25% report it).

My Dr. had me increase my estrogen add-back, and suggested I take glucosamine/chondroiten (I already was). After a week the estrogen had no effect, so he suggested we stop at 5 Lupron injections. He had me started low-dose birth-control pills (Levlen ... progesterone dominant) in an attempt to retain the abdominal benefits of the Lupron, while hoping to help my joint pain.

After 10 days ... there has been no change. I like the idea of not having periods for another 3 months on continuous BCPs ... but I am very concerned that the joint pain is not going away.

Interesting thing is ... I NEVER had any kind of joint pain prior to this. It began after the Lupron, and I was told it was a "known" effect. It is "supposed" to go away after I stop the Lupron. It hasn't yet. It hasn't for many of you. Because I've had no other "Lupron side effects" to speak of ... it can't be explained away as something else.

So ... I would really apprecaite hearing all your stories related to joint pain and arthritis like pain. And anything that has worked for you in relieving it. I would love to know if you've been able to get a definitive diagnosis too.

Thanks so much for your help!

I got my lupron from the good ole CVS pharmacy. I took three shots of this stuff, one shot a month for three months. I paid $20 per shot, my insurance covered the rest. Looking back, I really wish my insurance hadn't paid for this stuff. With a regular price of $425.00 per shot, maybe I wouldn't have been able to afford to take it!

Why were you given lupron? I had fibroids, one of which was quite large. My doctor wanted to give me lupron in order to shrink the fibroid before performing a myomectomy. Sounded like a good idea at the time. He also told me that since I was in such great shape physically that I would bounce back quickly. Well, needless to say, it's been over a year and I'm still waiting for that BIG BOUNCE!

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DateTime: 4/10/2001 10:11:30 PM

I am post Lupron for 10 years.
Yes, 10! years.
Worst mistake of my life at 30 to take Lupron for 9 months.
Have lost 10 years.
Muscle and bone pain everywhere every minute of each day.
Has not gotten much better with time.
Hope your experience won't be as bad.

=========

Sep-9 11:01 pm
I took lupron for endo. I had laser surgery in Dec. I was told that if I took lupron too, it shouldn't come back anytime soon. I wish I still had my endo. My last injections was 7/27/01 I still have not had a period. I keep hoping that I will have a period and everything will be fine. How long before your cycle returned? When did you realize that you were not yourself? I have felt out of controll, "Not Normal" since my 2nd injection, but was dumb enough to believe them when they said it wasn't the lupron. Thanks for everything. I've enjoyed communicating with everyone.

======

Sep-11 4:33 am

I guess it was after my second injection that I had the feeling that what I was experiencing just couldn't be "normal." The hot flashes I could handle, especially in comparison to everything else that happening. But I just kept forging ahead the best I could. After all, this was all supposed to help make me better, right? So then I had the myomectomy and I thought that soon all this would be behind me and I would be better than ever and be able to get back to being my "normal" self again, only without the heavy periods. Well, my periods are a lot lighter now, that being about the only good thing that came out of all this. But the rest of me is definitely NOT normal and I don't know if I ever will be again.

I believe my periods started up again about a month after my surgery, which would have been about two months after my last injection. So maybe yours will start sometime soon. Hopefully you'll get back to "normal" in that regard, anyway. Hang in there!

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Sep-29 5:38 am

I would suggest filling out a MEDWATCH form for the FDA. A doctor Does NOT have to do it for you!!!!!! www.fda.gov/medwatch It's one of the best things you can do for yourself and others. They need to know how many of us there are!

I suppose this goes without saying, but I hope you found or are looking for a new doctor.

Have you tried talking to your PCP or Primary doctor about your Lupron problems? Some of us have also had good luck with Neurologists and/or Rheumotologists. Depending on what your symptoms are. I use them all. Currently my _PCP is my biggest ally! She is really great. If you can find a doctor concerned with women's health issues, that might help. You could interview staff over the phone so you don't waste a trip. Then I would state your problems somewhat "matter of factly". I mean to say that It, Lupron, is part of your health history that caused your health problems. State it as YOU know it to be true. Take some time, when you can, to write everything down. I really found this to be helpfull to not just my doctors but for myself as well. It was sort of thereputic. I asked family and friends to help fill in the large holes in my memory. I also used medical records to fill in my complaints and get an accurate time line.

Well, these are just a few things you can do for you...I know it's difficult! It will be difficult for a while!

As your parents may be doing now, mine had to deal with their own guilt as well. Even though I was an adult, they watched me go through all this. I was living at home when I took Lupron. They knew I wasn't "right". but my doctor was insistant. My father still struggles with it. It's been 9 yrs. He faxes me stuff all the time and if there is ANY pro-lupron report in his local paper his is the first on the phone blasting the reporter or marching down to the office to tell off the editor. This problem effects everyone.

good Luck!

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Lupron, Infertility, and Women as Guinea Pigs

By Nicholas Regush Redflagsweekly.com

It's a disgrace. A drug named Lupron that is unapproved by the Food and Drug Administration for treatment of infertility is being used widely at infertility clinics.

There is no surveillance to speak of, no adequate research being done, and little or no informed consent. It's become a free-for-all and a glaring example of why modern medicine, drug companies and the FDA cannot be easily trusted.

Lupron, manufactured by Tap Pharmaceuticals Inc., is approved for treatment of men with advanced prostate cancer and for treatment of endometriosis and uterine fibroids.

That's it. Nothing more.

.....(section deleted) I'd like to issue a challenge to Tap Pharmaceuticals and any medical body or doctor to pony up the "real" science that has been done to support the contention that the use of Lupron for treatment of infertility is safe and effective, over both the short-term and long-term.

Any public revelations that solid safety and efficacy data exist to support the use of Lupron in the treatment of

infertility could be viewed as reassurance to women that they are not guinea pigs in some giant medical experiment - which I believe they are.

As things stand, for example, there are already many serious questions about the use of Lupron in the treatment of endometriosis, an approved indication. The studies supporting the approval were amazingly scant, and long-term research has seriously gone missing.

Endometriosis is a condition in which pieces of the lining of the uterus are found in other parts of the body, especially in the pelvic cavity. These pieces of endometrium respond to the menstrual cycle and bleed. Because the blood cannot escape, it builds up and causes the development of small or large painful cysts.

Lupron is a synthetic-like hormone that is said to act on this process by suppressing the ovaries and is supposed to temporarily interrupt estrogen output. This creates a drug-induced menopause. The goal of treatment is to shrink any lesions produced via endometriosis.

Many women with endometriosis who are given Lupron injections have horrendous side-effects, including cardiac arrythmias, dizziness, swelling, chest pain, depression and confusion, bone pain, extreme fatigue, vision loss, high blood pressure, and nausea. Some of the women claim their side-effects last long after treatment is completed.

TAP says its product is safe and that the normal function of the pituitary-gonadal system is usually restored within three months after Lupron injections are discontinued. The FDA agrees with the company.

It's fine for TAP to say their product is safe, but quite another to produce evidence on the basis of well-controlled long-term research that the pituitary-gonadal system is not altered in any way by Lupron.

Meanwhile, IVF doctors often use the very same drug - Lupron -for the treatment of infertility, an unapproved

indication.

Usually Lupron injections are begun approximately one week after ovulation. The idea is to suppress female hormones that normally can produce one mature egg. Shutting off the body's production of hormones enables the IVF doctors to use hormonal preparations that can lead to multiple egg development.

Fine, but where's the solid science on safety and efficacy?

Red Flags Weekly March 11, 2000

DateTime: 8/31/2000 11:57:27 AM

The alcohol wipes used to wipe the arm or butt after a lupron shot are to be considered "hazardous". In "Chemotherapy Care Plans Handbook" by M.B.Burke, G.M. Wilkes & K. Ingwersen (1998), lupron (leuprolide), a GnRHa, is listed in the "commonly used cytotoxic and hazardous drugs" list. In the Appendix of this book, there is an 'Illustrated Guide to Handling of Cytotoxic and Hazardous Drugs', and it states: "After administration of drug, place all gauze and alcohol wipes into a hazardous chemical waste container; wash hands upon removal of gloves."

Published medical reports have noted the occurrence of abnormal pregnancy outcomes associated with the use of lupron - 43.5% in one 1996 study (Fertility and Sterility, Abstract P-34, Program Supplement, April 1996, p.A27). In 1999, the first study was conducted on the long-term follow-up of children born after inadvertent administration of GnRHa in early (undetected) pregnancy. In the six children studied, a major congenital malformation and four neurodevelopmental abnormalities, including epileptic disorder, attention deficit hyperactivity disorder, motor difficulties and speech difficulties, were seen. The conclusion was that "[t]his observation of neurodevelopmental abnormalities in four of six children in the study group justifies the need for long-term follow-up of more children previously exposed to GnRHa." (Human Reproduction, 1999;14(10):2656). In addition, a follow up letter published in response to this article stated that "[t]he need for long term follow-up ... echoes the intuition of many clinicians." (Human Reproduction, 1999,15(6):1421). In a fairly comprehensive review of the published literature, the highest figure I came across, published in 1999, was "more than 340 pregnancies reported". Just from those articles

that I came across, I could count 407 reported inadvertent exposure to GnRHa (lupron, gonadorelin, buserelin, decapeptly, triptorelin, and suprefact) during pregnancy. Of those 407 pregnancies, I counted 316 births; only 7 of those 316 births had any follow-up - and 6 of those 7 are mentioned above (4 were found to have neurodevelopmental abnormalities and one of those also had a major congenital malformation).

I've learned that a major hospital's recovery room staff had a meeting regarding lupron and the issue of the recommendations for healthcare personnell to use protective gear when handling and injecting lupron. The conclusion of this meeting was that patients can receive their lupron injection at their post-op doctors visit as this particular recovery room decided it would no longer administer lupron. :)

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More to follow--these are items gathered initially (late March 2002)

The White House
President George W. Bush

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For Immediate Release
Office of the Press Secretary
April 10, 2002

President Bush Calls on Senate to Back Human Cloning Ban
Remarks by the President on Human Cloning Legislation
The East Room

1:18 P.M. EDT

[redacted] President's Remarks
view
listen

THE PRESIDENT: Well, thank you all so very much for coming to the White House. It's my honor to welcome you to the people's house.

I particularly want to honor three folks who I had the honor of meeting earlier: Joni Tada, Jim Kelly and Steve McDonald. I want to thank you for your courage, I want to thank you for your wisdom, I want to thank you for your extraordinary perseverence and faith. They have triumphed in the face of physical disability and share a deep commitment to medicine that is practiced ethically and humanely.

All of us here today believe in the promise of modern medicine. We're hopeful about where science may take us. And we're also here because we believe in the principles of ethical medicine.

As we seek to improve human life, we must always preserve human dignity. (Applause.) And therefore, we must prevent human cloning by stopping it before it starts. (Applause.)

I want to welcome Tommy Thompson, who is the Secretary of Health and Human Services, a man who is doing a fine job for America. (Applause.) I want to thank members from the United States Congress, members from both political parties who are here. I particularly want to thank Senator Brownback and Senator Landrieu for sponsoring a bill about which I'm going to speak. (Applause.)

As well, we've got Senator Frist and Senator Bond and Senator Hutchinson and Senator Santorum and Congressman Weldon, Stupak, and eventually Smith and Kerns. They just don't realize -- (applause) -- thank you all for coming -- they seem to have forgotten we start things on time here in the White House. (Laughter.)

We live in a time of tremendous medical progress. A little more than a year ago, scientists first cracked the human genetic code -- one of the most important advances in scientific history. Already, scientists are developing new diagnostic tools so that each of us can know our risk of disease and act to prevent them.

One day soon, precise therapies will be custom made for our own genetic makeup. We're on the threshold of historic breakthroughs against AIDS and Alzheimer's Disease and cancer and diabetes and heart disease and Parkinson's Disease. And that's incredibly positive.

Our age may be known to history as the age of genetic medicine, a time when many of the most feared illnesses were overcome.

Our age must also be defined by the care and restraint and responsibility with which we take up these new scientific powers.

Advances in biomedical technology must never come at the expense of human conscience. (Applause.) As we seek what is possible, we must always ask what is right, and we must not forget that even the most noble ends do not justify any means. (Applause.)

Science has set before us decisions of immense consequence. We can pursue medical research with a clear sense of moral purpose or we can travel without an ethical compass into a world we could live to regret. Science now presses forward the issue of human cloning. How we answer the question of human cloning will place us on one path or the other.

Human cloning is the laboratory production of individuals who are genetically identical to another human being. Cloning is achieved by putting the genetic material from a donor into a woman's egg, which has had its nucleus removed. As a result, the new or cloned embryo is an identical copy of only the donor. Human cloning has moved from science fiction into science.

One biotech company has already began producing embryonic human clones for research purposes. Chinese scientists have derived stem cells from cloned embryos created by combining human DNA and rabbit eggs. Others have announced plans to produce cloned children, despite the fact that laboratory cloning of animals has lead to spontaneous abortions and terrible, terrible abnormalities.

Human cloning is deeply troubling to me, and to most Americans. Life is a creation, not a commodity. (Applause.) Our children are gifts to be loved and protected, not products to be designed and manufactured. Allowing cloning would be taking a significant step toward a society in which human beings are grown for spare body parts, and children are engineered to custom specifications; and that's not acceptable.

In the current debate over human cloning, two terms are being used: reproductive cloning and research cloning. Reproductive cloning involves creating a cloned embryo and implanting it into a woman with the goal of creating a child. Fortunately, nearly every American agrees that this practice should be banned. Research cloning, on the other hand, involves the creation of cloned human embryos which are then destroyed to derive stem cells.

I believe all human cloning is wrong, and both forms of cloning ought to be banned, for the following reasons. First, anything other than a total ban on human cloning would be unethical. Research cloning would contradict the most fundamental principle of medical ethics, that no human life should be exploited or extinguished for the benefit of another. (Applause.)

Yet a law permitting research cloning, while forbidding the birth of a cloned child, would require the destruction of nascent human life. Secondly, anything other than a total ban on human cloning would be virtually impossible to enforce. Cloned human embryos created for research would be widely available in laboratories and embryo farms. Once cloned embryos were available, implantation would take place. Even the tightest regulations and strict policing would not prevent or detect the birth of cloned babies.

Third, the benefits of research cloning are highly speculative. Advocates of research cloning argue that stem cells obtained from cloned embryos would be injected into a genetically identical individual without risk of tissue rejection. But there is evidence, based on animal studies, that cells derived from cloned embryos may indeed be rejected.

Yet even if research cloning were medically effective, every person who wanted to benefit would need an embryonic clone of his or her own, to provide the designer tissues. This would create a massive national market for eggs and egg donors, and exploitation of women's bodies that we cannot and must not allow. (Applause.)

I stand firm in my opposition to human cloning. And at the same time, we will pursue other promising and ethical ways to relieve suffering through biotechnology. This year for the first time, federal dollars will go towards supporting human embryonic stem cell research consistent with the ethical guidelines I announced last August.

The National Institutes of Health is also funding a broad range of animal and human adult stem cell research. Adult stem cells which do not require the destruction of human embryos and which yield tissues which can be transplanted without rejection are more versatile that originally thought.

We're making progress. We're learning more about them. And therapies developed from adult stem cells are already helping suffering people.

I support increasing the research budget of the NIH, and I ask Congress to join me in that support. And at the same time, I strongly support a comprehensive law against all human cloning. And I endorse the bill -- wholeheartedly endorse the bill -- sponsored by Senator Brownback and Senator Mary Landrieu. (Applause.)

This carefully drafted bill would ban all human cloning in the United States, including the cloning of embryos for research. It is nearly identical to the bipartisan legislation that last year passed the House of Representatives by more than a 100-vote margin. It has wide support across the political spectrum, liberals and conservatives support it, religious people and nonreligious people support it. Those who are pro-choice and those who are pro-life support the bill.

This is a diverse coalition, united by a commitment to prevent the cloning and exploitation of human beings. (Applause.) It would be a mistake for the United States Senate to allow any kind of human cloning to come out of that chamber. (Applause.)

I'm an incurable optimist about the future of our country. I know we can achieve great things. We can make the world more peaceful, we can become a more compassionate nation. We can push the limits of medical science. I truly believe that we're going to bring hope and healing to countless lives across the country. And as we do, I will insist that we always maintain the highest of ethical standards.

Thank you all for coming. (Applause.) God bless.

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Not Ready For Human Cloning

By Bill Frist

Thursday, April 11, 2002; Page A29

Can one be an advocate for embryonic stem cell research while opposing human cloning experimentation? That's the question facing about 30 U.S. senators who have not yet taken a position on human cloning legislation to be brought before the Senate.

But we must first understand the similarities and distinctions between the two. It's important to understand that human "therapeutic" or "research" cloning is an experimental tool often confused with, but distinct from, embryonic stem cell research. Only then can we appropriately dissect a debate on the potential of the science vs. the restraint defined by ethics and moral concerns.

Most agree that human reproductive cloning, or the cloning of human beings, should be banned. The contentious issue is whether this ban should extend to all human cloning, including human embryo research cloning experimentation, a brand-new field. Advocates point to its potential to develop tissues that will not be rejected by a patient's immune system. They also argue for human cloning as a source of genetically diverse stem cells for research. Moreover, they say such experimentation will further our basic understanding of biology and life's origins.

But regardless of our religious backgrounds, most of us remain uncomfortable with the idea of creating cloned human embryos to be destroyed in an experiment.

As a physician and legislator who struggles with this inherent tension between scientific progress and ethical concerns, I focus on two fundamental questions: (1) Does the scientific potential of human research cloning experimentation justify the purposeful creation of human embryos, which must be destroyed in experiments? (2) Does the promise of human embryonic stem cell research depend on experimental human research cloning?

At this point in the evolution of this new science, I cannot justify the purposeful creation and destruction of human embryos in order to experiment on them, especially when the promise and success of human embryonic stem cell research do not depend on experimental research cloning.

President Bush last August outlined a scientifically and ethically balanced policy that allows federal funding of embryonic stem cell research for nearly 80 stem cell lines. This has opened the door to a significant expansion of embryonic stem cell research. Further, there are no restrictions on private research using stem cells from the thousands of embryos left over after in vitro fertilization. This research, too, is underway. The promise and hope for new cures is being investigated. And the promise of this research does not -- I repeat, does not -- depend on human embryo cloning.

Human cloning would indeed provide another source of stem cells -- this time by asexual reproduction. But a human embryo still has to be created -- then destroyed -- to produce these stem cells. Moreover, very little research cloning experimentation has been done with animals -- a prerequisite to any demands for such work in humans. Given the early state of this uncharted new science, the large number of federal cell lines and the unlimited number available for private research, I believe a sufficient number and range of cell lines are available.

As a heart transplant surgeon, I know intimately the challenges of transplant rejection. But I also know of multiple promising strategies to address this issue, such as the development of "tolerance strategies," improved pharmacologic immunosuppression and the manipulation of cell surface structure to make cells "invisible" to the immune system -- none of which carries the ethical burdens attached to human cloning.

No one can deny the potential that human cloning holds for increased scientific understanding. But given the serious ethical concerns this research raises, the fact that promising embryonic stem cell research will continue even under a cloning ban, the lack of significant research in animal models and the existence of promising alternatives, I am unable to find a compelling justification for allowing human cloning today.

The fact that we are even engaged in this debate testifies to the rapid and encouraging progress of science. As it moves forward, we will undoubtedly be forced to reexamine this issue. For now, the proper course is to stop short of allowing cloning research in humans but to enthusiastically embrace the public and private stem cell research that holds such great hope for those who suffer from a wide range of disorders and conditions, such as Alzheimer's disease, Parkinson's disease and diabetes.

The writer is a former heart and lung transplant surgeon and a Republican senator from Tennessee.

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CLONING INFORMATION

The Views of the United States on the Science and Ethical Implications of Human Cloning

Distributed by the US Delegation to the United Nations Meeting on a Treaty to Ban Human Cloning, February 26, 2002

A. The United States' Position

The United States supports a global and comprehensive ban on human cloning through somatic cell nuclear transfer, regardless of the purpose for which the human clone is produced. The United States believes that so-called "therapeutic" or "experimental" cloning, which involves the creation and destruction of human embryos, must be part of this global and comprehensive ban. Thus, the United States does not support a ban that is limited merely to "reproductive" cloning.

Any ban on human cloning should explicitly state that it does not prohibit the use of nuclear transfer or other cloning techniques to produce DNA molecules, organs, plants, tissues, cells other than human embryos, or animals other than humans.

In addition, we believe that nations should actively pursue the potential medical and scientific benefits of adult stem-cell research. Such research does not require the exploitation and destruction of nascent human life, nor does it open the door to the dehumanizing possibilities that will come with the cloning of human beings.

B. Scientific Background

Cloning refers to any process that results in the creation of an identical or nearly identical genetic copy of a DNA molecule, cell, or individual plant, animal, or human. Cloning occurs in nature. For example, identical twins are the product of a natural cloning event. There have also been recent scientific developments in cloning, such as the 1997 live birth of a sheep created using an experimental cloning method called "somatic cell nuclear transfer."

Somatic cell nuclear transfer is a cloning technique used by scientists to produce a nearly genetically identical copy of an existing animal. The product of somatic cell nuclear transfer is an embryo. In simple terms, this embryo is created by replacing the nucleus of a female egg cell with genetic material from a "somatic" cell (which is a cell from the body other than a sperm or egg cell). There is no involvement of sperm. The resulting embryo is a clone that is nearly genetically identical to the donor of the somatic cell. (Since the donor egg also contains non-nuclear DNA in subcellular structures called mitochondria, the clone's cells contain a very small amount of mitochondrial DNA from the donor egg cell. Thus, the clone is not exactly genetically identical to the somatic cell donor.)

Scientists conduct two types of experiments using somatic cell nuclear transfer. The first type of experiment, sometimes described as "reproductive" cloning, involves the creation of an embryo

through cloning, and its subsequent implantation into the uterus with the objective of creating a living animal. Animal reproductive cloning experiments have very high failure rates (around 95%) and often result in stillbirths, spontaneous abortions, or offspring with severe congenital abnormalities.

The other kind of experiment, sometimes described as "research," "experimental," or "therapeutic" cloning, involves the creation of a cloned embryo, which is then used to derive stem cells or (after the embryo is grown to a fetal stage) tissues for transplantation. For example, after growth to the blastocyst stage (5-9 days), the embryo is destroyed in order to derive embryonic stem cells that hold the potential for the development for cell replacement therapies. (Stem cells are discussed more fully in the attachment.) Hypothetically, therapies based on stem cells derived from cloned human embryos would not be subject to immune rejection if transplanted into the human donor of the somatic cell used for cloning. Other kinds of research on cloned embryos have also been attempted. Recently, researchers have reported that they have grown cloned animal embryos in an animal host uterus beyond the blastocyst stage and successfully extracted differentiated tissue for replacement therapy.

Whatever its purpose, cloning through human somatic cell nuclear transfer necessarily involves the creation of a living human embryo. For this reason, the technique raises profound ethical and moral questions and is highly controversial.

There are other cloning techniques that do not raise these moral and ethical concerns. For example, scientists routinely employ cellular or molecular cloning in their work to make genetically identical cells for research. Although these other cloning techniques could be used to develop therapies to treat disease, scientists do not use the term "therapeutic" to describe these techniques. Rather, as discussed above, the term "therapeutic" cloning is used by scientists to describe cloning by somatic cell nuclear transfer for therapeutic, as opposed to reproductive, purposes. This latter type of cloning is also described as "experimental" cloning, or "cloning for research purposes."

C. Ethical Implications of a Partial Ban Human Cloning

Human cloning for any purpose is an enormously troubling development in biotechnology. It is unethical in itself and dangerous as a precedent.

The possible creation of a human being through cloning raises many ethical concerns. It constitutes unethical experimentation on a child-to-be, subjecting him or her to enormous risks of bodily and developmental abnormalities. It threatens human individuality, deliberately saddling the clone with the genetic makeup of a person who has already lived. It risks making women's bodies a commodity, with women being paid to undergo risky drug treatment so they will produce the many eggs that are needed for cloning. It is also a giant step toward a society in which life is created for convenience, human beings are grown for spare body parts, and children are engineered to fit eugenic specification.

We cannot allow human life to be devalued in this way. Some have proposed to prohibit only so-called "reproductive" cloning, by prohibiting the transfer of a cloned embryo into a woman to begin a pregnancy in the hopes of creating a human baby. This approach is unsound.

First, a ban that prohibited only "reproductive" cloning, but left "therapeutic" or "experimental" cloning unaddressed, would essentially authorize the creation and destruction of human embryos

explicitly and solely for research and experimentation. It would turn nascent human life into a natural resource to be mined and exploited, eroding the sense of the worth and dignity of the individual. This prospect is repugnant to many people, including those who do not believe that the embryo is a "person."

Second, to ban "reproductive" cloning effectively, *all* human cloning must be banned. Under a partial ban that permitted the creation of cloned embryos for research, human embryos would be widely cloned in laboratories and assisted-reproduction facilities. Once cloned embryos are available, it would be virtually impossible to control what was done with them. Stockpiles of embryonic clones could be produced, bought and sold without anyone knowing it. Implantation of cloned embryos, an easy procedure, would take place out of sight, and even elaborate and intrusive regulations and policing could not detect or prevent the initiation of a clonal pregnancy. Once begun, an illicit clonal pregnancy would be virtually impossible to detect. And if detected, governments would be unlikely to compel the pregnancy to be aborted or severely penalize the pregnant woman for allowing the implantation or for failure to abort the pregnancy. A ban only on "reproductive"cloning would therefore be a false ban, creating the illusion that such cloning had been prohibited.

Third, a ban that permits embryonic clones to be created and forbids them to be implanted in utero legally *requires* the destruction of nascent human life and criminalizes efforts to preserve and protect it once created, a morally abhorrent prospect.

Fourth, there may be other routes to solving the transplant rejection problem, and there is to date no animal research to support the claim that cloned embryonic stem cells are therapeutically efficacious. A legal ban on "therapeutic" cloning would allow time for the investigation of promising and less problematic research alternatives such as "adult" stem-cell research. It would also allow time for policy makers and the public to develop more informed judgments about cloning, and for the establishment of regulatory structures to oversee applications of cloning technology that society deems acceptable.

Attachment Stem Cell Overview

Cloned human embryos produced through somatic cell nuclear transfer are potentially a source of human embryonic stem cells. They could also be used for other experimental purposes. This attachment provides some information about embryonic and adult stem cells.

Stem cells are cells that occur in animals at all stages of development, from the embryo to the adult. They have different properties and abilities, depending on the age of the organism and the location of the stem cells within the organism.

Embryonic stem cells are derived from a 5-9 day-old embryo and are able to generate nearly all the cell types of the body. To date, human embryonic stem cell research has been conducted using stem cells derived from embryos that were created in the course of in vitro fertilization and were no longer needed for that purpose.

Adult stem cells occur in small numbers throughout the bodies of adult mammals. Under normal conditions, they generate the cell types of the tissue in which they reside. Under certain experimental conditions in the laboratory, or even after transplant into a living animal, adult stem cells may be able to differentiate into the specialized cells of several different tissues.

All stem cells are unspecialized (undifferentiated) they do not have any specific structures that allow them to perform specific functions such as carry oxygen or fire an electrical signal. Unlike specialized cells such as muscle cells, blood cells, or nerve cells, which divide slowly or not at all, stem cells are also capable of dividing and renewing themselves for long periods (self-renewing). Importantly, stem cells retain the unique ability to give rise to specialized cells (differentiation), such as muscle, skin, or neurons.

Scientists believe that human stem cells embryonic and adult, directed to differentiated to specific cell types offer the possibility of a renewable source of replacement cells and tissues to treat a myriad of diseases.

What is Human Cloning?

In the public policy debate on human cloning, groups that support the cloning of human embryos for destructive research have raised questions as to what procedures are properly called human cloning. Even if one uses only definitions proposed by such groups, however, it is clear that only one bill pending in Congress qualifies as a ban on any kind of human cloning.

1. How is "cloning" defined by those who wish to allow cloning of embryos for research?

The National Academy of Sciences (NAS) defines "clone" and "cloning" as follows:
"Clone - 1) An exact genetic replica of a DNA molecule, cell, tissue, organ, or entire plant or animal. 2) An organism that has the same nuclear genome as another organism.
"Cloning - The production of a clone."
- NAS, *Scientific and Medical Aspects of Human Reproductive Cloning* (National Academy Press 2002), page E-4

Similarly, an original co-sponsor of the Specter/Harkin cloning bill (S. 1893), designed to allow human embryo cloning for research purposes, says:
"(T)he scientific term 'cloning' is defined as the creation of an exact genetic copy of an existing molecule, cell or organism."
- Senator Harry Reid (D-NV), letter to constituent, January 24, 2002

By these definitions, cloning has occurred as soon as a new organism is created that *genetically* copies an existing organism. To be a clone one need not be of identical age or identical stage of development compared to the original organism, but only a new organism of identical *genetic* makeup. *To ban cloning is to ban such creation of a new genetically identical organism.*

2. Is the new embryo created by somatic cell nuclear transfer an "organism"?

Since 1996, Congress has defined the early human embryo *outside* the womb as an "organism... that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells." Sec. 510 (b) of P.L. 107-116 (Labor/HHS/Education appropriations act for FY 2002).

This reflects a *consensus* even among government advisory boards which favor destructive embryo research. See the National Bioethics Advisory Commission (NBAC):
"Embryo - The developing *organism* from the time of fertilization until significant

differentiation has occurred, when the organism becomes known as a fetus." (Emphasis added)

- NBAC, *Cloning Human Beings* (Rockville, MD: June 1997), Vol. I, page A-2

Here is the National Institutes of Health definition:
"Embryo - In humans, the developing *organism* from the time of fertilization until the end of the eighth week of gestation..."

- *Stem Cells: Scientific Progress and Future Research Directions* (NIH, June 2001), page F-3

Congress specifically includes the cloned human organism under its definition of an embryo. While some outside groups speak of the embryo "from the time of fertilization," they also recognize that the new organism created by cloning qualifies as an embryo: "The Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg involves *the creation of an embryo*, with the apparent potential to be implanted in utero and developed to term."

- NBAC, *Cloning Human Beings*, op. cit., p. 3 (emphasis added)

The view of ethicists, stem cell researchers and the Clinton administration is also clear: In December 1998 testimony before the Senate Appropriations Subcommittee for Labor/HHS, witnesses from all sides of the embryonic stem cell debate (including an official of the Catholic bishops' conference and prominent embryonic stem cell researchers) agreed that an embryonic stem cell is *not* an embryo, because a human embryo is an organism of the human species and an embryonic stem cell is not. This key distinction was the basis for the HHS general counsel's 1999 legal opinion that the Clinton administration could legally fund research on stem cells from embryos, because stem cells are themselves not "organisms" and therefore not embryos. The Rabb memo cited Congress's definition of "embryo," and the December 1998 hearing, to support its case (Harriet S. Rabb, Memorandum to NIH Director Harold Varmus on "Federal Funding for Research Involving Human Pluripotent Stem Cells," Jan. 15, 1999, pp. 2-4).

3. Is the creation of a human embryo by cloning accurately called "*human cloning*"?

An affirmative answer to this question is demanded by the facts above: If the new organism created by cloning is a human organism (i.e., a human embryo), this is human cloning.

If there is any remaining doubt, we need only review the NAS's own definition of "embryo":

"**Embryo-** ...In medical terms, **embryo** usually refers to the *developing human* from fertilization (the zygote stage) until the end of the eighth week of gestation..." - NAS, op. cit., p. E-5.

The Brownback/Landrieu Human Cloning Prohibition Act, S. 1899, conforms to this accurate definition. It is the *only* pending bill that bans human cloning.

In fact there is no human cloning that does not proceed by creating an early human embryo. As cloning proponent Professor Lee Silver of Princeton University has written: "Scientists cannot make full-grown adult copies of any animal, let alone humans... Real biological cloning can only take place at the level of the cell..." - Lee Silver, *Remaking Eden* (Avon

Books 1997), p. 124.

4. Then what *is* banned by the Feinstein bill (S. 1758) and Harkin/Specter bill (S. 1893)?

These bills only ban *transfer* of an already-cloned human embryo into a uterus (or in the case of S. 1893, into a "substitute" for a uterus). Such transfer is a change of location – it does not create a new developing human, or make the embryo any more genetically identical to a previously existing individual than it was before, or change its status as an organism of the human species.

Embryo transfer is a well-known procedure, distinct from the nuclear transfer procedure used to do cloning. It is an essential part of reproduction by *in vitro* fertilization, and is exactly the same whether the embryo was created by fertilization or cloning. See NBAC's definition:
"Embryo transfer - the introduction of a preimplantation embryo into the uterus for growth and development." - NBAC, op. cit., p. A-2.

This is the procedure banned by the Feinstein and Specter/Harkin bills. They ban "embryo transfer" when a cloned embryo is involved.

These bills raise serious legal questions about the government's authority to regulate the kind of child a woman may bear in her womb. They also raise practical problems -- at the stage of development where embryo transfer might be attempted, there is no reliable way to distinguish a cloned embryo from a fertilized one. Most importantly, however, this procedure is simply not cloning. It does not create an organism, but changes the location of an organism already created.

5. The NAS report on cloning uses several vague and incompatible definitions of "reproductive cloning."

For policy reasons the NAS wants to describe as "cloning" only the transfer of a cloned embryo to a womb (for which it offers the term "reproductive cloning"). But it offers no justification for contradicting its own glossary's definition of cloning. In fact the NAS report at various points offers three different meanings for "reproductive cloning" – these contradict each other, and they all contradict the scientific definition in the report's own glossary.

The text speaks of "reproductive cloning" as the transfer of a cloned embryo to a uterus (NAS, page 6-6). This contradicts the NAS's own glossary. Elsewhere the text refers to "reproductive cloning" as creating a new "individual," and seems to equate "individual" with a born infant (NAS, page 2-8). At yet another point the text equates "reproductive cloning" with "cloning of *adult* animals" (NAS, page 1-1). Logically, under these latter definitions, a law that required killing all cloned humans at any time before birth (or at any time before reaching adulthood) could be seen as a "ban on reproductive cloning."

S. 1758 and S. 1893 ban the transfer of cloned human embryos into environments where they might survive to a later stage. But disrupting the further development of an organism is

very different from preventing its creation.

6. Efforts to create euphemisms for what is really human cloning

In the policy debate, euphemisms have been produced to avoid calling human cloning what it is:

a. Embryo cloning for research purposes is merely "nuclear transplantation" or "somatic cell nuclear transfer," as contrasted with "reproductive cloning."

In fact somatic cell nuclear transfer, or nuclear transplantation, are the terms for the cloning procedure itself. This procedure is what efforts at human cloning, whether for experimental or "reproductive" purposes, have *in common*. Even the NAS report says that "reproductive" cloning "involves a process called nuclear transplantation or somatic cell nuclear transfer" (NAS, p. 1-1).

b. "Nuclear transplantation to produce stem cells" (NAS, p. 2-5)

This makes even less sense. Nuclear transplantation into an egg does not produce stem cells – it produces an embryo, which can then either be placed in a uterus (embryo transfer) or destroyed for research. Some researchers want to use cloning to produce human embryos, then kill the embryos for their stem cells. Proponents of cloning are trying to obscure this fact. If a woman delivered a baby solely to obtain his or her kidney for transplantation into someone else, would we say she had given birth to a kidney?

c. "Therapeutic cloning"

This term is already being discarded by researchers, since the idea that anything "therapeutic" may come from this procedure is speculative at best. This is another euphemism for experimental cloning in which embryos are created to be destroyed. There is, of course, nothing "therapeutic" in the cloning process itself, or in the lethal harm that will be done to the cloned embryo.

d. "DNA-regenerative medicine"

This strange hybrid phrase was first used at a February 5, 2002 Senate hearing on cloning. It makes the least sense of all. To be sure, there is such a thing as the cloning of DNA strands, a standard biological practice that does not produce an embryo and is not banned by *any* pending bill. There is also an entire field known as regenerative medicine, which chiefly uses adult stem cells and other non-embryonic tissues. Neither of these has much relevance to human cloning.

In short: Relying on definitions provided by the proponents of human cloning for research purposes, we can see that the use of somatic cell nuclear transfer to make human embryos (for whatever purpose) is the only procedure under debate that is accurately called human cloning. Members of Congress who wish to ban other activities should call them by their scientifically accepted names – not hijack the clear and well-defined term "cloning" for other purposes.

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TESTIMONY OF

MICHELINE M. MATHEWS-ROTH, M.D.

TO

THE SUBCOMMITTEE ON CRIMINAL JUSTICE,
DRUG POLICY AND HUMAN RESOURCES
OF THE U.S. HOUSE OF REPRESENTATIVES

TESTIMONY ON THERAPEUTIC CLONING

Micheline M. Mathews-Roth, M.D.

I am Dr. Micheline Mathews-Roth. I am a physician doing clinical and basic research on a rare genetic disease called erythropoietic protoporphyria (EPP). I am an associate professor of medicine at the Harvard Medical School, and a Physician at the Brigham and Women's Hospital: both institutions are in Boston, Massachusetts. I want to make it clear that I am not speaking as a representative of either of these institutions, but as an individual physician and medical researcher. I regret that I cannot be here to present my testimony in person, but I am pleased that written testimony is also accepted.

It is important for legislators, and for that matter, the public, to understanding exactly what is involved in therapeutic cloning, or as it is also called, research cloning, and also somatic cell nuclear transfer. The purpose of therapeutic cloning is to obtain embryonic stem cells to be developed into cells or tissues or organs to be used to treat a serious disease, such as Alzheimer's disease or diabetes or Parkinson's disease, that the donor of the somatic cell has. The theoretical advantage of using cells and tissues derived from cloned embryonic stem cells is that there should be no immunological rejection of cells or tissues formed from them when these are transplanted into the nucleus donor to treat his or her disease.

However, there is an important scientific fact which must be remembered about embryonic stem cells, whether they are obtained from excess embryos produced for in-vitro fertilization (IVF) or whether they are obtained from cloned embryos: although embryonic stem cells are not embryos themselves, the only way to obtain them at the present time is to destroy - that is, to kill - a growing young human of 5 to 7 days of life, because at this age it has reached the blastocyst stage of its development, and remove its "inner cell mass", the group of embryonic stem cells that the growing young human contains. **To put it bluntly, in therapeutic cloning, a human being is made to start its life for the sole purpose of killing it when it gets to be 5 to 7 days old to obtain its stem cells.**

Let me now give you the scientific data to back up the statements I have just made. It is a fact of embryology that a member of the human species (or for that matter, of any other mammalian species) starts his or her existence as one cell, the zygote, the cell formed by the union of egg and sperm in the process of fertilization: this cell is the first cell of the new organism. This is true for babies whose development starts either when egg and sperm unite in the mother's body or when egg and sperm unite in a petri dish in the process of IVF. Two leading embryology text-books put it this way:

"Although life is a continuous process, fertilization is a critical landmark because, under ordinary circumstances, a new, genetically distinct human organism is thereby formed. This remains true even though the embryonic genome is not actually activated until 4-8 cells are present, at about 2-3 days [of the new human's life]." ("Human Embryology and Teratology" 2nd edition, R.. O'Rahilly & F. Muller, Wiley-Liss, New York, 1996)

"Zygote. This cell results from the union of an oocyte and a sperm. A zygote is the beginning of a new human being (i.e. an embryo). The expression "fertilized ovum" refers to a secondary oocyte (ovum) that is impregnated by a sperm: when fertilization is complete, the oocyte becomes a zygote." ("The Developing Human. Clinically Oriented Embryology" 6th edition, K. L. Moore & T. V. N. Persaud, W.B. Saunders, Philadelphia, 1998).

In therapeutic cloning, as well as in reproductive cloning, a new human being also starts its development as one cell - the cell which is formed by introducing a somatic cell nucleus (such as a skin cell's nucleus) into a donated egg cell after the egg cell's nucleus has been removed. This new cell is the cloned individual's zygote, the first cell of the new cloned human. The cell is then stimulated, which causes it to start to divide, and it divides and undergoes the same stages of development that embryos developing in their mother's body or in IVF do. In reproductive cloning, the developing young human would be implanted into the mother's uterus. In therapeutic cloning, the young human is allowed to develop and grow for about 5 to 7 days until it reaches the blastocyst stage and then it is killed so that its stem cells can be harvested. To help you understand the scientific data I have just described, I am including two illustrations with my testimony: 1) "Timetable of Human Prenatal Development", reproduced with permission from the Moore and Persaud textbook, and 2) a chart comparing normal reproduction, making stem cells, and reproductive and therapeutic cloning (designed by me). You can see what the blastocyst and its inner cell mass of stem cells looks like, and how it develops.

It should be obvious from the scientific data I have presented here, that producing embryonic stem cells from a blastocyst obtained from either therapeutic cloning or from excess IVF embryos results in the death of a very young human being, a "new genetically distinct human organism". What we have to ask ourselves is: **do we as a society really want to allow the bringing into existence of many young humans for the sole purpose of killing them to obtain their useful parts, even for the laudable purpose of alleviating the suffering of other members of our species?** This is what sanctioning therapeutic cloning really means. And, it seems to me that it is a form of blatant discrimination - against very young humans - a vicious form of ageism, saying that they are not worth protecting from deliberate killing..

We have to remember that there is no guarantee that we will be able to master the process of directing embryonic stem cells from either cloned embryos or IVF embryos into developing into the kinds of differentiated cells or tissues we need for therapy without causing harm to the recipient of these cells or tissues: we are years away from achieving the goal of safe and effective embryonic stem cell therapy. I would urge the members of both the Senate and the House of Representatives to ban research on human embryonic stem cells, to avoid the killing of the thousands of young humans, which will be necessary to obtain this goal. I also strongly urge our legislators to encourage work (by increasing funding to the National Institutes of Health) on animal embryonic stem cells, specifically on primate embryonic stem cells, as well as to encourage work on human and animal adult stem cells. This way, scientists could really determine what we can make embryonic stem cells do (or not do), without killing any very young humans in the process. If indeed studies in primates prove that there are some things which embryonic stem cells really can do that adult stem cells cannot do (in spite of the fact that adult stem cells are proving to be just about as versatile as embryonic stem cells in making the cells needed to treat significant diseases), then methods could be developed, again first developing them in primates, to either obtain a few stem cells from a blastocyst without killing it (analogous to early embryo biopsy presently done for obtaining cells for genetic testing of growing embryos), or to cause somatic cell de-differentiation into stem cells without forming an embryo and having to kill it. We must indeed continue the development of cures for human diseases - but we must do this by following the Hippocratic principle of first doing no harm to bona-fide members of our own species.

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By K.L. Moore and T.V.N. Persaud, W.B. Saunders & Co., New York, 6th ed., 1998.

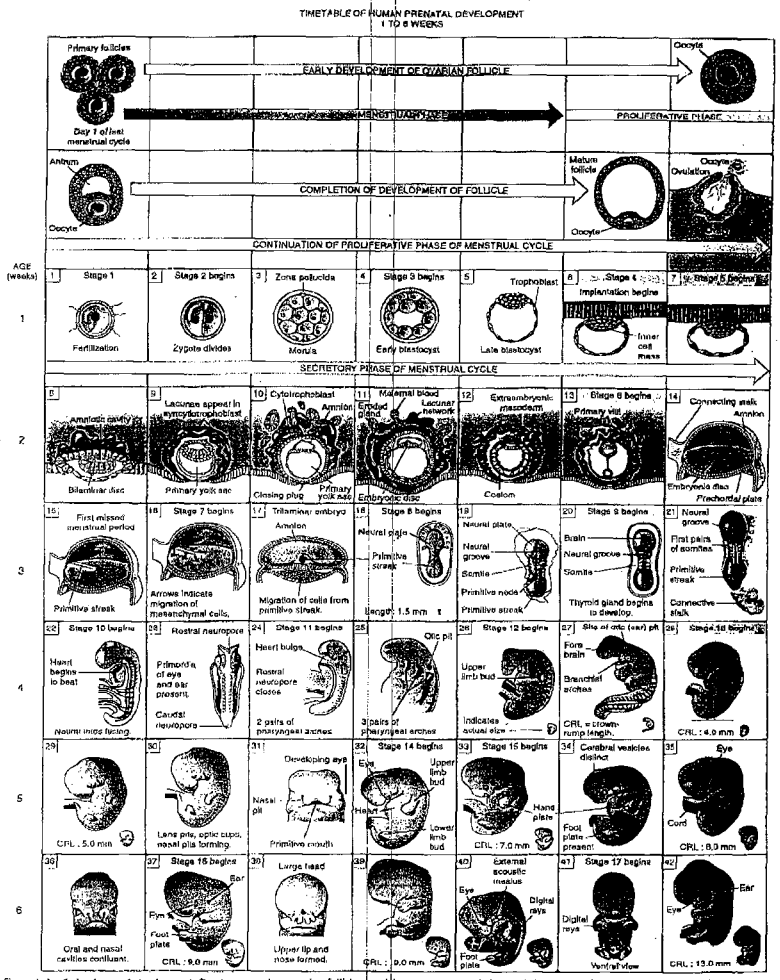


Figure 1–1 Early stages of development. Development of an ovarian follicle containing an oocyte, ovulation, and the phases of the menstrual cycle are illustrated. Human development begins at fertilization, about 14 days after the onset of the last menstruation. Cleavage of the zygote in the uterine tube, implantation of the blastocyst, and early development of the embryo are also shown. For a full discussion of embryonic development, see Chapter 5. Beginning students should make no attempt to memorize these tables or the stages (e.g., that Stage 3 begins on day 4 and Stage 5 on day 7).

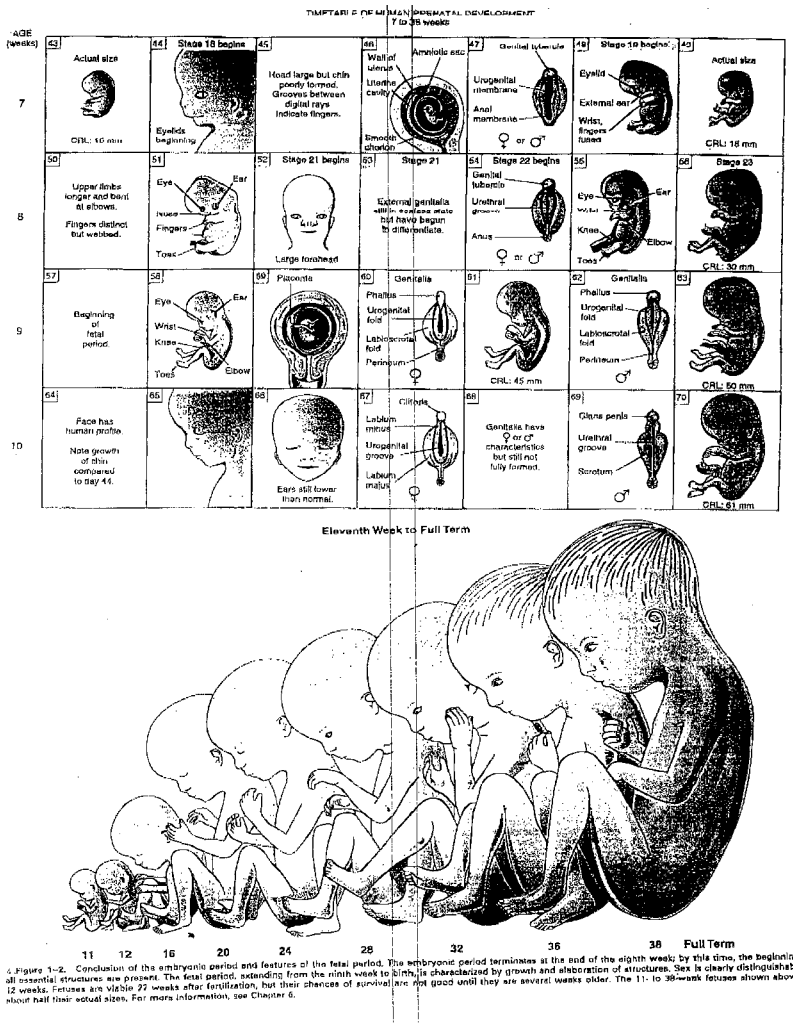
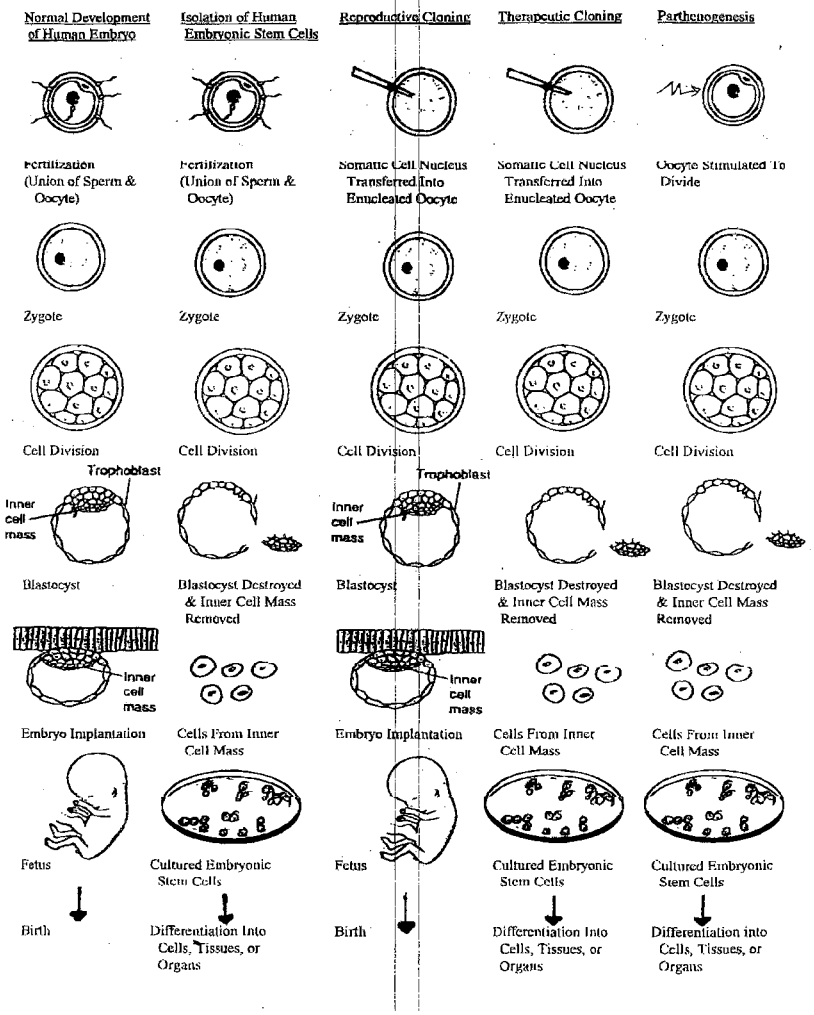


Figure 1–2. Conclusion of the embryonic period and features of the fetal period. The embryonic period terminates at the end of the eighth week; by this time, the beginnings of all essential structures are present. The fetal period, extending from the ninth week to birth, is characterized by growth and elaboration of structures. Sex is clearly distinguishable by 12 weeks. Fetuses are viable 22 weeks after fertilization, but their chances of survival are not good until they are several weeks older. The 11- to 38-week fetuses shown above are about half their actual sizes. For more information, see Chapter 6.

COMPARISON OF NORMAL REPRODUCTION, MAKING STEM CELLS AND CLONING



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Research Cloning? No.

By Charles Krauthammer

Friday, May 10, 2002; Page A37

Proponents of research cloning would love to turn the cloning debate into a Scopes monkey trial, a struggle between religion and science. It is not.

Many do oppose research cloning because of deeply held beliefs that destroying a human embryo at any stage violates the sanctity of human life. I respect that view, but I do not share it. I have no theology. I do not believe that personhood begins at conception. I support stem cell research. But I oppose research cloning.

It does no good to change the nomenclature. The Harry and Louise ad asks, "Is it cloning?" and answers, "No, it uses an unfertilized egg and a skin cell."

But fusing (the nucleus of) a "somatic" cell (such as skin) with an enucleated egg cell is precisely how you clone. That is how Dolly the sheep was created (with the cell taken not from the skin but from the udder). And that is how pig, goat, cow, mouse, cat and rabbit clones are created.

The scientists pushing this research go Harry and Louise one better. They want to substitute the beautifully sterile, high-tech sounding term SCNT -- "somatic cell nuclear transfer" -- for cloning. Indeed, the nucleus of a somatic cell is transferred into an egg cell to produce a clone. But to say that is not cloning is like saying: "No, that is not sex. It is just penile vaginal intromission." Describing the technique does not change the nature of the enterprise.

Cloning it is. And it is research cloning rather than reproductive cloning because the intention is not to produce a cloned child but to grow the embryo long enough to dismember it for its useful scientific parts.

And that is where the secularists have their objection. What makes research cloning different from stem cell research -- what pushes us over a moral frontier -- is that for the first time it sanctions the creation of a human embryo for the sole purpose of using it for its parts. Indeed, it will sanction the creation of an entire industry of embryo manufacture whose explicit purpose is not creation of children but dismemberment for research.

It is the ultimate commodification of the human embryo. And it is a bridge too far. Reducing the human embryo to nothing more than a manufactured thing sets a fearsome desensitizing precedent that jeopardizes all the other ethical barriers we have constructed around embryonic research.

This is not just my view. This was the view just months ago of those who, like me, supported federally funded stem cell research.

The clinching argument then was this: Look, we are simply trying to bring some good from embryos that would otherwise be discarded in IVF clinics. This is no slippery slope. We are going to put all kinds of safeguards around stem cell research. We are not about to start creating human embryos for such research. No way.

Thus when Sens. Tom Harkin and Arlen Specter were pushing legislation promoting stem cell research in 2000, they stipulated that "the stem cells used by scientists can only be derived from spare embryos that would otherwise be discarded by in vitro fertilization clinics." Lest there be any ambiguity, they added: "Under our legislation, strict federal guidelines would ensure [that] no human embryos will be created for research purposes."

Yet two years later, Harkin and Specter are two of the most enthusiastic Senate proponents of creating cloned human embryos for research purposes.

In testimony less than 10 months ago, Sen. Orrin Hatch found "extremely troubling" the just-reported work of the Jones Institute, "which is creating embryos in order to conduct stem cell research."

The stem cell legislation Hatch was then supporting -- with its "federal funding with strict research guidelines," he assured us -- was needed precisely to prevent such "extremely troubling" procedures.

That was then. Hatch has just come out for research cloning whose entire purpose is "creating embryos in order to conduct stem cell research."

Yesterday it was yes to stem cells with solemn assurances that there would be no embryo manufacture. Today we are told: Forget what we said about embryo manufacture; we now solemnly pledge that we will experiment on only the tiniest cloned embryo, and never grow it -- and use it -- beyond that early "blastocyst" stage.

What confidence can one possibly have in these new assurances? This is not a slide down the slippery slope. This is downhill skiing. And the way to stop it is to draw the line right now at the embryo manufacture that is cloning -- not just because that line is right, but because the very notion of drawing lines is at stake.

Charles Krauthammer is a member of the President's Council on Bioethics. These views are his own.

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A secular argument against research cloning.

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BODY:
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The Problem

You were once a single cell. Every one of the 100 trillion cells in your body today is a direct descendent of that zygote, the primordial cell formed by the union of mother's egg and father's sperm. Each one is genetically identical (allowing for copying errors and environmental damage along the way) to that cell. Therefore, if we scraped a cell from, say, the inner lining of your cheek, its DNA would be the same DNA that, years ago in the original zygote, contained the entire plan for creating you and every part of you.

Here is the mystery: Why can the zygote, as it multiplies, produce every different kind of cell in the body--kidney, liver, brain, skin--while the skin cell is destined, however many times it multiplies, to remain skin forever? As the embryo matures, cells become specialized and lose their flexibility and plasticity. Once an adult cell has specialized- differentiated, in scientific lingo--it is stuck forever in that specialty. Skin is skin; kidney is kidney. Understanding that mystery holds the keys to the kingdom. The Holy Grail of modern biology is regenerative medicine. If we can figure out how to make a specialized adult cell dedifferentiate--unspecialize, i.e., revert way back to the embryonic stage, perhaps even to the original zygotic stage--and then grow it like an embryo under controlled circumstances, we could reproduce for you every kind of tissue or organ you might need. We could create a storehouse of repair parts for your body. And, if we let that dedifferentiated cell develop completely in a woman's uterus, we will have created a copy of you, your **clone.**

That is the promise and the menace of cloning. It has already been done in sheep, mice, goats, pigs, cows, and now cats and rabbits (though cloning rabbits seems an exercise in biological redundancy). There is no reason in principle why it cannot be done in humans. The question is: Should it be done?

Notice that the cloning question is really two questions: (1) May we grow that dedifferentiated cell all the way into a cloned baby, a copy of you? That is called reproductive cloning. And (2) may we grow that dedifferentiated cell just into the embryonic stage and then mine it for parts, such as stem cells? That is called research cloning.

Reproductive cloning is universally abhorred. In July 2001 the House of Representatives, a fairly good representative of the American people, took up the issue and not a single member defended reproductive cloning. Research cloning, however, is the hard one. Some members were prepared to permit the cloning of the human embryo in order to study and use its component parts, with the proviso that the embryo be destroyed before it grows into a fetus or child. They were a minority, however. Their amendment banning baby-making but permitting research cloning was defeated by 76 votes. On July 31, 2001, a bill outlawing all cloning passed the House decisively.

Within weeks, perhaps days, the Senate will vote on essentially the same alternatives. On this vote will hinge the course of the genetic revolution at whose threshold we now stand.

The Promise

This is how research cloning works. You take a donor egg from a woman, remove its nucleus, and inject the nucleus of, say, a skin cell from another person. It has been shown in animals that by the right manipulation you can trick the egg and the injected nucleus into dedifferentiating--that means giving up all the specialization of the skin cell and returning to its original state as a primordial cell that could become anything in the body.

In other words, this cell becomes totipotent. It becomes the equivalent of the fertilized egg in normal procreation, except that instead of having chromosomes from two people, it has chromosomes from one. This cell then behaves precisely like an embryo. It divides. It develops. At four to seven days, it forms a "blastocyst" consisting of about 100 to 200 cells.

The main objective of cloning researchers would be to disassemble this blastocyst: pull the stem cells out, grow them in the laboratory, and then try to tease them into becoming specific kinds of cells, say, kidney or heart or brain and so on.

There would be two purposes for doing this: study or cure. You could take a cell from a person with a baffling disease, like Lou Gehrig's, **clone** it into a blastocyst, pull the stem cells out, and then study them in order to try to understand the biology of the illness. Or you could begin with a cell from a person with Parkinson's or a spinal cord injury, **clone** it, and tease out the stem cells to develop tissue that you would reinject into the original donor to, in theory, cure the Parkinson's or spinal cord injury. The advantage of using a cloned cell rather than an ordinary stem cell is that, presumably, there would be no tissue rejection. It's your own DNA. The body would recognize it. You'd have a perfect match.

(Research cloning is sometimes called therapeutic cloning, but that is a misleading term. First, because therapy by reinjection is only one of the many uses to which this cloning can be put. Moreover, it is not therapeutic for the **clone**--indeed, the **clone** is invariably destroyed in the process--though it may be therapeutic for others. If you donate a kidney to your brother, it would be odd to call your operation a therapeutic nephrectomy. It is not. It's a sacrificial nephrectomy.)

The conquest of rejection is one of the principal rationales for research cloning. But there is reason to doubt this claim on scientific grounds. There is some empirical evidence in mice that cloned tissue may be rejected anyway (possibly because a **clone** contains a small amount of foreign- mitochondrial--DNA derived from the egg into which it was originally injected). Moreover, enormous advances are being made elsewhere in combating tissue rejection. The science of immune rejection is much more mature than the science of cloning. By the time we figure out how to do safe and reliable research cloning, the rejection problem may well be solved. And finally, there are less problematic alternatives--such as adult stem cells--that offer a promising alternative to cloning because they present no problem of tissue

rejection and raise none of cloning's moral conundrums.

These scientific considerations raise serious questions about the efficacy of, and thus the need for, research cloning. But there is a stronger case to be made. Even if the scientific objections are swept aside, even if research cloning is as doable and promising as its advocates contend, there are other reasons to pause.

The most obvious is this: Research cloning is an open door to reproductive cloning. Banning the production of cloned babies while permitting the production of cloned embryos makes no sense. If you have factories all around the country producing embryos for research and commerce, it is inevitable that someone will implant one in a woman (or perhaps in some artificial medium in the farther future) and produce a human **clone.** What then? A law banning reproductive cloning but permitting research cloning would then make it a crime not to destroy that fetus--an obvious moral absurdity.

This is an irrefutable point and the reason that many in Congress will vote for the total ban on cloning. Philosophically, however, it is a showstopper. It lets us off too early and too easy. It keeps us from facing the deeper question: Is there anything about research cloning that in and of itself makes it morally problematic?

Objection I: Intrinsic Worth

For some people, life begins at conception. And not just life--if life is understood to mean a biologically functioning organism, even a single cell is obviously alive--but personhood. If the first zygotic cell is owed all the legal and moral respect due a person, then there is nothing to talk about. Ensoulment starts with Day One and Cell One, and the idea of taking that cell or its successor cells apart to serve someone else's needs is abhorrent.

This is an argument of great moral force but little intellectual interest. Not because it may not be right. But because it is unprovable. It rests on metaphysics. Either you believe it or you don't. The discussion ends there.

I happen not to share this view. I do not believe personhood begins at conception. I do not believe a single cell has the moral or legal standing of a child. This is not to say that I do not stand in awe of the developing embryo, a creation of majestic beauty and mystery. But I stand in equal awe of the Grand Canyon, the spider's web, and quantum mechanics. Awe commands wonder, humility, appreciation. It does not command inviolability. I am quite prepared to shatter an atom, take down a spider's web, or dam a canyon for electricity. (Though we'd have to be very short on electricity before I'd dam the Grand.)

I do not believe the embryo is entitled to inviolability. But is it entitled to nothing? There is a great distance between inviolability, on the one hand, and mere "thingness," on the other. Many advocates of research cloning see nothing but thingness. That view justifies the most ruthless exploitation of the embryo. That view is dangerous.

Why? Three possible reasons. First, the Brave New World Factor: Research cloning gives man too much power for evil. Second, the Slippery Slope: The habit of embryonic violation is in and of itself dangerous. Violate the blastocyst today and every day, and the practice will inure you to violating the fetus or even the infant tomorrow. Third, Manufacture: The very act of creating embryos for the sole purpose of exploiting and then destroying them will ultimately predispose us to a ruthless utilitarianism about human life itself.

Objection II: The Brave New World Factor

The physicists at Los Alamos did not hesitate to penetrate, manipulate, and split uranium atoms on the grounds that uranium atoms possess intrinsic worth that entitled them to inviolability. Yet after the war, many fought to curtail atomic power. They feared the consequences of delivering such unfathomable power--and potential evil--into the hands of fallible human beings. Analogously, one could believe that the cloned blastocyst has little more intrinsic worth than the uranium atom and still be deeply troubled by the manipulation of the blastocyst because of the fearsome power it confers upon humankind.

The issue is leverage. Our knowledge of how to manipulate human genetics (or atomic nuclei) is still primitive. We could never construct ex nihilo a human embryo. It is an unfolding organism of unimaginable complexity that took nature three billion years to produce. It might take us less time to build it from scratch, but not much less. By that time, we as a species might have acquired enough wisdom to use it wisely. Instead, the human race in its infancy has stumbled upon a genie infinitely too complicated to create or even fully understand, but understandable enough to command and perhaps even control. And given our demonstrated unwisdom with our other great discovery--atomic power: As we speak, the very worst of humanity is on the threshold of acquiring the most powerful weapons in history--this is a fear and a consideration to be taken very seriously.

For example. Female human eggs seriously limit the mass production of cloned embryos. Extracting eggs from wom en is difficult, expensive, and potentially dangerous. The search is on, therefore, for a good alternative. Scientists have begun injecting human nuclei into the egg cells of animals. In 1996 Massachusetts scientists injected a human nucleus with a cow egg. Chinese scientists have fused a human fibroblast with a rabbit egg and have grown the resulting embryo to the blastocyst stage. We have no idea what grotesque results might come from such interspecies clonal experiments.

In October 2000 the first primate containing genes from another species was born (a monkey with a jellyfish gene). In 1995 researchers in Texas produced headless mice. In 1997 researchers in Britain produced headless tadpoles. In theory, headlessness might be useful for organ transplantation. One can envision, in a world in which embryos are routinely manufactured, the production of headless **clones**--subhuman creatures with usable human organs but no head, no brain, no consciousness to identify them with the human family.

The heart of the problem is this: Nature, through endless evolution, has produced cells with totipotent power. We are about to harness that power for crude human purposes. That should give us pause. Just around the corner lies the logical by-product of such power: human-animal hybrids, partly developed human bodies for use as parts, and other horrors imagined--Huxley's Deltas and Epsilons--and as yet un imagined. This is the Brave New World Factor. Its grounds for objecting to this research are not about the beginnings of life, but about the ends; not the origin of these cells, but their destiny; not where we took these magnificent cells from, but where they are taking us.

Objection III: The Slippery Slope

The other prudential argument is that once you start tearing apart blastocysts, you get used to tearing apart blastocysts. And whereas now you'd only be doing that at the seven-day stage, when most people would look at this tiny clump of cells on the head of a pin and say it is not inviolable, it is inevitable that some scientist will soon say: Give me just a few more weeks to work with it and I could do wonders.

That will require quite a technological leap because the blastocyst will not develop as a human organism unless implanted in the uterus. That means that to go beyond that seven-day stage you'd have to implant this human embryo either in an animal uterus or in some fully artificial womb.

Both possibilities may be remote, but they are real. And then we'll have a scientist saying: Give me just a few more months with this embryo, and I'll have actual kidney cells, brain cells, pancreatic cells that I can transplant back into the donor of the **clone** and cure him. Scientists at Advanced Cell Technology in Massachusetts have already gone past that stage in animals. They have taken cloned cow embryos past the blastocyst stage, taken tissue from the more developed cow fetus, and reimplanted it back into the donor animal.

The scientists' plea to do the same in humans will be hard to ignore. Why grow the **clone** just to the blastocyst stage, destroy it, pull out the inner cell mass, grow stem cells out of that, propagate them in the laboratory, and then try chemically or otherwise to tweak them into becoming kidney cells or brain cells or islet cells? This is Rube Goldberg. Why not just allow that beautiful embryonic machine, created by nature and far more sophisticated than our crude techniques, to develop unmolested? Why not let the blastocyst grow into a fetus that possesses the kinds of differentiated tissue that we could then use for curing the donor?

Scientifically, this would make sense. Morally, we will have crossed the line between tearing apart a mere clump of cells and tearing apart a recognizable human fetus. And at that point, it would be an even smaller step to begin carving up seven- and eight-month-old fetuses with more perfectly formed organs to alleviate even more pain and suffering among the living. We will, slowly and by increments, have gone from stem cells to embryo farms to factories with fetuses in various stages of development and humanness, hanging (metaphorically) on meat hooks waiting to be cut open to be used by the already born.

We would all be revolted if a living infant or developed fetus were carved up for parts. Should we build a fence around that possibility by prohibiting any research on even the very earliest embryonic clump of cells? Is the only way to avoid the slide never to mount the slippery slope at all? On this question, I am personally agnostic. If I were utterly convinced that we would never cross the seven-day line, then I would have no objection on these grounds to such research on the inner cell mass of a blastocyst. The question is: Can we be sure? This is not a question of principle; it is a question of prudence. It is almost a question of psychological probability. No one yet knows the answer.

Objection IV: Manufacture

Note that while, up to now, I have been considering arguments against research cloning, they are all equally applicable to embryonic research done on a normal--i.e., noncloned--embryo. If the question is tearing up the blastocyst, there is no intrinsic moral difference between a two-parented embryo derived from a sperm and an egg and a single-parented embryo derived from a cloned cell. Thus the various arguments against this research--the intrinsic worth of the embryo, the prudential consideration that we might create monsters, or the prudential consideration that we might become monsters in exploiting post-embryonic forms of human life (fetuses or even children)--are identical to the arguments for and against stem-cell research.

These arguments are serious--serious enough to banish the insouciance of the scientists who consider anyone questioning their work to be a Luddite--yet, in my view, insufficient to justify a legal ban on stem-cell research (as with stem cells from discarded embryos in fertility clinics). I happen not to believe that either personhood or ensoulment occurs at conception. I think we need to be apprehensive about what evil might arise from the power of stem-cell research, but that apprehension alone, while justifying vigilance and regulation, does not justify a ban on the practice. And I believe that given the good that might flow from stem-cell research, we should first test the power of law and custom to enforce the seven-day blastocyst line for embryonic exploitation before assuming that such a line could never hold.

This is why I support stem-cell research (using leftover embryos from fertility clinics) and might support research cloning were it not for one other aspect that is unique to it. In research cloning, the embryo is created with the explicit intention of its eventual destruction. That is a given because not to destroy the embryo would be to produce a cloned child. If you are not permitted to grow the embryo into a child, you are obliged at some point to destroy it.

Deliberately creating embryos for eventual and certain destruction means the launching of an entire industry of embryo manufacture. It means the routinization, the commercialization, the commodification of the human embryo. The bill that would legalize research cloning essentially sanctions, licenses, and protects the establishment of a most ghoulish enterprise: the creation of nascent human life for the sole purpose of its exploitation and destruction.

How is this morally different from simply using discarded embryos from in vitro fertilization (IVF) clinics? Some have suggested that it is not, that to oppose research cloning is to oppose IVF and any stem-cell research that comes out of IVF. The claim is made that because in IVF there is a high probability of destruction of the embryo, it is morally equivalent to research cloning. But this is plainly not so. In research cloning there is not a high probability of destruction; there is 100 percent probability. Because every cloned embryo must be destroyed, it is nothing more than a means to someone else's end.

In IVF, the probability of destruction may be high, but it need not necessarily be. You could have a clinic that produces only a small number of embryos, and we know of many cases of multiple births resulting from multiple embryo implantation. In principle, one could have IVF using only a single embryo and thus involving no deliberate embryo destruction at all. In principle, that is impossible in research cloning.

Furthermore, a cloned embryo is created to be destroyed and used by others. An IVF embryo is created to develop into a child. One cannot disregard intent in determining morality. Embryos are created in IVF to serve reproduction. Embryos are created in research cloning to serve, well, research. If certain IVF embryos were designated as "helper embryos" that would simply aid an anointed embryo in turning into a child, then we would have an analogy to cloning. But, in fact, we don't know which embryo is anointed in IVF. They are all created to have a chance of survival. And they are all equally considered an end.

Critics counter that this ends-and-means argument is really obfuscation, that both procedures make an instrument of the embryo. In cloning, the creation and destruction of the embryo is a means to understanding or curing disease. In IVF, the creation of the embryo is a means of satisfying a couple's need for a child. They are both just means to ends.

But it makes no sense to call an embryo a means to the creation of a child. The creation of a child is the destiny of an embryo. To speak of an embryo as a means to creating a child empties the word "means" of content. The embryo in IVF is a stage in the development of a child; it is no more a means than a teenager is a means to the adult he or she later becomes. In contrast, an embryo in research cloning is pure means. Laboratory pure.

And that is where we must draw the line. During the great debate on stem-cell research, a rather broad consensus was reached (among those not committed to "intrinsic worth" rendering all embryos inviolable) that stem-cell research could be morally justified because the embryos destroyed for their possibly curative stem cells were derived from fertility clinics and thus were going to be discarded anyway. It was understood that human embryos should not be created solely for the purpose of being dismembered and then destroyed for the benefit of others. Indeed, when Senator Bill Frist made his impassioned presentation on the floor of the Senate supporting stem-cell research, he included among his conditions a total ban on creating human embryos just to be stem-cell farms.

Where cloning for research takes us decisively beyond stem-cell research is in sanctioning the manufacture of the human embryo. You can try to regulate embryonic research to prohibit the creation of Brave New World monsters; you can build fences on the slippery slope, regulating how many days you may grow an embryo for research; but once you countenance the very creation of human embryos for no other purpose than for their parts, you have crossed a moral frontier.

Research cloning is the ultimate in conferring thingness up on the human embryo. It is the ultimate in desensitization. And as such, it threatens whatever other fences and safeguards we might erect around embryonic research. The problem, one could almost say, is not what cloning does to the embryo, but what it does to us. Except that, once cloning has changed us, it will inevitably enable further assaults on human dignity. Creating a human embryo just so it can be used and then destroyed undermines the very foundation of the moral prudence that informs the entire enterprise of genetic research: the idea that, while a human embryo may not be a person, it is not nothing. Because if it is nothing, then everything is permitted. And if everything is permit ted, then there are no fences, no safeguards, no bottom.

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'Why Not?' Isn't Good Enough

Scientists' case for cloning is unsatisfactory.

BY DANIEL HENNINGER
Friday, April 19, 2002 12:01 a.m.

The U.S. Senate is about to take up and debate the issue of human cloning--whether to ban it outright, or to allow the technology for therapeutic purposes alone. On one familiar level, this is frightening. Normally the Senate confines its mental energies to such matters as highways for West Virginia and tossing logs onto bonfires around fallen executives. Perhaps sensing their lack of standing as philosophes, some senators at the dawn of this debate have grafted themselves to a letter signed by 40 Nobel laureates, who unified themselves to denounce President Bush's proposed ban on human embryo cloning experimentation.

The senior senator from Massachusetts (Ted Kennedy, for readers under 30), announced the other day that "Congress was right to place medicine over ideology in the past, and we should do the same again." Arlen Specter sees the banners taking America back to the "Dark Age."

The 40 Nobelists, including a few economists, expressed their fears this way: "By declaring scientifically valuable biomedical research illegal, Senator Brownback's legislation, if it becomes law, would have a chilling effect on all scientific research in the United States" and would "send a strong signal to the next generation of researchers that unfettered and responsible scientific investigation is not welcome in the United States." Who said scientists no longer believe in absolutes?

William F. Buckley Jr. once famously wrote that he'd rather be governed by the first 100 names in the Boston phone book than by the Harvard faculty. All things considered, I'd rather have the cloning issue decided, just now, by the first 100 names in the U.S. Senate than all the Nobel laureates in America.

This is saying something, insofar as I'm not sure what Teddy Kennedy is talking about, though presumably if the enemy that day was ideology, his side won. More to the point, I might prefer putting more faith in science than the World's Greatest Deliberative Body on this decision if we were living in 1952 and not 2002. A lot has changed since then and on balance for the better. These 40 Nobelists have contributed mightily to a better life for all. Science triumphed through those years, however, by staying loyal to the rigor it imposes on falsity and truth. But now, when science has driven itself, and us, to a point where we must decide whether its work with human biology will be moral, or not moral, we not only lack equal intellectual rigor for the task, we indeed may have no rigor at all anymore.

Let's begin with the final paragraph of the Nobelists' letter, wherein they swear off cloning a

person: "We, the undersigned, urge that legislation to impose criminal and civil sanctions against attempts to create a cloned human being be enacted." There, in all of 22 words, is the concession they offer to a world of concerns about the slippery slope of this technology: Trust us; we, the undersigned, won't do it. But I don't trust them.

The subject of this column is not therapeutic cloning itself. Nor do we wish here to take up the problems the biotech industry has had finding new-product flow that will redeem the unfulfilled promises it made to investors. Biotechnology's prospect of alleviating disease such as Parkinson's and Alzheimer's is too great to simply say no, never. My argument is with the way we think now, with what has come to be known as the postmodernist intellectual tradition, a real force in the culture of ideas in academia, media and politics. For some 30 years its way of thinking about the world has taken a great many victory laps in the arenas of history and politics. But I wouldn't let these people within 100 miles of deciding an important debate about genetics.

Lacking a quarter-million words of space to explain, we'll attempt a summary. For most of the 20th century, until the 1960s, modernists challenged tradition and authority by asking "Why?" The postmodernists, however, believe this form of challenge to be a quaint waste of time. They face any hard issue and reply: "Why not?" Thus, your objection to human embryo replication or assisted suicide or partial-birth abortion, however forcefully argued, has no particular ethical or moral standing. It's "interesting," at most.

They'll say, "No one's talking about cloning humans." But that's disingenuous. Postmodernists as a matter of, well, ideology, don't recognize the validity of stand-still limits like that. And I think a lot of them will issue this guarantee as a means to win the policy debate now, confident they'll be able to wear down inhibitions to the next steps over time, if not here, elsewhere. In an elegant reduction, the DNA Nobelist James Watson (an anti-ban letter-signer) once said: "What the public wants is not to be sick, and if we help them not to be sick, they'll be on our side."

Last week President Bush gave a speech supporting a ban in which he worried about a time when "human beings are grown for spare body parts and children are engineered to custom specifications, and that's not acceptable." In more than a few circles today this is read as almost up-from-the-swamp fundamentalism. One major editorial summed up the postmodernist's dismissal in four words: "The President's Narrow Morality."

This is self-assured moral trumping, and any veteran of the policy wars is by now used to how this the game is played. It's been fun, sometimes. But on this one subject--what it will mean to manipulate the basis for human life or to "discard" human embryos--winning by characterizing the opposition as narrow moral bumpkins just isn't going to be good enough. Simply asserting that your opponents don't care about mitigating disease with technology isn't good enough. The cloning issue will remain a political and intellectual mess unless its proponents engage the other side and just this once make a more philosophically rigorous case for opening this door and stepping through.

Absent that, and it really is absent from public view so far (more mental effort went into justifying the Endangered Species Act), we are better off letting Congress decide what will be cloned. Whatever its manifest faults, Congress is the way we discover and define our common interests. Its members are at least answerable to their constituents. Too much of the scientific and intellectual pantheon has come to believe its politics is answerable only to whatever happens to be in its own head, that day. I know for a fact which I prefer.

Mr. Henninger is deputy editor of The Wall Street Journal's editorial page. His column appears Fridays in the Journal and on OpinionJournal.com.

CONGRESSIONAL TESTIMONY

Briefing for Senate Staff on Cloning
April 10, 2002

Statement by James Kelly
Activist for Spinal Cord Injury Treatment
Fort Worth, Texas

Five years ago I was climbing Mount Shavano in Colorado with my wife. A month later I fell asleep on a warm afternoon while driving across Montana. I've been paralyzed ever since.

Every year, twenty-six million Americans are diagnosed with diseases or suffer injuries that stem cells might help cure. Ten thousand of these Americans will have my condition, spinal cord injury (SCI). I never thought I'd end up like this when I was healthy and climbing mountains, yet here I am. I'm saying this because I want you to understand that this issue's outcome will eventually affect your future as much as mine. To drive this point home, my chances of having SCI were one in thirty thousand. Your chance of waking up someday to find that your life might depend on the course this issue takes is one in eleven...*every year*. For all our sakes, we need to learn about cloning and make the right decision.

Since everyone has an agenda, let me be upfront about mine. I don't belong to a political party. I don't belong to an organized religion. And I don't have views on abortion. My sole interest in the cloning debate is that its outcome not needlessly slow the advance of cures. I say *cures*, not just *a cure for spinal cord injury*. Knowing as I do one form of Hell, my skin crawls at the thought of pulling others into a similar pit just so I can get out of mine. Because of my *pro-cures* priority I'm 100% in favor of Senator Brownback's cloning legislation. Here are my reasons:

A. Cloning is too expensive to be part of a medically available therapy.

Dr. Wise Young of Rutgers is a well known SCI researcher who supports all *scientifically* valid neuroscience, including cloning. Yet he says: "*In my opinion, it will probably not be politically or economically feasible to clone stem cells for every individual.*" In simple terms, even if cloning's genetic mutation and reliability problems can be overcome, it will still be too expensive to use on an individual patient basis. So where's the *therapy* in *therapeutic* cloning? Either we need stem cells with our own DNA or not. If we do, cloning is too expensive, so why waste resources on it when adult stem cells already fit our DNA needs? If we don't, what is cloning good for? As Dr. Young says: "If adult stem cells prove to be as potent and as efficacious as embryonic stem cells, they will be a cheaper and safer source of stem cells for therapy."

B. Cloned embryonic stem cells are not needed to cure spinal cord injury.

The primary obstacle to reversing paralysis due to SCI has nothing to do with replacing specialized cells, which adult, fetal, and embryonic stem cells have shown they can do. Most scientists today consider reconnecting broken nerve connections at the injury site as the main challenge. Depending on the level of injury some neurons may need to be replaced, and axons

below the injury may need to be remyelinated -- but unless we overcome the inhibitory "glial scar" at the injury site, all the stem cells in the world won't help. Several avenues are being developed today to address this pivotal issue, none of which involve cloning or embryonic stem cells. No peer-reviewed study has shown a use for cloning in *any* SCI application, including neuron replacement and remyelination; and no one claims it has anything to offer regarding the bridging of the injury site.

C. Cheaper, safer, and further developed avenues already exist to address the conditions that cloned embryonic stem cells someday *may* address.

The NIH, the Christopher Reeve Paralysis Foundation, and most scientists advocate a "leave no stone unturned" policy for curing SCI and other conditions. And if we were in the stone age of medical research this might be a logical course. But we're not. We know why the spinal cord's broken connections won't reconnect, and we have several promising ways to address this problem. At least four genetically matched adult cell types have been shown in animals to remyelinate the brain and spinal cord (with one of these already in MS clinical trials at Yale). Three of these cell types (neural, bone marrow, and skin stem cells) can replace damaged central nervous system neurons. *None* of these adult cells is beset by the safety and performance problems inherent in cloned embryonic stem cells - genetic mutations, tumor formation, and (according to a recent study in trying to treat immune deficiency in mice using cloned embryonic stem cells) even immune response rejection. Yet advocates of "therapeutic cloning" say we should embark on years of expensive, highly speculative research that may have no therapeutic value -- in order to "leave no stone unturned."

Adult stem cells (that already have the patient's DNA) have also been shown to replace heart cells, blood cells, liver cells and pancreatic tissue. They've been successfully used to treat leukemia, traumatic brain injury, heart disease, stroke, Parkinson's disease, and immune deficiency syndrome. More research is needed to expand and perfect their use, and to develop other avenues with more immediate clinical potentials than cloning. But *expanding* and *perfecting* are a far cry from embarking on new, expensive, highly speculative research with the *potential* to someday *duplicate* what's already being done more cheaply, more safely, and more efficiently by adult stem cells and other avenues.

D. The medical availability of these avenues could be slowed or blocked if valuable resources are wasted on cloning.

Resources spent on one line of research cannot be spent on others. And contrary to the fantasies of those who say we can support *all* research, including adult cells, embryonic stem cells, and now *cloned* embryonic stem cells, America doesn't have a bottomless pit of money begging to be spent on science for the sake of science. If a major effort is made to advance cloning, other avenues will inevitably suffer. More promising research in SCI has been abandoned in the past because of willful development of an inferior avenue. As a result, it may be that half of those paralyzed by SCI today are needlessly so. In cloning we have the sickening possibility of repeating this grave mistake on a colossal scale.

E. I don't like being used.

I think it's highly immoral for researchers to encourage the sick, crippled, and dying to cut their own throats by supporting cloning, a research avenue whose extremely speculative potential lies somewhere in a distant and hazy future, to the detriment of proven avenues that offer more than futile hope.

AMERICANS TO BAN CLONING

CONGRESSIONAL TESTIMONY

Briefing for Senate Staff on Cloning
April 10, 2002

Statement by Joni Eareckson Tada
Director Emeritus,
Christian Council on Persons with Disabilities
Research Cloning from a Disability Perspective

My heart goes out to newly injured people who have suffered spinal cord damage. No one understands better their desire for a cure than me. Thirty five years ago when I broke my neck and became a quadriplegic, I was desperate for anything - "please, doctors, researchers, do anything" - that would repair my spinal cord and give me back use of my legs and hands. Acute disability does that: it screams for reprieve, demanding that a cure be gained at *any* cost.

Thirty five years later, my perspective has changed. Time makes one look at the broader implications - not how embryonic stem cell research would impact the individual, but society as a whole. Yes, my husband and I still encourage spinal cord injury research and cure, but not to the degree that the *benefits* of a possible cure outweigh the *serious and permanent consequences.*

For me, and tens of thousands of people with disabilities, the security of human dignity and respect for human life is paramount to securing a cure. The rights of people with disabilities - especially those who are disadvantaged and weak - are safeguarded in a society that honors life and treats humanity with respect. However, the weak and infirm are exposed in a society that thinks nothing of creating a class of human lives for the explicit purpose of exploitation. This is the Pandora=s Box that research cloning would open. Ironically, the disabled would be the first to be threatened in a world where eugenics and the bio-tech industry set the moral agenda. It=s an impersonal world that uses the guise of "cure" while devaluing the very human life it purports to help.

Historically, people with disabilities have *never* fared well in utilitarian societies, where right versus wrong doesn=t count but only whether or not "it will work." One prominent pro-cloning advocate, in his testimony before the Senate, said that "the duty of government is to do the greatest good for the greatest number" - yet it was this ideology which paved the way for the extermination of hundreds of thousands of people with disabilities in World War II. Rather, the duty of government is to safeguard the rights of the weak and marginalized; in so doing, the rights of all are upheld. This strikes at the heart of the cloning debate. If we criminalize the care and nurturing of an entire class of human beings - as would be the case if experimental cloning were legalized - then the character of our helping society would erode.

As a person with a disability, that=s not the kind of world I want. I do not want research benefiting me at the expense of other human life. I do not want a society that establishes in law a class of embryos that it is a crime *not* to destroy. I don=t want valuable resources, now dedicated to safe and promising adult stem cell research, to be diverted for cloning experimentation. There are scientific data showing that stem cells can be obtained from the blood of the umbilical cord, from neural tissue, bone marrow and skin cells.

I join countless Americans with disabilities in deploring the "harvesting" of human life; I find it shameful that some of my associates with disabilities are using their physical impairment as a plea to promote research cloning, and I am offended that words like "helpless victim" and "being trapped in a useless body" are used to sway the sympathies of legislators. Rather, let us influence our society with reasoned judgment, strength of character, and a commitment to improve our culture, not diminish it.

I encourage disabled people, their families and friends to say no to cloning and persuade the Senate to pass the Brownback-Landrieu bill.

AMERICANS TO BAN CLONING

CONGRESSIONAL TESTIMONY

Briefing for Senate Staff on Cloning
April 10, 2002

Statement by Jean D. Peduzzi-Nelson, Ph.D.
Research Associate Professor
University of Alabama at Birmingham
Neuroscientist Working on Treatments for Spinal Cord Injury

I strongly oppose research involving human cloning and human embryonic stem cell research, based on experimental animal studies and clinical trials, because it is more likely to *harm than help* people with a disease or injury. My reasons for saying this are:

1. Cloning has not been shown to be effective in directly treating any injury or disease in experimental animal studies that form the essential basis for clinical trials. Success in preclinical animal trials is the first step in going to clinical trials. Numerous preclinical trials for spinal cord injury and other injuries or diseases have already had positive results using other avenues. Cloning has never even been tried in treating most injuries or diseases. Cloning is still in the realm of 'wild speculation.'

2. Cloning has never even been tested in the treatment of spinal cord injury in experimental animals. Most publicity is about use of cloning in spinal cord injury. However, there is no evidence that this is a useful prospect for treatment. Several other treatments (person's own stem cells, matrix, growth factor, and immunological methods) hold great promise.

3. In cases where cell therapy is proven effective, the best cells to use are the person's own cells (rather than embryonic human stem cells or cloned human cells), because these would be safer, easier and more feasible. This is a readily available source of cells that does not require use of human egg or nuclear (DNA) transfer. It avoids possible disease transmission, rejection, and the problem of overgrowth, and represents a viable therapy plan. Therapeutic cloning, if ever successful, would be cost prohibitive as a treatment plan.

4. This line of research would divert the limited funds available for research from promising areas of research. Research is always prioritized into most promising areas. It is not possible to go in every theoretical direction, for limited funding is available in research.

5. Significant risks are associated with cloning. There is a general lack of understanding about the reasons for the medical problems in cloned animals. The problem may be due to lack of imprinting (a control mechanism in the cell to turn on half of each of the duplicate genes) or due to foreign mitochondrial DNA or lack of proper environment for growth.

In my own research area of spinal cord injury, several avenues are likely to be successful in the near future (assuming adequate funding), especially if used in combination:

1. **The Patient's Own Stem Cells**: There is no need to waste valuable research funding on other sources of cells, because stem cells and other useful cell types are plentiful in the adult human. At Cedars-Sinai Hospital in California, Dr. Michel Levesque has multiplied a Parkinson's patient's own brain cells in culture and then used them to successfully treat that patient; these studies are continuing. Other researchers have found that bone stromal cells obtained from a simple bone biopsy procedure can form nerve cells. Recently Dr. Lars Olson, a prominent researcher in spinal cord injury, found that bone stromal cells can promote functional recovery after spinal cord injury in animals. Other cell types, found in the olfactory system (sense of smell), have also been used to promote recovery in experimental spinal cord injury. Using a person's own cells eliminates any problems of tissue rejection (the problem cloning is supposed to solve); it also eliminates the possibility of disease transmission, and avoids the problem of uncontrolled growth and tumor formation that has hounded embryonic stem cell research.

2. **Matrix Material**: Various matrices are being developed for use in spinal cord injury to act as bridging material across the injury site. They provide a substrate for growth that allows remodeling of the damaged area in the spinal cord. These matrices can be mass-produced and sterilized, providing a simple tool for the surgeon to use in repair of the spinal cord. Using one of these matrices in my own research, published last year in the Journal of Neuroscience Research, I found functional improvement in rats with severe, chronic spinal cord injuries. Blood vessels, glial (support) cells, and axons (nerve cell processes) grew into these artificial matrices. Matrices can be used in combination with cells from adults, growth factors or other treatments to produce even greater functional improvement.

3. **Growth Factors**: In recent years a variety of growth factors, including neurotrophic factors and cytokines, were found to protect and stimulate growth after injury in the nervous system. While there is some difficulty in getting these factors to the injury site, new delivery methods are being developed to target particular cell types in the spinal cord. A growth factor called neurotrophin-3 has promoted partial functional recovery after experimental spinal cord injury; interleukin-10, a cytokine, has significantly improved function after acute spinal cord injury in rats. The growth factors are used to overcome inhibitors known to be present at the injury site. Certain growth factors actually stimulate endogenous stem cells to divide and mature, thus may avoid the need for transplantation.

4. **Immunological Method**: The immune system that fights disease and foreign material in our body has been found to play a key role in spinal cord injury. Components of myelin (the insulating coat on axons) actually inhibit the growth of axons. By supplying antibodies to a component of myelin after spinal cord injury, Dr. Martin Schwab has found regeneration of the axons that originate in the brain. In other studies by Dr. Michal Schwartz, stimulation of the immune response to myelin has prevented complete paralysis in animal studies; her work is now in clinical trials in humans.

To claim that human embryo cloning is the only, or even one of the more promising, roads to spinal cord injury treatment is a disservice to the hundreds of dedicated researchers who have brought us to the brink of successful treatments. This is no time to divert our attention to a morally controversial, medically unproven and scientifically speculative avenue such as experimental cloning.

AMERICANS TO BAN CLONING

CONGRESSIONAL TESTIMONY

Briefing for Senate Staff on Cloning
April 10, 2002

Statement by Thomas P. Dooley, Ph.D.
CEO, IntegriDerm and Altruis
Co-Founder and Former President, BIO of Alabama

It is my distinct honor to address you today as a biotechnology scientist, entrepreneur, and advocate for economic development within the biotechnology industry. My expertise in these capacities is demonstrated by the fact that I am the CEO and founder of two scientific companies, IntegriDerm--a biopharmaceutical company, and ALtruis--an Internet healthcare company with likely the world's largest collection of healthcare and biotech informational websites.

In addition, I was the co-founder and former president of Alabama's biotechnology industry trade organization, and I am very pleased at the rate of growth of economic development in Alabama's life science industry. I resigned as President of this organization in March 2002 solely as a result of my opposition to policy statements by the Biotechnology Industry Organization that favor unrestricted use of human cloning research methods for the production of early stage human embryos intended for destruction.

Human cloning for any reason is unnecessary and immoral. There is no scientific, medical, or moral imperative to clone human beings or to produce human embryonic stem cells via embryo destruction. It should be noted that "reproductive cloning" and so-called "therapeutic cloning" both utilize the same unnatural manipulations of early stage human embryos. Since human life starts as a single cell embryo by conception using natural means or by somatic cell nuclear transfer in the case of cloning experiments, cloned human embryos - no matter how small - represent human beings with the potential to give rise to adults if implanted in the uterus. The difference between "reproductive" and "therapeutic" cloning is merely semantic and differs only in the intentions for their ultimate use.

As a biotechnology industry insider I can say confidently that there are no valid justifications to produce human clones either for reproductive reasons or for the generation of human embryonic stem cells. Two online commentaries provide the rationale for moral and scientific opposition to both human cloning and embryonic stem cell research: www.e-human-cloning.com and www.e-stem-cell.com. Alternative research approaches and therapies for various diseases are available and are being pursued by researchers, thus abrogating the so-called "need" for human embryonic stem cell research. Viable alternatives include adult stem cells, biotechnology-derived recombinant proteins, pharmaceuticals, and surgical and radiological intervention. In addition, funding by the National Institutes of Health or the private sector for these alternative approaches is likely to produce excellent results with comparable or greater potential to aid in the healing of human maladies.

Conversely, the moral imperative to preserve the sanctity of human embryonic life should overrule the desires by scientists and physicians who seek to manipulate human embryos for

financial gains and/or mere scientific interests. Morality should be elevated above money. And, some forms of scientific enquiry should not be permitted by society.

The Senate bill S. 1899 advocated by Senator Sam Brownback is an excellent piece of legislation deserving the support of the entire U.S. Senate, President Bush, and the citizens of the U.S.A. This bill parallels an identical bill sponsored by Congressman Dave Weldon that passed overwhelmingly in the U.S. House of Representatives last year. I encourage the U.S. Senate to pass Senator Brownback's bill to ban human cloning, as all human cloning for any reason is unnecessary and immoral.

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CONGRESSIONAL TESTIMONY

Briefing for Senate Staff on Cloning
April 10, 2002

Statement by Anton-Lewis Usala, M.D.
Clinical Professor of Pediatric Endocrinology
Brody School of Medicine, East Carolina University
Founder, Encelle Inc.

Chronic disease states such as Type 1 Diabetes, Parkinson=s Disease, and Spinal Cord Injury result from the destruction of specific cells. Replacement of these tissues may provide immense relief, and possibly cure, of the disease.

One approach to replace these tissues is to find acceptable transplantation sources and implant donor cells into a patient. If these cells are derived from a source other than the patient, there will be problems with rejecting the Aforeign@ transplant material. Cloned patient cells (cells that are induced to replicate with the same DNA template as the patient) do not have foreign markers and theoretically would not be rejected. However, cloned cells as well as other cells still must overcome the problem of appropriate integration into the transplant site in order to replace the function of the destroyed tissue.

Shortly after conception, a human being has a unique DNA template from which *all* other cells (except some germ cells) are generated. A differentiated heart cell has the same DNA template as a differentiated skin cell, and they both have the same DNA template as the undifferentiated cells early in embryogenesis. Different areas of the DNA template are promoted and repressed, resulting in different cell functions. What areas of the DNA template are promoted and repressed are largely determined by environmental factors outside the cell. Thus, it is hypothetically possible to induce *any* cell to become any other kind of cell, if the right environment were provided.

The developing embryo is surrounded by different proteins and factors than later in development, but the DNA template remains the same throughout a person=s life. One hypothesis is that if the correct embryonic environment could be duplicated, a patient=s cells might be induced to regenerate in a given site, as they rapidly do during embryogenesis. This would result in totally compatible, integrated replacement tissue for the disease being treated.

This concept was tested in an FDA monitored feasibility study in which patients with chronic diabetic foot ulcers were injected with an artificially made embryonic matrix at the ulcer site. Within days, all the patients experienced rapid diminution of ulcer size, with apparent regeneration of skin, blood vessels, and surrounding structures. In animal studies, the new tissue resulting from exposure to the embryonic-like matrix was determined to be structurally identical to non-wounded areas, without the usual scarring that is normally seen with healing lesions. Since the new tissue derived from the patient=s own tissue, there was seamless integration with no evidence of rejection.

Transplantation strategies, whether derived from foreign donors or cloned cells from patients themselves, are clearly not the only approach to replace damaged tissues. Other avenues are

much further along in clinical trials, and should be considered as a first approach for study. Claims that only embryonic stem cells, or cloned tissues, can overcome problems of rejection are false. Indeed, the patient=s existing cells provide the most rational source for fully integrating replacement tissues, as occurred during embryogenesis.

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AMERICANS TO BAN CLONING

CONGRESSIONAL TESTIMONY

Briefing for Senate Staff on Cloning
April 10, 2002

Statement by Yuri Mantilla, LLM, MA
Counsel for Hispanic Affairs and Human Rights
Family Research Council

The international human rights system was created as a reaction to the atrocities committed in World War II. Today, we are facing similar atrocities, but with different names. The cloning of human beings represents a gross violation of fundamental human rights norms including the right to life, the right of non-discrimination and the right to equality.

Cloning is often discussed as if there were two different kinds of cloning, "therapeutic" and "reproductive." In reality, there is only one type of cloning, "reproductive." Once a human embryo has been created, all human rights norms and principles are applicable to that human person.

Human cloning violates fundamental human rights. In therapeutic cloning, the human embryo is created to be killed and used in research experiments. This is a violation of the right to life, which is recognized as a fundamental human right in the Universal Declaration of Human Rights, the Inter - American Convention of Human Rights and other important international instruments.

The cloning of human beings is also a violation of the Nuremberg Code, which was written in response to the atrocities committed by the Nazi regime. According to the code: 'No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur." So-called "therapeutic cloning" kills embryonic human beings and therefore violates the Nuremberg Code.

We must continue to defend and promote fundamental human rights and we must reject attempts to use human persons as objects of lethal experimentation.

Human cloning exploits women, promotes racists views of life and is a form of slavery. Cloning reduces a class of human beings to the status of objects and property.

According to a Time/CNN poll, 90% of Americans oppose human cloning. Hispanic culture highly values the life of the child, before and after birth. Because of this, I ask the Hispanic community to oppose any bill that seeks to legalize the cloning of human beings. We must understand that there is no such thing as "therapeutic cloning." Respect for human dignity, since the time of conception, of each human being is the foundation for the moral, economic and social development of any civilized nation.

In what kind of world are we going to live?

One in which respect for human rights and dignity are the foundation of society, or one in which

might makes right?

The promotion of human rights and human dignity should prevail against the financial power of the bio-technologyical industry and its attempts to promote human cloning.

Yes to human dignity and human rights!

Yes to the Brownback/Landrieu Bill!

No to human cloning!

Together we can!

Juntos Podemos!

Presented at a meeting sponsored by Faith and Law and the Wilberforce Forum's Council for Biotechnology Policy, April 23, 2002, on Capitol Hill.

Cloning and the Biotechnology Crisis: Toward a Strategy

Nigel M. de S. Cameron

Dean, The Wilberforce Forum; Director, Council for Biotechnology Policy; Founding Editor, Ethics and Medicine

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When back in February of 1997 the announcement was made that for the first time a mammal had been cloned, Dolly the sheep was instantly famous as the centerpoint of a huge and still gathering debate about biotechnology, human nature, and the capacity of our public institutions to respond to what many have seen as their greatest challenge.

For back of the many particular questions of this debate lies the great question for public policy: can our democratic institutions frame a proportionate response to the exponential demands that biotechnology will make on the fabric of human society? As government pursues its traditional priorities of national defense and adroit economic management, a stealth agenda of greater import has begun to break the surface: the question of the future of human nature. Since democratic government has evolved in a period of settled conviction about such fundamental questions, it is little surprise that our institutions find this new and fateful challenge to be traumatic.

Ten years ago I wrote an essay that reviewed the meager Christian contributions to bioethics debate. I cited Creasey's famous book on *The Decisive Battles of History*. History does not turn entirely on military strategy and the tactics that can make all the difference to an engagement. There are vast forces at work in what Samuel Huntington has memorably called the "clash of civilizations," and we know well that so much of the modern world is explicable only in terms of the internal clash within "western culture" of its Judeo-Christian roots and their Enlightenment critique. But to note that there are great historical forces at work is never to suggest inaction or fatalism on our part. As the history of warfare makes plain, there is nothing "inevitable" about the outcomes of many of the great clashes of powers and their military forces.

This has been neatly illustrated by the recent surge of interest in so-called "counter-factuals" - scholarly explorations of might-have-beens had decisions and engagements gone another way. We could engage in some of our own. Had we been fatalists in the eighteenth century the church would have taken Enlightenment advice and essentially resigned herself to some kind of Unitarian accommodation with nascent secularism. And the nineteenth century, the greatest century of missionary expansion in which, not least, America was comprehensively evangelized and bequeathed the deep-rooted religious conviction to which we have fallen heir, would simply not have happened.

Fatalism is no part of the Christian worldview. One thing we do learn from history is that action can pay; strategically focused, timely, wise activism, modeled in such heroes as William Wilberforce, can change the future. By steadily and skillfully engaging the slave-trade, and slavery, in the British Empire, he fought one of our civilization's most decisive battles. And he laid

the foundations for abolition here in the United States, and for its belated echo in the civil rights movement a centiury later.

During the past year I have been invited to debate human cloning on many colleges and university campuses, often in tandem with Greg Pence, whose book *Who's Afraid of Cloning?* is an eloquent defense of baby cloning as a reproductive right. Last week we were at the University of North Dakota, and as he made his usual rights claims he coupled them with a common and cancerous argument that I hear on all sides: biotechnology is here to stay; we can't prevent it; the industry and the market will shape it; so whatever our views may be, there is not very much we can do.

In my rebuttal, I asked who, in fact, is in favor of choice? Pence is saying that as a community we have no choices. My case is that we can, we must, shape our future. We must decide what it is we choose for the human community. It is in our hands to frame policy that will give us a biotechnology that serves us. The alternative, a biotechnology that we serve, is the great threat that hangs over the 21st century.

I welcome the cloning of Dolly as an object-lesson, one that we could hardly have expected so early in the roll-out of the new biotech. Here is our opportunity to educate ourselves and our community, to discern what Leon Kass has called the wisdom of repugnance, and to develop the outlines of policy. In the prospect of human cloning we gaze into an image of biotechnology setting its own pace for the human species; the twin dimensions of biotech as hubris and horror; as it were, the marriage of Faust and Frankenstein, a sampling of the new powers that we are taking to ourselves.

Cloning stands first in a succession of waves of technological development that, one after another and in combinations we cannot predict, are set to break upon the moral structures of our culture in this generation. It is intertwined with the patenting of genetic material that has suddenly made this field hugely attractive to investors and crippled the public good motivation of researchers. Back of it lies the prospect of "germline" gene interventions - modifications of the germ cells that are inheritable by succeeding generations, as we become able not just to pick but to "design" our babies. And, back of that, lie developments in cybernetics and nanotechnology that take us beyond biology to its control and replication in the manufacture of devices of intelligence and enhancement, and the integration of human and mechanical. While there are serious debates about such issues as whether artificial intelligence will enable us to replicate and supersede the life of the human mind, there is no question that each of these waves of technological advance and corporate opportunity will pose afresh the question at the heart of our culture: what does it mean to be human?

Because in each case we are confronted with a cornucopeia of possibility - whether for healing or enhancement or control. We may expect that the appeal will be intense, and the attraction of particular applications marketed to us with full force. The policy parameters we agree today will set the tone for tomorrow and what it will bring. And that of course is the exact reason that the bio-industrial complex is so deeply committed to resisting policy of any kind. For them, as for us, this is round one of a great struggle; and every succeeding round will be easier for the side that wins at the outset.

Which is one reason the cloning issue is of such momentous significance. As we engage in a debate focused on the experimental use of clonal embryos, it is vital for us to understand that while there are parallels with the moral and policy discussions over the experimental use of in vitro embryos, this is not that debate. The distinctive character of cloning as the capacity to manufacture our own kind has slipped from center stage. Yet every act of cloning is "reproductive," and to whatever end the clonal embryo is put, it represents the first decisive step

across the line that separates the kind of beings we are from the kind of things we make; thus Homo faber, man the maker, begins to make himself - and in the sublimest of all ironies in a single fateful act both elevates himself to the role of creator and degrades that same self to the status of a manufacture.

This act is stupefying in its scope, and Faustian in its hubris. Humankind simultaneously claims the role of God while being reduced to playing the part of a mere thing, the dust of the earth out of which we were made and to which we foolish creatures choose to return ourselves; to become, in the president's recent phrase, commodity rather than creation.

From a theological perspective the significance of both these sides of the coin is plain. In this attempt to serve as our own creator, we are revealed as usurpers, capable only of manufacture. That Faustian bargain is the only one on offer. For the task of creator is personal to God, and his election of the inter-personal mystery of human sexuality as the context for procreation preserves his creatorhood absolutely. The most that his human creatures can do is, as we say, to "ape" his role, parody it, and reduce it to the mechanistic and industrial processes at which we are so good and for which indeed we were made. The ambiguity of the clonal human, as both creature and product, Homo sapiens hijacked by Homo faber, moves us decisively toward what the posthumanists call the "singularity" - that state they envisage in which the distinction between human being and manufactured being is over, and a seamless dress weaves together our humankind and what we have made. It anticipates the union of "mecha" and "orga," to cite one of the (few) memorable contributions of Spielberg's movie AI.

It's worth noting that outside small academic circles this discussion is being carried on in science fiction and its movies, from *Brave New World* onwards. Perhaps the most powerful is *Gattaca*, about a society in which genetic information destroys human dignity; it happens also be to a fine movie for many other reasons. *The Matrix* anticipates a world in which the machines have taken over.

Bill Joy, co-founder of Sun Microsystems, set out the most striking scenario in his now famous jeremiad, "Why the Future doesn't Need Us" - in which he claims that genetics, robotics, and nanotechnology between them will through some mixture of accident and intent result in either the destruction of the human species, or its supplanting, through some biological or mechanical meltdown or the triumph of machine intelligence. One does not need to buy the whole thesis to acclaim his comprehensive framing of the issues. And at the heart of this secular analysis lies a single theological issue: the threat to humanity that is posed by fallen human creativity; the dominion mandate from Genesis 1 to "subdue the earth" divorced from its Biblical context in human dignity made in the image of God.

Human cloning therefore crosses the Rubicon, taking us for the first time into the manufacture of our own kind. Until now the depth of our imaginative depravity had to be content with new forms of killing, the legacy of Cain and Abel. We confront now a new kind of sin, a fresh fulfilment of our conflicted fallen nature, the lineal descendant of the Tower of Babel. This is our best opportunity to begin to frame public policy for biotechnology around an issue of high profile that has resonated with the public conscience.

So how should we respond? Never before have the stakes for humankind been so high - the manufacture and, in due course, the reconstruction of our own nature. And the challenge comes to us full-force at that time in the history of our civilization when we are perhaps least able to resist. While our churches remain full (at least here in the United States), the web of Judeo-Christian defaults that have long nourished the values of our culture and fed its moral vision is steadily being re-set by our cultural elite; a process greatly aided by the generally pietistic and withdrawn character of our Christianity. It remains to be seen whether Christian commitment to

the prolife cause, the single striking exception, can be morphed into a broad engagement with biotechnology.

That brings us to the question of strategy. Those of us who are, broadly speaking, Christian cultural conservatives have not had much of one. It is hard to develop strategy when the initiative lies elsewhere, although it is even more necessary. Famously asked what was his strategy on coming into office, Churchill temporized: "it is to wage war, by land and sea." At that same level, ours is always to resist evil and to promote good. But how shall we do it?

I have already remarked that the debate over human cloning has offered a wonderful opportunity for the education of the conscience of the world, as we move toward C.S. Lewis' chilling "Abolition of Man." The pro-life movement has for the first time been drawn, though with hesitancy and some reluctance, out of its single focus on abortion. And, as pro-choice law professor Lori Andrews and I declared in a joint op-ed in the *Chicago Tribune* last August 8, a watershed has been crossed in collaboration between political progressives and conservatives, prolife and prochoice. The occasion of the op-ed was a House Commerce hearing on cloning at which, we claimed, one of the great moments of political theater of our generation was acted out, as representative pro-choice and progressive environmental figures lined up behind legislation that originated with the pro-life community.

Two strategic issues here emerge in very clear form. First, co-operation between those who have been and remain foes on the abortion issue will be central to the long-term task of engaging the emerging biotech agenda, as issues as diverse as germline interventions (inherited genetic modifications), gene patenting issues, genetic discrimination, and down the line nanotechnology and artificial intelligence loom as the great questions to be faced by our generation. Secondly, the pro-life community needs to upgrade both its understanding of and commitment to questions that go far beyond abortion and that are of at least equal and arguably greater gravity to conscience and our civilization.

Let me be practical. Some of us have been working hard to use this current year as the great cloning educational opportunity. We have been active on both these fronts. Within the conservative Christian community, we have established as a Wilberforce affiliate the Council for Biotechnology Policy, with members including leaders of Christian medical and legal communities as well as bioethics experts and figures highly esteemed in the prolife community. The Council has begun its own strategic reflections, and plans to take on an increasingly public role as the focus of the Christian mind on the biotech agenda.

Secondly, we have moved to consolidate the coalition with the generally prochoice progressives. The *Tribune* op-ed was followed within weeks by a very private meeting that has led to others, and Lori Andrews and I expect soon to announce the formation of a Coalition on Biotechnology and the Human Future.

These are both, at present, shells; but they are shells, as it were, designed to house strategies.

1. The church strategy. The strategy of engaging the prolife community and the wider church in moral education and political action on the biotech agenda is as vast in its implications as it is vital, not simply to asserting sanity and humanity in public policy but in maintaining the distinctives of the Christian community itself. This is both a grassroots education task and a nationwide political priority. It has plain, inescapable implications for our prolife organizations, whose fidelity to their mission-focus on elective abortion has been as commendable as it could soon become unwise. For this is not mission-creep, it is rather a dawning awareness that the question of the dignity of human life, manifested for a generation almost entirely in the threat posed by abortion, is suddenly and dramatically broadened into an altogether more radical

assault on human nature in which the direct killing of the unborn threatens to be superseded in awfulness by the transcendent crimes of genetic manipulation, the re-design of human nature, and through mechanisms such as cloning the manufacture of whole classes of compromised human beings.

The problem is well illustrated by the fact that for many prolifers experimental (so-called therapeutic) cloning in plainly wrong since it kills the unborn. Live-birth cloning (so-called reproductive) may be ruled out on safety grounds, but as to cloning *in itself*, they find it hard to take a view. They thus become the only group more opposed to experimental cloning than to the birth of clonal babies. Indeed, I have teased some of my friends with this question: what would a prolife view be if, *per impossibile*, it could be shown that it was actually "safer" to clone babies than to conceive and carry them the natural way? Would prolifers then favor cloning? The problem arises when abortion is seen not as a profound moral evil, but as the paradigm for moral evil. I am not suggesting that we have a calculus readily to hand (which is one reason why utilitarianism is so hard to sustain) - since goods and evils may be incommensurable. How do we compare, let us say, an act of abortion, with an act of lifelong slavery? How do we compare a rape with lifelong discrimination based on genetic information? My point is simply that it is not right to take the horror of elective abortion as the canon of evil in medicine and biotechnology. It is, as it were, symptom and not disease; and there are many such symptoms of medical science infected by a loss of vision for human dignity. Our prolife Christian community, and its organizations, must urgently address these vast questions or we shall be overtaken by evil events and the dignity of all of us radically undermined.

2. The political strategy. The significance of our presently tentative rapprochement with the broadly (though not entirely) prochoice progressive community cannot be understated, and must form the keystone of our political strategy as we engage the range of biotech questions. At one level we are all used to working in *ad hoc* coalitions, on issues such as religious freedom and prison rape. Some of these projects are narrower than others, but they tend to focus on one bill or one debate. That is our precedent as we move into this potentially broader and enduring coalition. The specific cloning question has brought us together, although ironically there has been less common ground here than there is on other biotechnology issues; some progressives favor a moratorium on experimental cloning, together with a ban on the birth if clonal babies, although in general they have been supportive of our common effort for a comprehensive ban.

But as we have discussed the ramifications of cloning and the broad issues raised by biotechnology, we have rapidly identified eight or ten issues on which we expect to find large areas of common ground and the capacity for long-term political collaboration. It is generally true to say that the conscientious forces within our culture are grouped on the right and the left, wearing political labels that are assuming less significance as politics becomes more eclectic and all our political traditions are steadily secularized. A creeping libertarianism across the entire spectrum contrasts with the "social conservatism" of both left and right who uphold the central place of values and conviction in the framing of public policy.

Let me end with this. Brownback-Landrieu is the only way to deal with human cloning. We need to ban every application of the Dolly technology to humankind, to strangle this route to human commodification at birth. We need to learn not to heed the siren-calls of the bio-industrial complex as they offer us instant cures for deadly diseases that we all know, even if they were forthcoming, would take a generation to be developed; and that could be developed, perhaps more readily, in other and ethical ways. We need to help our political leaders resist the blandishments of celebrity advocates and naive Nobelists, by drawing on the good sense of the American people to whom they must give account. Above all, we need to educate the Christians in ethics and science and policy, so that the church is able to serve as salt and light at this moment of greatest crisis for the culture.

Web resources:

Wilberforce.org
CloningInformation.org
Cbhd.org
TheCbc.org

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April 15, 2002 Monday

SECTION: WASHINGTON WIRE; PHYLLIS SCHLAFLY

LENGTH: 827 words

HEADLINE: 42202SCHLAFLY

Ban cloning, without an Enron loophole

BYLINE: Phyllis Schlafly Copley News Service

BODY:
We realize what a fundamental difference the 2000 election made to America when we read that The New York Times has accused President George W. Bush of having a "narrow morality." Nobody could have made such an accusation against the previous White House occupant!

What is it that makes his views narrow? Was it reminding us that "life is a creation, not a commodity" and that children are not "products to be designed and manufactured"? Was it advising us that "advances in biomedical technology must never come at the expense of human conscience"?

Was it saying that, "as we seek to improve human life, we must always preserve human dignity"? Was it warning us not to "travel without an ethical compass into a world we could live to regret"? It really wasn't Bush's words that The New York Times found "disturbing" so much as his "black-and-white tone." Yet, most people do perceive killing in tones of black and white and, in Bush's words, "wrong" and "unethical."

Bush announced that he wants to ban human cloning, i.e., creating human embryos that are genetic replicas of adults. The controversy arises because some people assert there are two kinds of cloning: bad reproductive cloning and good experimental cloning (also called research or therapeutic cloning).

According to the National Academy of Sciences, the first step in all cloning is "nuclear transplantation" or "somatic cell nuclear transfer." This produces a cell that divides several times to produce an embryo composed of about 150 cells.

If the embryo is implanted in a woman's uterus, a baby can be born nine months later, and that's called reproductive cloning. Alternatively, the cells can be removed from the embryo to make stem cell lines for experimentation and the embryo is killed; that's called research or therapeutic cloning.

The difference between reproductive cloning and cloning for research is not scientific; it is political and rhetorical. It's only the use of the embryo that is different.

There is widespread agreement that we should ban the former, but profit-oriented lobbies have raised a big ruckus by asserting that cloning-for-research might hold promise for the treatment of Parkinson's and

other diseases.

There is growing skepticism among scientists, however, about the effectiveness of research cloning and its possibility to cure diseases.

Chasing pie in the sky down the cloning road would take valuable resources away from the development of more promising avenues.

Clinical tests provide far more evidence that processes to conquer disease can come from stem cells from umbilical cord blood and from adults, of which there is an almost unlimited supply.

Scientists estimate that it would take at least 50 eggs to create one viable cloned embryo, while all the other embryos would die or be killed. At that rate, getting matched tissues for 16 million Parkinson's patients would require 800 million women's eggs.

It defies all that we know about human nature to believe that, if research cloning were allowed, it would never be used for reproductive purposes. Such a rule would be impossible to enforce, even if we stationed a policeman in every laboratory.

The press is already reporting news of foreign scientists who plan to **clone** humans. These threats come in spite of the fact that the laboratory cloning of animals required dozens of attempts and produced spontaneous abortions and terrible abnormalities.

You don't have to have a particularly vivid imagination to recognize that President Bush was correct when he said that authorizing therapeutic cloning would lead to experimental human beings, "embryo farms," and "a society in which human beings are grown for spare body parts and children are engineered to custom specifications."

The House last year overwhelmingly (265-162) passed a good bill that would prohibit human cloning for any purpose, and would further prohibit the importation of medical therapies developed from cloning technology. S.1899 is sponsored in the Senate by Sam Brownback (R-Kan.) and more than two dozen other senators, and the president has promised to sign the bill if it passes.

Strenuous efforts are currently being made to weaken Brownback's bill. Those who oppose human cloning must make sure the Senate bill passes without an Enron loophole, i.e., allowing the results of mischievous activities in foreign countries to be imported for the profit of U.S. residents.

It would defeat the whole purpose of a ban on human cloning if U.S. laboratories were allowed to experiment on **clones,** or use products made from **clones,** brought in from other countries.

The overwhelming majority of Americans agree with President Bush that "no human life should be exploited or extinguished for the benefit of another." If we are going to stop cloning before it starts, it is important for the Senate to act immediately.

Phyllis Schlafly is a lawyer and conservative political analyst.

LOAD-DATE: April 16, 2002

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The Mirror

May 7, 2002, Tuesday

SECTION: NEWS; Pg. 7

LENGTH: 153 words

HEADLINE: CLONE DOC GUILTY OVER DIRTY OP

BYLINE: Fiona Cummins

HIGHLIGHT:
GUILTY: Antinori

BODY:

MAVERICK fertility doctor Severino Antinori was yesterday found guilty of having an unsterilised operating theatre which damaged a patient's ability to have children.

The controversial professor, who claims he is planning to **clone** the world's first baby, now faces a huge compensation claim in the civil courts. The woman, who was then 34, developed an infection while having IVF treatment in 1994 at Antinori's clinic yards from the Vatican.

She was taken to hospital but lost her unborn baby and one of her ovaries, impairing her prospects of a future child.

A court in Rome fined the professor a nominal pounds 125 for causing culpable injuries. He was also ordered to pay into court a provisional sum of pounds 3,000 pending the outcome of the civil case.

Antinori said: "Justice has lost here.

"This is a guilty verdict brought about by the religious authorities who are against me."

LOAD-DATE: May 7, 2002

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The Boston Globe

January 13, 2002, Sunday ,THIRD EDITION
Correction Appended

SECTION: METRO/REGION; Pg. A1

LENGTH: 1951 words

HEADLINE: FIRM FACES UNCERTAIN FUTURE WHILE TOILING WITH EMBRYOS

BYLINE: By Raja Mishra, Globe Staff

BODY:
WORCESTER - The first security card opens the door. A second opens the freezer housing human eggs. Only after clearing those checkpoints can scientists at Advanced Cell Technology here begin their work. Out comes the egg's DNA, in goes another adult's DNA. Chemicals are injected. A human embryonic **clone** is born.

They have done this dozens of times in the last two months. Talk radio blares in the background. A video camera hovers. To date, every one of the cloned embryos has died before it could produce the stem cells the scientists sought. But ACT vows to continue until one embryo yields the prized cells.

On the outside, this small biotech firm is one of the most controversial companies in America. It has been a target of President Bush, who seeks to outlaw all human cloning. The US Senate, in coming weeks, will consider criminalizing the firm's work. But inside ACT's tidy lab there is no hesitation. Scientists here display a quiet resolve to **clone and clone** again until the firm makes its point: Human embryonic cloning can revolutionize medicine.

"I've been in some controversial places. But this is by far the most extreme," said ACT's medical director, Dr. Robert Lanza.

These are heady, complicated times for the privately held Worcester company. Its work, more than any other lab or company, has forced the public to weigh ethics against medical progress.

And its relationship with the US government grows increasingly contradictory.

In coming weeks, the US Senate plans to debate a human cloning ban, a bill that in effect targets ACT alone. No other US company is known to be trying to **clone** a human embryo. Bush champions the ban, even singling out ACT for condemnation.

But at the same time, one wing of his administration - the US Food and Drug Administration - has quietly encouraged the firm's cloning work.

In August, with ACT's headline-grabbing human cloning announcement imminent, the company briefed enthusiastic FDA officials on its ambitious plans, according to company officials present at the private

meeting.

At that same meeting, FDA officials discussed eventually conducting clinical trials on medical treatments derived from human embryo **clones.** And they compelled ACT officials to sign an affidavit promising not to **clone** embryos for the purpose of creating new human beings, explaining that such a document would provide cover for their work, according to Lanza.

"It was a very amicable affair," he said. "They were thankful that we took the time to come down to the FDA to brief them about our activities. They said the meeting helped them tremendously, and that they hoped we would think of them as a resource."

The FDA has declined comment on its dealings with ACT, but a spokeswoman cited recent federal mandates giving the agency authority over all human cloning-derived medical applications.

Lanza, 45, runs ACT's cloning effort, housed in a cramped office suite in Worcester's booming biotech corridor. Born in Boston and raised in Stoughton, he published his first scientific paper while attending Stoughton High School and was accepted to the University of Pennsylvania's medical school before finishing 12th grade.

The author of numerous texts on organ transplants, Lanza grew frustrated as patient after patient rejected transplanted organs. And then a sheep **clone** was born.

"Dolly happened and that was it," said Lanza. "That was the answer."

In 1998, he sought out ACT, which was at the fore of animal cloning science. He met a receptive CEO in Michael West, an ambitious scientist with a taste for pushing boundaries.

Now the company views cloned human embryos as a treasure chest of treatments: Individual patients would **clone** themselves; the embryos would grow for a few days, yielding stem cells, and the primordial cells would be coaxed into brain, heart, muscle or whatever tissue the patient required. Rejection would not be a problem because the tissue would genetically match the patient.

The first hurdle in advancing this approach was human cloning itself. No one had done it. In the late summer and fall of last year, ACT made 19 attempts to **clone** human embryos, succeeding 11 times. Most of the embryos died within hours. But three lasted for two days, developing four to six cells. If they had lived about a week, long enough to grow into 60 to 100 cells, stem cells could be harvested.

But the process requires a delicate act of nurturing that ACT has yet to master.

"If ACT succeeds, I happen to think that's going to be very important," said Dr. George Daley, a prominent embryonic stem cell researcher at the Massachusetts Institute of Technology-affiliated Whitehead Institute. "But it's a very labor-intensive process. It's a real challenge."

To accomplish even the first step - creating a successful cloned embryo - requires a deft combination of knowledge and technique. ACT hired the steadiest hands in the field from around the world, people known for their ability to pierce and poke at delicate microscopic cells, to suck and insert DNA without damaging them. Still, months were spent producing the first **clone.**

The next step - growing them - is perhaps more complex. ACT's embryos sit in petri dishes, far from the nurturing environment of the womb. They appear silver under the microscope, dwarfed by the hair-thin

pipettes used to feed them. The embryos require a precise and elusive mix of nutrients to develop properly. And they need just the right amount of oxygen. ACT scientists, peering for hours through microscopes, adjust these with each experiment, seeking the magic combination. But to date, the embryos have withered and died in their dishes.

As ACT continues its laboratory trial and error, involving the death of microscopic human embryos at each turn, some cloning opponents said the firm's work confirms their worst fears, that the destruction of large numbers of human embryos would become a routine feature of medical research.

"This is like the '30s, when the Nazis had no moral qualms about conducting experiments on and destroying people they considered subhuman," said Ray Neary, former president of Massachusetts Citizens for Life, who organized a protest at ACT last month.

Lanza, a Roman Catholic who supports abortion rights, appears squarely focused on how to move forward. The combined progress of his lab and that of other stem cell researchers could quickly produce treatments ready for testing in patients, he said.

"I could be in clinical trials next year, if I had the OK," said Lanza.

To that end, ACT officials this summer contacted the FDA. In August, they flew down to meet with Kathryn Zoon, director of the FDA's Center for Biologics Evaluation and Research, and her staff, which has jurisdiction over all human embryonic cloning applications. Lanza and West presented their ambitious plans, including their then-unrevealed effort to **clone** the first human embryo.

FDA officials outlined potential governmental hurdles, ACT scientists said. The FDA officials, along with getting ACT to promise not to allow any cloned embryos to become fully formed humans, also offered encouragement.

"They were wonderful. We have an excellent relationship," said Lanza.

ACT's stunning November announcement that it had created the first human embryo **clones** reignited calls in Congress to ban all forms of cloning. The US House passed such a ban earlier this year. The Senate plans to take up the matter in either February or March. Massachusetts Senator Edward M. Kennedy plans to lead a push to modify the bill to allow work on cloned embryos while preserving the ban on cloning humans, according to his aides.

But Bush supports the House's approach. If the Senate approves, ACT would be legislated out of business. With this looming, the company has found it hard to raise the money to push its science forward, said Lanza.

Nonetheless, ACT has conducted several notable experiments in cow cloning, still unpublished, the company said. Heart tissue was grown with stem cells from a cloned cow embryo, then successfully transplanted. Using the same process, a functioning miniature cow kidney was created and transplanted. And a similar process yielded high-potency cow immune cells, according to ACT.

Lanza said these experiments are "proof of principle" that ACT's vision can be realized.

A security guard has recently been stationed at the firm's Worcester offices and many of its 50 employees are wary of all the attention. But Lanza said he was surprised at the timidity of the blacklash. The protests have been quiet and small. And he counts only two threatening letters.

Far more profuse, he says, are the pleas for help. During a recent interview he held up a letter from a quadriplegic man who lives in the Tamil Nadu state of India, complaining of a "vegetable existence" and urging Lanza to "continue to carry on your research with compassion."

"This is not some academic debate," said Lanza. "This is reality. This is why we push forward."
SIDEBAR: THE PROCESS PLEASE REFER TO MICROFILM FOR CHART DATA.

CORRECTION-DATE: January 13, 2002, Sunday

CORRECTION:
Because of a reporting error, a Page 1 story last Sunday on Advanced Cell Technology of Worcester misstated the number of times that the company failed in human embryonic cloning attempts. ACT has acknowledged only eight failures to date. The story also incorrectly said that the US Food and Drug Administration asked ACT to sign a letter promising not to use cloning for reproductive purposes. The letter was conceived and drafted by ACT, not the FDA.

GRAPHIC: PHOTO CHART, Medical director Robert Lanza doing research on cow cells at Advanced Cell Technology. / GLOBE STAFF PHOTO / JANET KNOTT

LOAD-DATE: February 5, 2002

The Associated Press State & Local Wire

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January 13, 2002, Sunday, BC cycle

SECTION: State and Regional

LENGTH: 768 words

HEADLINE: Worcester company races to create human embryos as Washington pushes and pulls

DATELINE: WORCESTER, Mass.

BODY:
On the outside, Advanced Cell Technology is one of the most controversial companies in America. President Bush has targeted the company, and the U.S. Senate will soon consider criminalizing the firm's work.

But inside ACT's tidy lab, scientists quietly resolve to continue cloning human cells, guided by the firm belief that human embryonic cloning can revolutionize medicine.

"I've been in some controversial places. But this is by far the most extreme," ACT's medical director, Dr. Robert Lanza, told The Boston Globe. The company's relationship with the U.S. government is increasingly contradictory.

In coming weeks, the Senate plans to debate a human cloning ban, a bill that effectively targets ACT, as no other U.S. company is known to be trying to **clone** a human embryo. Bush champions the ban, and has even singled out ACT for condemnation.

At the same time, the U.S. Food and Drug Administration has encouraged the firm's work, company officials say.

In August, the company briefed FDA officials on its plans on the eve of the company's human cloning announcement, according to company officials present at the private meeting.

At that meeting, FDA officials discussed future clinical trials on medical treatments derived from human embryo **clones.** And they compelled ACT officials to sign an affidavit promising not to **clone** embryos to create new human beings, explaining that such a document would provide cover for their work, according to Lanza.

"It was a very amicable affair," he said. "They were thankful that we took the time to come down to the FDA to brief them about our activities. They said the meeting helped them tremendously, and that they hoped we would think of them as a resource."

The FDA declined comment on its dealings with ACT, but a spokeswoman cited recent federal mandates

giving the agency authority over all human cloning-derived medical applications.

Lanza, 45, runs ACT's cloning effort. In 1998, he sought out ACT, which was at the forefront of animal cloning science, where he met CEO Michael West, an ambitious scientist with a taste for pushing boundaries.

The company views cloned human embryos as a potential treasure trove of treatments. Embryos cloned from patients would yield stem cells to be used for brain, heart, muscle or any other tissue the patient required. Rejection would not be a problem because the tissue would genetically match the patient.

The company cleared the first hurdle in advancing this approach late last summer and fall, when ACT attempted to **clone** human embryos 19 times and succeeded 11 times.

Most of the embryos died within hours, but three lasted for two days, developing four to six cells. Had they lived about a week, they would have grown into 60 to 100 cells from which stem cells could have been harvested.

The as-yet unreached goal of growing cells is complex. Lanza, a Roman Catholic who supports abortion rights, is focused on how to move forward. The progress of his lab, with that of other stem cell researchers, could quickly produce treatments ready for testing in patients, he said.

"I could be in clinical trials next year, if I had the OK," said Lanza.

To that end, ACT officials this summer contacted the FDA. In August, they met with Kathryn Zoon, director of the FDA's Center for Biologics Evaluation and Research, and her staff, which has jurisdiction over all human embryonic cloning.

Lanza and West presented their plans, including their then-unrevealed effort to **clone** the first human embryo.

FDA officials outlined potential governmental hurdles, ACT scientists said. The FDA officials offered encouragement while asking for a promise not to **clone** embryos into fully formed humans.

"They were wonderful. We have an excellent relationship," said Lanza.

ACT's November announcement that it had created the first human embryo **clones** reignited calls in Congress to ban all forms of cloning.

The U.S. House passed a ban earlier this year. The Senate plans to take up the matter in February or March. Massachusetts Senator Edward M. Kennedy plans to lead a push to allow work on cloned embryos while preserving the ban on cloning humans, according to his aides.

Bush supports the House's approach. If the Senate approves the actions, ACT would be legislated out of business.

Lanza said that lives are stake, citing encouragement he's received, such as from a man from India who wrote urging the company to "continue to carry on your research with compassion."

"This is not some academic debate," said Lanza. "This is reality. This is why we push forward."

GRAPHIC: AP Photos Pursuing

LOAD-DATE: January 14, 2002

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The Boston Globe

May 16, 2002, Thursday ,THIRD EDITION

SECTION: BUSINESS; Pg. E1

LENGTH: 662 words

HEADLINE: RESCINDING ADVANCED CELL GRANTS URGED LAWMAKERS WANT US TO PULL $1.9M AFTER MISSPENT-FUNDS REPORT

BYLINE: By Raja Mishra, Globe Staff

BODY:
Several Washington lawmakers yesterday pressured the Bush administration to rescind almost $1.9 million in federal research grants awarded to Worcester's Advanced Cell Technology Inc., after federal investigators reported the company recently misspent about $150,000 in government funding while conducting animal cloning experiments.

The controversy stems from an April 26 report by US Department of Health and Human Services investigators which recommended that Advanced Cell be forced to refund the misspent money to the government. Company officials said they are waiting for a formal request from federal health officials before taking action.

"If [the National Institutes of Health] wants us to repay the money, then I assume we will comply with that," said Gunnar Engstrom, Advanced Cell's chief financial officer. "But we have not received a request for anything." Though such requests are not uncommon in the complex world of federal research funding, in this case they involve a company at the center of a heated national debate. The US Senate is preparing to debate the criminalization of all human cloning research, which would effectively end Advanced Cell's high-profile attempts to derive medical cures from week-old human embryos.

The probe into the company was ordered by 32 anticloning Washington lawmakers after Advanced Cell revealed in November its scientists were attempting to **clone** the first human embryos.

But after inspecting Advanced Cell's tiny Worcester offices and combing through its records, federal investigators found the scientists there had not spent taxpayer dollars on human cloning, which would be illegal under current funding rules.

Despite those findings, 17 GOP House members yesterday sent a letter to the Bush administration stating: "ACT may have used taxpayer funds to subsidize its human cloning activities, but since its accounting records are so poor, the HHS inspector general cannot find any 'evidence' . . . this is by no means an exoneration of ACT nor proof positive that taxpayer funds should be entrusted to these human cloners."

The letter, circulated by Representative Joe Pitts, a Pennsylvania Republican, called on the White House to issue a more severe punishment against Advanced Cell than the April 26 report recommended: Force

the company to return about $1.9 million in federal research grant money it has been awarded over the last three years for animal cloning experiments.

Engstrom yesterday called the effort a "smear campaign."

"I think we have here an attempt to get ACT linked to human cloning. But we oppose human reproductive cloning," he said. The firm has said it has no plans to produce cloned babies, although it is openly attempting to create medical treatments through therapeutic cloning, which involves harvesting stem cells from week-old cloned embryos.

The nine-page April 26 report recommended that Advanced Cell return $149,917 it has spent from its government grants. The report charged that the company improperly billed the government for $35,000 in salary costs on one grant. Engstrom said the grant in question was old and the company lacked the documentation to exonerate itself.

In addition, the report charged that the company spent about $114,000 on equipment it was not authorized to buy. Engstrom said the expenditure was approved by the NIH, and if there was an error, it was committed by NIH.

Finally, investigators leveled a broader charge at Advanced Cell: "We have continuing reservations regarding ACT's ability to continue as a going concern," they wrote, citing a independent audit of the company from 2000 that found numerous weaknesses in the company's financial books. Engstrom said the company was currently on solid footing.

"Why did they put in a comment that dates back over a year?" he said. "I can only assume they had a desire to hurt the company."

Raja Mishra can be reached at rmishra@globe.com.

LOAD-DATE: May 16, 2002

May-13-02 11:38am From-HHS ASL/Human Services 202-690-6750 T-400 P.002 F-739

Department of Health and Human Services

OFFICE OF INSPECTOR GENERAL

REVIEW OF NATIONAL INSTITUTES OF HEALTH GRANTS AT ADVANCED CELL TECHNOLOGY, INC

JANET REHNQUIST
INSPECTOR GENERAL
APRIL 2002
A-01-02-01500

May-13-02 11:38am From-HHS ASL/Human Services 202-690-5750 T-400 P.003/013 F-739

DEPARTMENT OF HEALTH & HUMAN SERVICES OFFICE OF INSPECTOR GENERAL

Office of Audit Services
Region I
John F. Kennedy Federal Building
Room 2425
Boston, MA 02203
(617) 565-2684

APR 26 2002

CIN: A-01-02-01500

Michael West, Ph.D.
President and CEO
Advanced Cell Technology, Inc.
One Innovation Drive
Worcester, MA 01605

Dear Dr. West:

The purpose of this letter is to provide you with the results of our review of the National Institutes of Health's (NIH) three grant awards made to Advanced Cell Technology, Inc. (ACT). The objectives of our audit were to: (1) determine whether the costs charged to the three NIH grants were allowable; and (2) ensure the funds were not expended, either directly or indirectly, in support of human cloning activities under the terms of the grants and applicable Federal regulations.

Based upon our review, we believe that $149,917 of the $214,146 in direct costs claimed to date for the three NIH grant awards are unallowable costs. Specifically, we are questioning equipment costs totaling $114,417 charged to two ongoing grants and salary expenditures of $35,500 charged to a completed grant. Additionally, we found no evidence that NIH funds supported ACT's human embryo cloning activities.

We noted that ACT's independent public accountants questioned ACT's ability to continue as a going concern considering its cash and working capital positions. We also have concerns regarding ACT's financial viability and the impact this would have on the continuity of research under the ongoing grants. We have additional concerns regarding the continuity of NIH-funded research considering the stated intent of its Principal Investigators (PI) to leave ACT shortly.

We recommend that ACT refund the grant awards $149,917 of the $214,146 in costs claimed as of March 15, 2002. We also recommend that ACT refrain from charging the NIH-funded grant awards additional costs until ACT is able to: (1) fully implement effective accounting policies and procedures; (2) provide evidence of a long term financing commitment demonstrating its ability to continue as a going concern; and (3) ensure the continuity of the NIH-funded research.

INTRODUCTION

BACKGROUND

The ACT is a commercial biotechnology corporation located in Worcester, Massachusetts. On November 26, 2001, researchers at ACT reported the cloning of a human embryo using somatic cell nuclear transfer. The Department of Health and Human Services (HHS) appropriation language prohibits the Department's funding from being used for: (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero. The Secretary of HHS has requested the Inspector General to determine whether any Federal grant funds have been used to support ACT's human embryo cloning research.

ACT has received the following three grant awards from HHS through the NIH:

- A completed small business innovation research grant (SBIR) for the "Creation of Cloned Cattle Lacking the Prion Gene" totaling $99,729 in direct costs for the period August 1, 1999, through January 31, 2001. The NIH grant number is R43 NS38382-01.

- An ongoing grant for "Defining Critical Parameters of Mouse Cloning" for $1,556,748 in total costs; $967,503 in direct costs and $589,245 in indirect costs for the period September 2001 through August 2006. The NIH grant number is R01 HD42320-01 (R01).

- An ongoing grant for "Enhanced Gene Targeting in Mammals" for $267,000 in total costs; $150,000 in direct costs and $117,000 in indirect costs for the period September 2001 through August 2003. The NIH grant number is R21 GM65194-01 (R21).

Both of the ongoing grants were restricted in the use of funds awarded for indirect costs. That is, ACT could not draw down awarded indirect costs in excess of 10% for fringe benefits associated with salaries and wages until ACT received an approved indirect cost rate. As of March 15, 2002, ACT had not submitted its indirect cost rate proposal to NIH for approval. ACT has not claimed any indirect costs on either open grant award and indirect costs were not budgeted on the SBIR.

OBJECTIVES, SCOPE AND METHODOLOGY

Our review was conducted in accordance with generally accepted government auditing standards. The objectives of our audit were to: (1) determine whether the costs charged to the three NIH grants were allowable; and (2) ensure the funds were not expended, either directly or indirectly, in support of human cloning activities under the terms of the grants and applicable Federal regulations.

To accomplish these objectives, we:

- Reviewed the three NIH grant applications and award documents to obtain an understanding of the nature of the grants and the types of costs involved.
- Reviewed applicable regulations including the Code of Federal Regulations and the Public Health Service (PHS) and NIH Grants Policy Statements.
- Conducted a walkthrough of the ACT facility in Worcester to determine if the NIH funded research areas were isolated from the human cloning research areas.
- Reviewed expenditures from the NIH grants to ensure they were adequately supported in accordance with Federal regulations.
- Reviewed ACT's financial management system, including the policies and procedures manual, to determine whether it met Federal requirements for safeguarding assets and ensuring costs were assigned to projects commensurate with benefits received.
- Interviewed the PIs on the two ongoing NIH grants and reviewed their documentation to determine whether research was actively being performed.

We did not rely on the internal control structure at ACT because written policies and procedures were not in place and ACT had neither a formal nor informal system for charging salaries to projects in proportion to the benefits received. We performed our fieldwork at ACT in Worcester, Massachusetts from January 2002 through February 2002. Our draft report was issued to ACT on March 18, 2002. The ACT's written comments are summarized on pages six and seven and appended in their entirety to the report (See Appendix).

FINDINGS AND RECOMMENDATIONS

Based upon our review, we found that $149,917 of the $214,146 in direct costs claimed to date for the three NIH grant awards are unallowable costs. Additionally, we found no evidence that NIH funds supported ACT's human embryo cloning activities.

We noted that ACT's independent public accountants questioned ACT's ability to continue as a going concern considering its cash and working capital positions. We also have concerns regarding ACT's financial viability and the impact this would have on the continuity of research under the ongoing grants. We have additional concerns regarding the continuity of NIH-funded research considering the stated intent of its PIs to leave ACT shortly. We discuss these areas in more detail below.

UNALLOWABLE COSTS

SBIR Grant

ACT charged direct costs of $99,729 to the completed SBIR grant. Through our testing of invoices and other support, we were able to obtain reasonable assurance that the non-salary expenditures totaling $64,229 were allowable costs. However, we were unable to verify that the salaries charged to the grant were attributable to the grant because ACT does not utilize an effort reporting (i.e., workload distribution) system as required by Federal regulations and the PHS and NIH Grants Policy Statements. As a result, we believe that the $35,500 in salary expenditures charged to the SBIR grant by ACT are unallowable costs.

R01 and R21 Grants

As of March 15, 2002, ACT had charged $114,417 in equipment expenditures to the two ongoing grants. Yet, the grants' applications and awards showed $0 in budgeted expenditures for equipment with nearly 100% of direct costs going to salary with each grant requiring full time research associates in addition to the PIs' efforts. ACT stated that NIH approved the use of grant funds to pay for the equipment because the grants were considered "modular" grants.

Our review showed that the equipment costs charged to the grants appeared to be questionable. In this regard, the equipment was on loan to the PIs in 1999 who, at the time, were working at Rockefeller University in New York. The PIs, before coming to ACT, used the loaned equipment to conduct research at Rockefeller University. The distributor loaned the equipment for a period of 15 months allowing the PIs time to obtain a grant to fund the equipment. Subsequently, ACT paid the distributor $114,417 in January 2002 for the equipment. Our review of the equipment transaction also disclosed that:

- the use of grant funds to purchase equipment described in one of ACT's grant applications as "already available for this project" and the fact that ACT did not staff the projects in accordance with the terms of the grant awards significantly reduces the scope of research possible;

- ACT has not conducted any research under the grant to which $35,000 in equipment was charged and we were unable to determine the extent of research conducted on the second grant because ACT does not have a system in place to distribute salaries in proportion to the benefits received; and

- the PIs stated intent to leave ACT for positions overseas by April 30, 2002, casts significant doubt as to the reasonableness of continuing to fund these grants.

Subsequently, we contacted each of the awarding Institutes and informed them of the information stated above. Upon learning of this information, officials at the Institute responsible for the R21 grant said they would not have approved the equipment expenditure. Officials at the Institute awarding the R01 grant expressed concern at the waste of a year of research funding and would make a decision about disallowing the transaction upon reviewing our report. As a result, we are questioning the allowability of $114,417 in equipment expenditures.

SEPARATION OF FEDERAL FUNDS FROM HUMAN CLONING ACTIVITIES

Although the PI on the SBIR grant donated a cell to be used for the cloning of a human embryo, we found no evidence that NIH funds supported ACT's human cloning activities. This PI is also ACT's Director of Research and has access to all ACT laboratories. However, since no indirect costs were charged to the NIH grants, none of his activity in his capacity as Director of Research was allocated to the grants. We also verified that the laboratories for Federally sponsored research projects are physically separated from the laboratory used for human cloning activities.

ADVANCED CELL TECHNOLOGY'S ABILITY TO CONTINUE AS A GOING CONCERN

In its audit report on ACT's financial statements for the two years ended December 31, 2000, ACT's independent public accountants questioned ACT's ability to continue as a going concern considering ACT's cash and working capital positions. At our entrance conference in January, ACT's Chief Financial Officer (CFO) said bridge loans had been arranged for the short term. In addition, he assured us long term financing was available. Later in February, the CFO allowed us to review a term sheet providing for long term financing available upon ACT's acceptance by signing. However, as of the date of this report, we had not been provided a signed copy of these terms indicating the necessary financing has been put in place. As a result, we have continuing reservations regarding ACT's ability to continue as a going concern and the impact this would have on the continuity of research under the ongoing grants.

RECOMMENDATIONS

We recommend that ACT refund the grant awards $149,917; $114,417 for equipment charged to the R-01 and R-21 grants, and $35,500 for salaries charged to the SBIR grant. We also recommend that ACT refrain from charging the NIH-funded grant awards additional costs until ACT is able to:

- fully implement effective accounting policies and procedures for all areas, including an adequate system for the distribution of salaries;

- provide evidence of a long term financing commitment demonstrating its ability to continue as a going concern and protect the government's interests; and
- ensure the continuity of the Federally funded research considering the decision of the PIs to leave ACT shortly.

AUDITEE COMMENTS

In its response to our March 18, 2002 draft report, ACT did not disagree with the validity of the facts presented in the report. However, ACT did not address our recommendations to: (1) refund the grant awards $149,917; $114,417 for equipment charged to the R-01 and R-21 grants and $35,500 charged to the SBIR grant; and (2) refrain from charging the NIH-funded grants awards until specific conditions outlined in the recommendations section of our report were met. Below, we have included ACT's relevant comments and additional OIG comments. The full text of ACT's comments are included as an APPENDIX to this report.

SBIR Grant

Auditee Comments

In its response, ACT acknowledged it could not identify the exact hours worked on the SBIR grant because of the absence of an effort reporting system. However, ACT maintains that since the grant was completed and findings reported, it is clear time was spent on performing the activity under the grant.

Additional OIG Comments

Since ACT did not have an effort reporting system in place to account for the distribution of salaries, it was unable to provide support for personnel that actually worked on the SBIR grant and the number of hours charged to the grant by personnel. Therefore, we believe that the $35,500 in salary expenditures charged to the SBIR grant by ACT are unallowable costs.

R01 and R21 Grants

Auditee Comments

In its response to our audit of the two ongoing grants, ACT requests we clearly state there has been no misappropriation of funds associated with the equipment purchase. ACT states that the NIH grant officer approved the use of grant funds for the equipment purchase. ACT maintains that although NIH may have erred in approving the equipment purchase, ACT acted in accordance with NIH's instructions. As to the continuity of the research, ACT acknowledges the PIs are leaving ACT for positions overseas. As a result, ACT will abandon the R-21 grant. However, ACT intends to name a new PI for the R-01 grant and it will submit the PI's name to NIH for approval shortly.

Additional OIG Comments

Our report does not state, nor do we imply, that ACT misappropriated grant funds to purchase the equipment. However, we did question the allowability of the equipment costs charged to the grants based upon the facts surrounding the equipment purchase as detailed in our report. Upon review of the additional information we provided, the officials responsible for the R-21 grant stated they would not have approved the use of grant funds for the equipment purchase had they known the details of the transaction. We continue to recommend that ACT refund the grant awards $149,917 for equipment charged to the respective grants.

Although ACT has decided to abandon the R-21 grant, the continuity of Federally funded research on the R-01 grant is still in question due to the issues stated in our report. Therefore, we continue to recommend that ACT refrain from charging this grant award until NIH approves appointment of a new PI and ACT establishes effective accounting procedures and provides evidence of its ability to continue as a going concern.

Advanced Cell Technology's Ability to Continue as a Going Concern

Auditee Comments

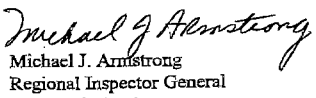
The ACT takes issue with our reporting on ACT's viability as a going concern. ACT states that its independent auditors raised the going concern issue in the 2000 audit and ACT has since operated for over one year, indicating the statement in the auditors' report was cautionary. ACT further states that as a private company it has neither the obligation nor desire to publicly disclose the terms of financing discussed with its private investors and will not provide OIG with a signed termsheet. ACT believes the "*going concern*" reference in the report is not applicable and is potentially damaging to the Company because OIG reports are public documents. Thus, ACT requests the "*going concern*" reference that originated in the independent auditors' 2000 financial statement report be removed from our report.

Additional OIG Comments

Our report clearly states the question of ACT's financial viability was raised in ACT's independent auditors' financial statement report for the two years ended December 31, 2000. During the course of our audit, ACT did not provide evidence that it had resolved the question of its financial viability.

In order to facilitate identification, please refer to Common Identification Number A-01-02-01500 in all correspondence relating to this report.

Sincerely yours,



Michael J. Armstrong
Regional Inspector General
for Audit Services

May-13-02 11:41am From-HHS ASL/Human Services 202-690-5750 T-400 P.011/013 F-739

APPENDIX

April 17, 2002

U.S. Department of Health and Human Services
Room 2425
John F. Kennedy Federal Building
Boston, MA 02203

Attention: Richard A. Navarro, CPA

RE: Common I.D. Number A-01-02-01500

Dear Mr. Navarro:

First, regarding your comments about our prior *SBIR Grant.* As you have pointed out, ACT did not have an effort reporting system at the time of this grant, and consequently we agree that the Company cannot identify the exact hours worked on this grant. We would like to emphasize, however, since the grant was completed and findings reported, it is clear that the time was spent on performing the activity under the grant.

Second, regarding the *R01 and R21 Grants.* We request that the report would state more clearly that there has been no misappropriation of funds associated with this equipment purchase. When requested by the PI, NIH explicitly approved the use of funds to purchase this equipment. Prior to drawing the funds, the Company's Accounting Manager subsequently confirmed the NIH approval directly with the grant officer at NIH, who confirmed that this expenditure was indeed allowed under the grants. It is possible that NIH made a mistake when it approved this purchase, but the Company acted in accordance with the instructions it received from NIH.

The PIs of these grants are leaving ACT, and will soon relocate to the Riken Center for Developmental Biology in Kobe, Japan.

- ACT will not assign a new PI to the grant entitled "Enhanced Gene Targeting in Mammals." This grant will be abandoned.
- ACT has not yet made the decision as to the named PI for the grant entitled "Defining Critical Parameters of Mouse Cloning." We will submit that name for approval shortly.

Third, regarding the "*going concern*" mentioned in the 2000 audit. We would like to clarify that ACT is a privately held company, funded by private sources. As many biotechnology companies, we raise funds periodically to meet our financing needs. At the time of the 2000 audit the Company's cash position was such that our independent auditors issued a going concern in their audited report. The Company has since operated for over one year, which would indicate the statement in the auditors' report was on the cautionary side. As a private company ACT has neither an obligation nor a desire to

publicly disclose the terms discussed with potential investors in the company and can therefore not provide OIG with a copy of a signed termsheet. We believe this reference in your report is inapplicable and potentially damaging to the Company if put in the public domain. We would respectfully request that reference to the "going concern" in the 2000 audit be removed from your report. Copies of current termsheets are available for review by a designated OIG representative under confidentiality.

Sincerely,

Michael D. West, Ph.D.
President and Chief Executive Officer

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