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ROUNDTABLE ON HEALTH TECHNOLOGY

HEARING

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE

ONE HUNDRED EIGHTH CONGRESS

FIRST SESSION

ON

EXAMINING HEALTH TECHNOLOGY, FOCUSING ON NANOTECHNOLOGY, INCLUDING THE DANGERS AND SOCIETAL IMPLICATIONS, MARKET BARRIERS AND CHALLENGES OF INTERDISCIPLINARY RESEARCH, AND THE FEDERAL ROLE OF FUNDING, COORDINATION, AND PRIORITY SETTING

SEPTEMBER 23, 2003

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ROUNDTABLE ON HEALTH TECHNOLOGY

TUESDAY, SEPTEMBER 23, 2003

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The committee met, pursuant to notice, at 10 a.m., in room SD–430, Dirksen Senate Office Building, Senator Gregg, (chairman of the committee), presiding.

Present: Senators Gregg and Murray.

OPENING STATEMENT OF SENATOR GREGG

The CHAIRMAN. Let me begin the hearing. It is ten o'clock. I expect we will have members wandering in and wandering out. There is a lot going on, plus I guess the traffic is a disaster this morning, which is too bad, but typical, I guess.

Let me first say on this subject, technology, that this committee is extremely interested in this issue because of its implications specifically to health care, obviously, which are dramatic. The fact that if we look to the future, this appears to be the science and the area where we are going to see an acceleration of more than geometric proportions, nano proportions, that will dramatically affect everything we do, I suspect, but especially affect our health care as we deliver it in this country and the world.

As I look at the American experience as we move into this century and we see that so much of our manufacturing in a free market economy is moving overseas, our capacity as a nation to compete is going to be tied to our capacity to lead technologies which lead the world, and nanotechnology is clearly one of those areas where we, as a Nation, need to lead and are leading and the government has an obligation to be a sister in this effort.

And so I wanted to hold this hearing today, first to get a thumbnail sketch as to what is happening in the area, but second, to hear ideas as to what we should be doing, if anything, beyond what the government is already doing, and interestingly enough, we appear to be involved in this fairly aggressively already, which is hopefully good news. And third, issues that we see coming down the road which we need to address as a matter of public policy—ethics issues, things which we need to address early so that they don't become bumps or impediments to the expansion of the technology and the use of the technology in a variety of different ways.

The CHAIRMAN. I very much appreciate the fact that the witnesses are here today and we have such an expert group. Dr. Schloss is the National Human Genome Project researcher in this area and, of course, NIH is making a major effort in this area. The

NSTC, which is the National Science and Technology Council, which coordinates the activities in this area, is the representative from NIH on that.

Dr. Dehmer is with the Basic Energy Sciences Office at Oak Ridge, and this is an area where we have a huge interest in nanotechnology research and appreciate her taking the time to be here.

Dr. Stupp is the Director of the Institute for Bioengineering and Nanoscience in Medicine at Northwestern, which is on the cutting edge of the use of this area of technology in an interdisciplinary way.

And Todd Lizotte is from New Hampshire and has actually commercialized some activities in this area that are exciting, especially in the use of very small penetrating micro lasers that allow for the introduction of extremely small holes and various applications.

I appreciate your all taking the time to come here. Why don't we just begin. I want to do this sort of in a discussion format, and so I would suggest that each of you sort of give us what your thoughts are in five or 10 minutes and then we will move on to discussion, hopefully between you folks and me and whoever else comes by, as to where we are going.

Dr. Schloss?

STATEMENTS OF JEFFREY A. SCHLOSS, M.D., NATIONAL HUMAN GENOME RESEARCH INSTITUTE, WASHINGTON, DC.; PATRICIA M. DEHMER, PH.D., DIRECTOR, OFFICE OF BASIC ENERGY SCIENCES, DEPARTMENT OF ENERGY, WASHINGTON, DC.; SAMUEL I. STUPP, PH.D., DIRECTOR, INSTITUTE FOR BIOENGINEERING AND NANOSCIENCE IN MEDICINE, NORTHWESTERN UNIVERSITY, CHICAGO, ILLINOIS; AND TODD LIZOTTE, VICE PRESIDENT, RESEARCH AND DEVELOPMENT, NANOVIA, LP, LONDONDERRY, NEW HAMPSHIRE

Dr. SCHLOSS. Thank you, Senator Gregg, for the opportunity to come this morning. I have probably got way too many slides, and I understand that. I have a lot of examples at the end. We will go through a number of them, and then when we have seen enough examples, we will stop.

We have probably all heard the definition—I have put it in here just to make sure that people understood what we are talking about. Research and development at the atomic molecular or macromolecular levels, so we are being fairly inclusive there. The scale is important. It is one-to-100 nanometers, and we really focused on this idea of a fundamental understanding of phenomena and materials and this idea of creating and using structures, devices, and systems with novel properties because of the size scale. So all of those things have to come together to comprise this new field of nanoscience and nanotechnology.

So from the biology or health perspective, I am thinking of—a number of us are thinking of this in at least two ways that are not totally mutually exclusive—they overlap a lot—one of which is the idea that nanotechnology is operating at the same size scale as biological processes. So this offers us really a unique vantage point from which to interact with the biology of life. One of the key

issues there is we can really work and study biology at the single molecule level.

The other aspect of this is that nanotechnology has grown up in other fields generally, in the physical sciences, and these fields have generated a number of incredibly important materials, devices, and tools that we can apply with the appropriate research to biological systems. And so we can fundamentally understand biological systems and use that information to translate out into utility for biology and medicine and for other areas of technology, and then we can also bring into biology the discoveries from other fields.

So we coordinate nanotechnology research at NIH through the Bioengineering Consortium, or BEACON, and we need to do something like that, because with 27 institutes and centers, we need a central way to deal with this, and this just represents the various components of the NIH that are involved in this process.

You will notice actually that we have three other agencies that are represented in the lower right-hand corner who participate in BEACON activities, and this is one of the ways that we can coordinate across agencies.

One of the important activities of BEACON has been to hold a series of symposia where we reach out to various communities that have, in many cases, not been the typical NIH communities and use this as an opportunity for people to meet each other, to understand the vision of other scientific fields as related to biology and medicine and also to understand how we can do business at NIH differently in order to promote research in those areas. And as you see, one of these was in nanoscience and nanotechnology back in June of 2000.

So the support for nanotechnology at NIH occurs through a number of different kinds of programs. A few of them actually say nanotechnology in the program announcement, but most of them actually don't. Because the mission of the NIH is, of course, diagnosis and treatment of diseases, they tend to be framed in that context, but there are many opportunities to apply nanotechnology ideas in those contexts.

So this is just a list of program announcements that have been generated through BEACON, through this trans-NIH efforts, and the first two are specifically for nanoscience and nanotechnology. The first is for sort of standard research grants that NIH would provide to research institutions, colleges, universities, and the second is through the SBIR program to help these kinds of ideas and tools get out through commercialization. The others are more general programs that BEACON has developed, again, through the auspices of all the institutes of the NIH, under which people can apply for nanotechnology and nanoscience research support.

And then this is just the list of a few of the many program announcements from institutes, usually from consortia of institutes, under which nanotechnology can be supported, and I have broken them down just for the examples here into sort of the different areas of basic research or sensors or tissue engineering, disease and syndrome research, and diagnostics and therapeutics to give some idea of the breadth of areas where we believe nanotechnology is going to be important in the context of NIH.

So our investment in nanotechnology has well more than doubled in the time that the NIH budget has doubled. These are fairly conservative projections, I think, for the out years. Of course, 2003 isn't finished yet, so we will only tally that at the end of 2003. And we have actually new programs. The first program announcement I showed you is actually a new one where we received many applications, and I think our portfolio is likely to grow faster than this.

Through the National Nanotechnology Initiative, several grand challenges have been enunciated and the one for health care is clearly the one that is most relevant to NIH. And the areas where we think that our activities—where nanotechnology is going to be important are listed here, detecting disease very, very early, before there is any substantial deterioration of health, in the tissue regeneration area, and in therapeutics delivery.

So the rest of the slides are really examples. Obviously, there is a lot of information covered in each slide, and I won't go through it. I will try to point out some key issues.

So most of these slides represent projects that NIH is currently supporting. In a couple of cases, there was no good website or place where I could get nice illustrations, so I have illustrated it with other research that is not being supported by NIH, but in each case, it represents research that we are supporting in other grants.

And the other thing I have done here is not only indicate the grantee, but also the Institute of the NIH that is supporting it so that you will have some sense of the way that this crosses the NIH.

So this represents a material called quantum dots that allow us to do things that we have been able to do in the past with organic dyes, but probably a lot better than we were able to do it in terms of the different colors which we can use to indicate different cellular entities and also the kinds of signals we can detect in our imaging.

And so in this case, it is showing that we can use these quantum dots to label various proteins inside of cells and learn about them. These can also be used for imaging in whole animals, and this is just a study sort of to show you where we are. The key thing here is this—in this case, the quantum dots are coated with a material that didn't work very well, and I am just going to run this movie that runs over 60 minutes. All you are supposed to see here is that the signal except in the liver disappears very fast. When you coat it with a different material, the quantum dots stay in the blood circulation for 190 minutes.

So this is where we are. We are trying to learn how to use these materials to do in vivo imaging, in this case of a mouse—a mouse or a rat, sorry, I can't remember which—in order to be able to, in this case, visualize circulation, but this will be used potentially for labeling many other things in in vivo imaging.

This is another study also using in vivo imaging using quantum dots, again, a collaboration by the company that has commercialized these and Cornell University, in which they are doing much finer resolution of the circulation, of the circulatory system.

And I wanted to point out this additional item that was noted in this publication. No adverse effects on the mice were observed and the mice are being maintained to investigate long-term Q-dot toxicity. This is a very important point, clearly. We have to under-

stand how these nano scale materials interact with the body. We are now developing the tools, as you can see here, to be able to actually do that.

So there are a number of other sensor examples here in the slides. This is an example, instead of coating the outside of the nano material with materials that will allow for specific biological visualization here, it is the construction of the nano material itself that is going to produce fluorescent signals that can be visualized in the light microscope and that will indicate various interesting and important things about the cells' physiology.

Here is a use of carbon nanotubes that have very unique electrical properties. These tubes are one nanometer in diameter. They can be centimeters long. The idea here is to put something at the tip of the nanotube that will allow us to detect some specific biological molecule and then perhaps use these in catheters to detect things inside the body.

Another thing that this slide points out is partnerships between agencies. So in this case, it is a collaboration between the National Cancer Institute and NASA.

The next few slides, I won't talk about in detail. They are other kinds of sensors technologies that are being supported, in this case, under SBIR grants, the work coming from Harvard. Here is another one, work actually supported at Massachusetts General Hospital, and this is a technology that might be used not only to do diagnostics in test tubes, but also potentially in vivo imaging once again.

Quantum dots have many other uses in, for example, in high throughput screening. There are many other ways to do high throughput screening. There are some very, very novel ways to use nanotechnologies. In this case, it is for measuring DNA, information from DNA using a pore that is exactly the same size in diameter as a DNA molecule. This would be a very new approach to DNA sequencing. It uses new physics, new fabrication technologies, and there are partnerships all over the country that are working on this.

There are a number of aspects of tissue engineering, most of which I won't cover because Dr. Stupp is going to cover that, but there are two different approaches here. One is modifying existing approaches to tissue engineering and the other is create completely new ones.

There are examples in drug delivery, either for creating new ways to deliver existing drugs to make them more effective, or creating completely new drugs that didn't exist before, that work by different principles using nanotechnologies.

This is the last slide I will show. This is a multifunctional device based on some very elegant chemistry—beautiful molecules, actually—and the idea here is you will create a complex by this very tightly, carefully controlled chemistry where you could bring the complex to a very specific place in the cell, use this for biopsies or in vivo imaging in the whole person to find out where this material is localized to target a specific thing that has gone wrong, such as cancer cells, and use the same device to deliver therapeutics.

So I will stop there because I have run just a little bit long. I have additional slides that we can use later on to illustrate various points if that seems appropriation.

And so now I will close down my presentation and we will move to the next one.

The CHAIRMAN. Thank you, Doctor.

Dr. Dehmer?

Ms. DEHMER. Senator Gregg, Senator Murray, it is really a pleasure to be able to represent the Department of Energy here this morning. I am Pat Dehmer. I head the Office of Basic Energy Sciences in the Office of Science in the Department of Energy.

I have given a lot of talks on nanoscience to folks who don't have a lot of physical science training and I find that starting with a poster that I made several years ago is the best way to tell people what some of the challenges are.

This is the scale of things poster, and I am actually going to use—each one of these tics represents an increase of a factor of ten, so this might be ten, 100, 1,000, and so forth. This is a scale of increasing size.

The nano world, as Jeff said, is about one-to-100 nanometers. The micro world, which we are much more familiar with, is about one-to-100 micrometers. These two scales differ by a factor of 1,000.

Quite remarkably, until very recently, we were not able to see anything in the nano world. We could only see things in the micro world. And I think it is not an understatement to say that our ability to see atoms has driven both the nanotech and the biotech revolutions, and this came about relatively recently, in the last 30 or 40 years or so.

So let us just look at some of the things that nature makes in these various size ranges and some of the things that man makes in these various size ranges.

In the micro world, the world that we are familiar with, we have red and white blood cells, we have phylage, we have human hair, and if you want to get bigger, we have pesky things like dust mites and ants and mosquitoes sucking the red out of the things natural slogan. So this, we are very familiar with. We have been able to see these using visible light microscopes.

At the nano scale, things are more complicated. Here, we see atoms of silicon, solid silicon, spaced by a few tenths of a nanometer. Here, we see deoxyribonucleic acid, DNA, this wonderful polymer that transmits all the information of life. It is actually about 2.5 nanometers wide. If you go to a slightly larger biological molecule, a rotor, it is about ten nanometers wide. It is at the nanometer scale that Mother Nature starts assembling things, and it is at that scale that things start having their properties. Metals start having metallic properties, biological molecules start having the properties of living things. It is an extremely important world.

It took Mother Nature about three billion years to perfect these molecules. By contrast, man has been working at control over materials for a couple of thousand years if you ignore rock hand axes, which are about a million years old.

So what has man done? On the right hand side of the chart, in the micrometer scale region, you see these beautiful MEMS devices, micro-electro mechanical devices. A little tooth of one of these

gears is about the same size as a red blood cell. We have been able to drive downward in our industrial fabrication to the micron level, and one of our speakers here this morning, Mr. Lizotte, is going to tell us about some of the things that they have done in this size region.

However, if you go much lower than this, you can no longer do things with fabrication. You have to use a different way, a different approach. If you go way down to the level where Mother Nature starts putting things together, the atomic level, in a tour de force, we have been able—researchers have been able to move atoms literally one at a time into quantum structures, circles—this is a circle of atoms—or they have been able to make slogans. Everyone has seen the IBM slogan written with atoms. This is a tour de force and it is not likely to go into mass production if you physically have to move an atom one at a time.

The way that we are going to have to solve the problem of making nano structures is to do what Mother Nature did, to learn how to self-assemble nano structures to get what we want, and here is a self-assembled structure that another one of our speakers, Dr. Stupp, has made, and he will tell you more about that.

It is only through self-assembly that we are going to be able to make nano structures to do what we want to do, and the big challenge in the decades to come is to take different kinds of nano structures that nature hasn't thought about, put them together in various ways so that we can make things that nature hasn't done, and in particular, make things that are more robust than natural systems. Natural systems are remarkable, but they don't withstand high temperatures, high pressures, and other kinds of corrosive atmospheres.

So this, then, is the scale of things and it presents some of the challenges. One of the things that Jeff talked about is coupling things that man makes with things that nature has made, to make nano structures that live inside the body that can detect disease, that can act as sensors, and so forth.

So this, in a nutshell, is the scale of things and where we are in man's attempt to control materials at this scale.

So what is the role of the Department of Energy in all of this? The Department has several roles, and I alluded to one a moment ago when I said that it has only been recently that we have actually been able to see things at this size scale. If you look at the little tiny spectrum right in the middle of the chart, that is the visible light region, and things that are larger than that, you can see with a visible light microscope. For example, you can see red blood cells with a visible light microscope. Things that are smaller than that, you can't see. The laws of physics simply forbid you from looking smaller.

So in order to see things at the nano scale, we have to come up with probes that are themselves the size of atoms, and there are three kinds of probes that have emerged, X-rays, neutrons, and electrons. The Department of Energy recognized quite a few years ago that these would be extremely important probes of matter.

By the way, the discovery of each one of those—electrons, neutrons, and X-rays—was made about the turn of the last century

and they were so important that each one of them garnered for its discoverer the Nobel Prize.

These probes are so important that they have become the basis for major user facilities that are shown here. These are the user facilities for X-ray scattering and neutron scattering that are operated by the Office of Basic Energy Sciences and the Department of Energy. We operate four huge light sources around the country. We have three operating neutron facilities, one at Argonne, one at Oak Ridge, and one at Los Alamos. This is the spallation neutron source, a $1.4 billion construction project that is underway at Oak Ridge National Laboratory, and on the drawing board we have a fourth generation X-ray source.

Together, these plus the electron beam scattering centers that we also run, have really revolutionized our ability to see things. And again, it is not an understatement to say that the ability to see how Mother Nature puts things together has driven both the nanotech and the biotech revolutions, and this is one of the main contributions of the Department of Energy's Office of Science.

When the National Nanotechnology Initiative came along, we recognized the importance of these major facilities at the nano scale and part of the Office of Science's contribution to the NNI was to make user facilities for nanoscience that are sited alongside of these major facilities for seeing atoms, and these are shown here. Under construction right now, we have five user facilities for research at the nano scale at Brookhaven National Laboratory next to the National Synchrotron Light Source at Argonne National Laboratory. This is being funded joint by the State of Illinois and DOE, and it is appended to the advanced photon source, a major synchrotron.

We have one at Lawrence Berkeley National Laboratory, again, which is adjacent to the advanced light source. We have a center going up at Oak Ridge National Laboratory, which is attended to the spallation neutron source, and we have a center at Los Alamos and Sandia National Lab which is appended to the Lujan Neutron Scattering Center, plus also their facility for MEMS, which is extremely important.

So this is part of the contribution of the Department of Energy. Another part of the contribution is the support of fundamental research, and about 60 percent of the fundamental research in nanoscience that has been competed recently has gone to the university community.

This is an example in biomolecular materials, which I am not going to go over in the consideration of time.

This is one that is very interesting and it demonstrates a principle that sometimes you don't know what you are going to get out of fundamental research. This was a project at Argonne National Laboratory—where I spent my formative years, but not on this project—on ultrananocrystalline diamond, UNCD. And if you don't think of the University of North Carolina when you say that acronym, you are better than I am. This is ultrananocrystalline diamond, and what it shows is that the diamond film forms in grains that are at the nanometer size. This is about three to five nanometers across.

This diamond film has some extraordinary properties. It is as hard as natural diamond. It has low coefficient of friction. And these two properties mainly can be used as coatings that are hard and wear-resistant. It has very high electro-conductivity that can be varied by many orders of magnitude, and that means it is great for MEMS devices because it can be little electrical conductors. It has high field emission from micropoints—here are some micropoints—and that means it can be used as a signaling device because electrons can come off of it. It is chemically inert and it is bioinert and it is biocompatible, and those things are very important.

And here is one of the artificial retina projects that is ongoing now in the United States, and this film is at the back of the retina to help bring the image from the outside into the nerve cells in the eye.

So the folks who thought about making this diamond film never had a clue that it might be used some day in an artificial retina, and this is some of the magic of nanoscience.

So with that, I am going to thank you for your attention and I am going to turn it over to Sam.

The CHAIRMAN. Thank you, Doctor.

[The prepared information of Ms. Dehmer may be found in additional material.]

The CHAIRMAN. Dr. Stupp?

Mr. STUPP. Good morning. Thank you, Senator Gregg, Senator Murray, for the opportunity to brief you this morning on my views on nanotechnology and the future of medicine, which is what I was asked to do.

There is no need to define nanoscience, nanotechnology anymore. Dr. Schloss and Dr. Dehmer have done a great job of that. But I simply want to remind everybody that cells function through interactions among nanostructures. In fact, these are highly orchestrated——

The CHAIRMAN. Excuse me. I have got to take a call. I will be right back.

Mr. STUPP. Cells function and make life possible by highly orchestrated interactions among nanostructures. Most of those nanostructures are actually proteins. So with the capabilities that we have now to create nanostructures with basically any chemistry that is available in the planet, almost, then we are in a position to make artificial ones that can talk directly to the cells and then control cell behavior or probe cells.

Now, one of the interesting opportunities in this field is regeneration of body parts, regenerative medicine. Targeted drug delivery is another one, and, for example, the area of more humane chemotherapy or more effective chemotherapy could fall under this category. We could also use the nanostructures, the artificial ones, to, in fact, detect disease at very early stages.

The related opportunities, of course, that come with all this knowledge base have to do with biosecurity, for example, and certainly genome mapping, which is also very important in regenerative medicine, as well.

So let me focus on regenerative medicine, which I have used as an example, to illustrate how nanotechnology is embedded in this problem.

So, so far, this is what we do, what is illustrated here on the right-hand side. We stick metals and ceramics, huge chunks of metal, in fact, and ceramic and other materials, composite materials, to fix joints and to fix blood vessels with artificial polymers, for example. What we should be looking to into the future is essentially the left-hand side, that is, have a scheme that allows us to regenerate all tissues of the body in adulthood. This is the target.

Now, why is regenerative medicine important? Well, it is important certainly because humans are living longer now and they will probably continue to live even longer. And the current generation, of course, is very interested in high quality of life. Humans want to be, at least in developed countries, there is a lot of desire to be physically active and have a higher quality of life into a more advanced age. This is very much characteristic of generations now. So regenerative medicine, therefore, will have a great human impact.

But, of course, there are other issues, you know. For example, the societal implication here is to basically think about the fact that we then need to keep populations in a highly productive and ideal State into a more advanced stage, and that brings, of course, all kinds of problems.

The needs for regenerative medicine are many, but I wanted to focus on a few here which I think are important. Real progress in this field, which is highly interdisciplinary, will require combining the frontiers of technology, in this case nanotechnology, with biology and clinical medicine. This is all about interdisciplinary science and technology, and countries that do not know how to tackle with interdisciplinary science and technology will not win in this field, both from a human point of view, of course, and an economic point of view, because this is also an economic opportunity.

We have in this country many entrepreneurial bright students which are going to be attracted to this objective because this is one of the great biomedical challenges of the century, to be able to regenerate the human body. But they need to be backed up by an interdisciplinary culture which is not there yet. So this is an issue that we need to ask questions about all the time because no one has the right formula yet for interdisciplinary education and research. The universities need to deal with this constantly. The agencies, of course, have to deal with it, as well, and they have a very critical role to play.

The issue is that teams of scientists and engineers of different fields is not enough. What you really need is multilingual scientists and engineers that can effectively do interdisciplinary work.

Now, here are some of the great targets, in my view, of regenerative medicine. We certainly should have as a developed society, we should have a way to reverse paralysis, and we don't have a way to reverse paralysis now, reverse blindness. So what needs to be done here is spinal cord regeneration and retinal regeneration, for example. Heart regeneration is extremely important, as well, and this is something that afflicts a large section of the population. If we could do that after heart attacks, then quality of life would be much higher. The same thing with stroke, which is a problem for

almost a million people every year just in the U.S. There is need for cell therapies, basically to substitute for the pancreas that doesn't produce insulin, and here, regenerative approaches are also important, as well.

Everybody would like to have access to cartilage and adulthood, because that causes the damaged cartilage, which no one in this room can grow cartilage right now because I suspect there is no one here that is under 18. So it is all gone. If we have an injury in cartilage, it will cause a lot of pain, decrease quality of life, and this attempts to fix this problem. It is also a multibillion dollar business. So if we had solutions, it would be a very attractive problem.

No one knows how to repair bone universally, and, of course, bone repair is something that afflicts an extremely large portion of the population every year. And, of course, nobody dies with their original permanent teeth, which is another reality here. It would be great if we could regenerate enamel, for example, and not have to use dentures and all the porcelain and metal that gets placed in our mouths throughout life.

So how is nanotechnology embedded in this problem of regenerative medicine? Well, the key is that we need to have scaffolds. To regenerate tissues in adulthood is like building a building. You need a scaffold. So the scaffold is needed, which is made up of nanostructures that can talk directly to cells and instruct them on what to do next. Of course, a lot of the information to design the scaffolds, to design the nanostructures of the scaffold, need to come from genomic and proteinomic information so that we know which signals we are to provide to cells in order to regenerate different tissues.

We also need to be concerned with stem cell biology. We are going to have to know how we want to deal with that problem. And, of course, regulatory work, such as the FDA, will need to be important, as well.

So I want to illustrate the problem with this nanostructure which was developed in my laboratory. We basically, using the spirit of nanoscience and nanotechnology, went out to create an artificial nanostructure that would mimic collagen fibrils, because collagen fibrils are everywhere in your body. They are the most common component of the natural scaffold where cells live in the various tissues of the body. So having a way to create an artificial one where we can change, let us say, the chemistry here to customize it to neurons or to retina or to heart or to bone, is extremely important.

We were able to do that in the slide which you already saw in Dr. Schloss's and Dr. Dehmer's talks. It shows a molecular rendition of this nanostructure. Just to show you how interdisciplinary this activity is, this structure, which should be of great interest to the NIH community because it is for regenerative medicine, the fundamental science that was needed to develop it actually came from support from the Department of Energy. And so this shows you how difficult it is to predict where things are going to come from and why is it so important to constantly be interested in interdisciplinary science and research.

These nanostructures combine proteins, for example. So if we know from genomics and proteinomics what proteins make what tissues grow, we can stick them there by design using specific techniques. We can load the middle of the structure in that cargo compartment with drugs, like hydrophobic drugs, for example, that are important in creating strategies for regenerative medicine, to actually make them work in the clinic.

This slide shows you how those fibers really look like when they are in three dimensions, and that is a picture of the scaffold where the cells can be. And so they form networks and the networks have some strands which are single nanofibers, other strands which are groups of twos or threes.

We have been able to customize them for the spinal cord injury recently, a problem, and so we have already in the laboratory nanofibers which cause neuroprogenitor cells to differentiate specifically into neurons and very rapidly. So this slide is an illustration of that differentiation. The green says that they are neurons, and you see very, very extensive neurites coming out of a cluster of progenitor cells.

The most interesting aspect of this problem is that other cells like glial cells have not appeared in the presence of our scaffold. Glial cells are implicated in the spinal cord injury problem because glial cells, when there is a spinal cord injury, they create a scar which prevents neurons from reconnecting and then healing.

So these synthetic nanostructures were able to direct progenitor cells to go only into the direction of being neurons and nothing else, and normally, in materials that had been explored for this purpose, you get mixtures of cells. You get glial and neurons. And so this will be important for spinal cord injury repair.

Bone, which is very important for the entire population because we will always depend on a healthy skeleton. We can't move around with a fractured skeleton. We have problems, osteoporosis, for example, and all of these things that connect very much to high quality of life.

The same nanofiber, the same synthetic structure, we were able to customize it so that it would grow bone crystals very rapidly that mimic exactly those found in natural bone. We were able to reconstruct the crystallography and the nanostructure details of bone mineral present in natural bone using a different molecular structure in the nanofiber. So it is possible to customize this to different tissues.

In the case of cartilage, which is this yellow region shown here, and if you have a cartilage injury, you will be miserable for a long time and maybe the rest of your life because it is very difficult to regenerate it, we have found nanostructures in which chrondocytes, which are the cells of cartilage, can actually produce—remain in the phenotype that is characteristic of chrondocytes and produce the proteoglycons which are so critical to formation of cartilage.

This area right here indicated as PA gel is chrondocytes sitting on nanostructures. Over here, these are chrondocytes sitting on tissue culture plastic or some other material that is not designed, and so there, the cells lose the characteristic phenotype which allows them to produce cartilage. So it is a very exciting possibility that we actually can go in, design a nanostructure, and talk directly to

cells and get them—send them in pathways that will lead to regenerated tissues.

Another great target is the heart, and I think here the same thing will apply. We will need to find out what are the right signals, the right epitopes, as biologists call them, and growth factors that are necessary for this to happen.

Now, to conclude, I just want to give you a few thoughts about how I think we should proceed. It is clear that these artificial systems in regenerative medicine, which is the example I chose to use, they will be developed by highly creative teams of physical scientists, engineers, biologists, and clinicians, everybody working together. But all the members of the team will have to speak several languages. Otherwise, this will never happen.

So the interdisciplinary culture is not necessarily going to emerge spontaneously. There are people that are naturally interdisciplinary. Others are not naturally interdisciplinary, and Federal agencies, for example, can do a lot to promote that culture through the programs they create. I think NIH and DOE both are doing an excellent job so far, but I don't want to say that it is a perfect job yet because there is a lot of work to be done, and frankly, the formula is not there yet.

I think universities are willing to do technology transfer. That is another issue that is important here. We must be very much aware of the fact that large companies are really not doing the R&D work that is going to be necessary for this field. And the venture capitalists, which are terribly scared right now for whatever happened in the 1990s, are pulling back and they are not ready to invest in high-risk quantum leap projects. And so again, the Federal agencies need to intervene and help move these processes along.

I would say that we need to ask the question of whether or not our country is offering the best possible resources we can offer to make science an attractive career for young people. I question that. I am not really sure. We can discuss that later if you would like. But I think having those resources is critical for a segment of the population.

There is a segment of the population that goes into science that will be scientists no matter what you do, okay, so you don't need to do anything for those. But there is another segment that are undecided and they make selections about business careers, legal careers, medical careers, different careers, and going that pathway for accidental reasons sometimes or just because the right opportunities are not presented to them at the right time. So that is where we have to look, because I don't think we have just the large—we do not have the right number of people, of bright young people in this country going into science and engineering careers right now.

Business as usual will not do. I mean, to go after this particular objective that I have described to you. Thank you.

The CHAIRMAN. Thank you, Doctor.

Mr. Lizotte?

Mr. LIZOTTE. Good morning, Senator Gregg and Senator Murray. I appreciate this opportunity to come here. I am definitely very intrigued by a lot of the work that is happening.

I dealt in the area of practical, bring-it-to-the-market kind of areas and my discussion will be from a small business perspective,

some of the areas that we do in micro as we are transitioning and looking toward a future for nanotechnology.

One of the things, I will just introduce our company in general, what we see as transitioning from micro to nano, some of our products in homeland security and defense, and some of our traditional markets over the years, and I will end it with some closing statements.

NanoVia, I am the Vice President of R&D at NanoVia, and typically where we operate is we operate from the point of looking out into the universities and in the national labs and looking for opportunities, and that is when materials are created, when processes are created, even if in the basic scheme of things. A lot of the technology we deal with here is for micromachining or microengineering, microfabrication is technology that came out of the microelectronics industry. What we are doing is adapting it to applications which can be commercially viable.

Now, those commercial applications can be things as simple as computers. One of the areas that we focus on is the efficient attachment of chips, computer chips and processors to chip carrier devices. Also, in the area of microfluidic delivery, including catheter delivery, schemes for delivering drugs or therapeutic drugs, and also our latest technology stuff in pulmonary drug delivery.

Our services, once again, are geared toward the research, process, and equipment development within our marketplace, which is micro systems, or microelectromechanical systems and passive mechanical micro devices.

Some of the images you can see which we always throw up for scale purposes, the upper image there is a human hair with small sections cut out of it using our particular laser technology, and where you can see that, we can create very high finesse cuts through different materials without damaging the surrounding structure.

One of the things I like to do with talking to people about scale, especially when you are talking microtechnology and nanotechnology, is to say that in the micro scale, one micron is equivalent—if you look at a human hair is about 100 to 150 microns, whereas a nanometer is one-80,000th of the diameter of a human hair. So it is a very broad scale.

Now, as far as commercial development in nanotechnology from a small business perspective or getting it out into the commercial area, it is going to be a long coming. There is not going to be anything super-substantial in the new few years, other than maybe in the bio areas. But we do see some things, especially in materials, that we are interested in. We are looking at materials that can withstand, as was said earlier, different environments and utilizing that material in our processes.

One of the things that we kind of look at microtechnology is we say micro is the new macro for the United States. The traditional manufacturing of welded assemblings and stuff of that nature is really getting shipped offshore. Even from 1999, when we started out, we were developing a process to triple the throughput of chip packages for laptop computers and we really thought we had something. We pushed it forward and built a tool and what we found was all of the market between 1997 and about 2000 shipped to Tai-

wan and China. So with that much manufacturing overseas, we saw, well, there is probably not too much opportunity for us to build equipment in that area, so what we end up doing is licensing that technology, and we ended up licensing that technology to a Japanese concern.

But we doubled back and we focused on things that we felt were key areas where we could see a potential for manufacturing in the United States, and the areas we see, of course, are medical device and diagnostics, some of the microwave components or communications components and high-value-added products. We still see these being competitively built in the U.S. and we see a market there for us in the future.

One of the things that Dr. Stupp had talked about, which we are also very—we say is very important, is—we call it a multidiscipline education. One of the things that is interesting about engineers is that when engineers enter into a workforce, typically, they go into a company and they might have one discipline, myself as a mechanical engineer. But I entered into an organization which demanded that I know optics and I know lasers.

So what ends up happening is in that kind of an environment where profitability and you get delivering to the customers there, you learn those disciplines and you learn them rapidly. And over a short career of 10 years, you might also dabble in electronics or electricity for some applications or even semiconductor processes. So what happens is that in the manufacturing environment, we are creating engineers and manufacturing engineers who have multiple disciplines, and also in chemistry and such of that nature.

So we see ourselves as a small business and as a growing business in this market as being the facilitators of taking the technology that is developed in the laboratories and the universities and actually applying them to potentially commercial products.

Now, a lot of the things that we have been working on in regards to products, like I will just say from 15 years ago, you know, we started drilling holes in small devices for ink jet and now we are drilling—and those holes are anywhere from 100 microns to 75 microns, around the diameter of a human hair, and now we are drilling one-micron holes to facilitate the atomization of pharmaceuticals that can be delivered down into the deep lung.

What we see with the micro to nano is an opportunity for us to really stake a claim in this new market that is coming out, and what we see is one of the things that is a big barrier to some of the foreign competitors, specifically in the Far East. We tend to say that they operate in a herd mentality, which is typically an engineer or staff engineer within a facility, there will be ten people applied in the manufacturing floor to solve one problem.

I personally have consulted in Taiwan and I have seen this happen, where it takes them a long time to—and that is because they do not operate the same way we do and they also don't have a multidiscipline ethic in regards to when they get into the workforce. They only want to do their one job, and I see that as a benefit in regards to our competitiveness.

As far as this market, we see opportunities in new capital equipment requirements. As has been discussed, we only recently have been able to see down to an atomic level. That gives us the poten-

tial of actually developing the new tools that are coming out and I think we might have a strategic advantage there. Those tools can be built by companies like ourselves. Once the basic science has been done, we can apply it and productize it and bring it into the market.

One of the other things that is key in all these markets is U.S. companies hold a significant market share in most of the diagnostic aspects, in microelectronic ICs and communications devices. So I see that we have a strong position.

Here are some applications that we are doing in regards to the homeland security and defense. Off to the side, you can see this one micron diameter hole. To drill a one-micron hole is pretty easy if you do one. We do a thousand every second and multiple—we have a system which does even more than that every quarter of a second and we do it to a six sigma level, which basically is about one defect per million. That is a requirement, especially for drug delivery, because you can't have a situation in which someone tries it and it fails, especially if you are delivering maybe something therapeutic that they need immediately, say for diabetes or something like that.

We are working on some other applications in regards to making microstructures and even nanostructures. In our world, we look at nanostructures from our perspective at below a micron. So one micron is 1,000 nanometers, you know, a tenth of a micron, in that range, 100 nanometer range is really what we are calling our nano at this level at this point. And one of the things we are doing is structures for different types of ID, holographic ID for anti-counterfeit technology, and also some military applications for tagging military vehicles to identify them as friend or foe from aircraft and such, some interesting optical technology.

This is an example which I talk about in regards to pulmonary drug delivery and where I see that there is a potential here to kind of revive some of our traditional manufacturers. One of the things is we have an opportunity in some select areas to work on machine technology and get a foothold in there, process technology in regard to how the things are processed, the assembly technology, and in this case, we are talking about some traditional lamination and application which is done by people like make paper and such. But if some of these traditional corporations could transfer over into these newer areas, they could find newer markets and maybe higher value added markets, which could help them out and transition from old technology.

And then, of course, product technology. That is where the key is. You can have one element of it, but if you are selling the product, then you are talking about true manufacturing, and then, of course, down to the end user.

Some of our traditional markets, I already talked about, microelectronics packaging, single-dose commercial pulmonary drug delivery devices, which we look at potentially third-world medical applications for giving a lot of these countries the ability to do immunizations and stuff of that nature without very complex delivery systems, holographic and defractive optics, and fluid metering, which includes ink jet, because that is always a good market out there for us financially, but bio analysis. We do a lot in regard to

micro channel plates and some advanced stuff that we call "lab on a chip," and maybe even create devices which these people could use in regards to their work, basically, create devices which allow them to do their work easier or faster and such.

In closing, one of the things that we have been thinking about is what is the role of government in regards to small business. The Small Business Innovative Research grants are very interesting vehicles. Our experience with them, though, is that even if you get through the first phase, you are not going to get through the second phase. There is a potential you won't get to that second phase. And the thing is, is that a lot of the times, you will see a lot of these programs don't go past the first phase.

In a small business environment where we are looking at—where we have technology, we believe in our technology, and if we show a track record of success with our company, one of the things is we don't see the SBIR program as being very attractive, because what it does is it maybe gives you one piece, but it doesn't guarantee you to bring it to the next level of marketing it.

We are trying to see if there is a potential of talking about things where it is a small business entrepreneurial grant, where we are talking about something where we do have a product, or we have something which is maybe out of the laboratory which is fundamentally there but needs to be productized and is maybe a higher level of potential success.

The SBIR first phase grants are about the same level of risk. Our feeling is if there is a potential link, commercial entity, to one of these programs where it is just at the cusp of being productized, that would probably allow us to bring it into the mainstream and apply it. It is one thing that we are thinking of looking at.

And we look at these grants, looking at funding different levels of where these products come out.

Another area is a multiindustry alliance grant, and this would be something we have been contemplated and which we currently do without Federal funding, and that is we look for traditional manufacturers who maybe are, say, a molding company, and they are very good at what they do and they have very highly skilled or a highly-skilled workforce, but we need micro molding. And what we do is we introduce to them the micro molding concept, which gives them an entry into this market they have never even been exposed to. If there was a way in which we could look at some type of funding to bring certain products out this way, where we maybe link these different traditional manufacturers, maybe in different regions of the country and different disciplines and try to bring it together to maybe bring them into this new type of technology.

One of the things that, I think just as a final note, is that unless you have a workforce that can handle this type of technology, even if you develop it, you just can't bring it to market from a product level. One of the things that we have now is even with some of the students and stuff that are coming into the workforce is they just don't have the background in microtechnology, and now we are talking about nanotechnology. There is definitely a shortfall, as Dr. Stupp was talking about, in regards to their education and their ability to adapt into a micro world when they were educated at a macro level. That is definitely something.

We typically see about a three-year—we bring in an engineer, it will take them about 3 years to bring them up to speed on the process and the technologies that actually exist, and they are always changing. And that is if we keep them, we can retain them, because there are always opportunities being put forward.

That is all I have to say.

The CHAIRMAN. Thank you. It is especially interesting because of the basic technologies, which I think is a key issue for us as a Nation, so I appreciate that.

[The prepared information of Mr. Lizotte may be found in additional material.]

The CHAIRMAN. I was just wondering, these were excellent presentations and gave me some strong background here, I am sure Senator Murray, too, and these records will be available to others. But I am wondering, Dr. Stupp, you mentioned the regeneration. If you are a person out there today who has a spinal cord injury, that is exciting news, but is it realistic news? I mean, what is the time frame here when we move from the dream to some form of actual reality, if there is such a time frame that is predictable?

Mr. STUPP. I think—well, it is probably reasonable to say that this might happen in, say, 10 years, maybe five to 10 years. Five would be very optimistic, but I think it is reasonable within 10 years.

However, the discovery by definition is not predictable and there could be breakthroughs that will accelerate the process. I think that it would probably come in stages, and so even earlier than 10 years, we may see very small steps that can be taken to at least return some motion to paralyzed individuals. Maybe they won't have a normal life, but it will be slightly better than it is today.

The CHAIRMAN. And, Dr. Schloss and Dr. Dehmer, what should we do in the area of funding? Is it more funding or is there more focus? Should we reorient programmatic activity to accelerate Dr. Stupp's dream here, which appears to be just over the horizon?

Dr. SCHLOSS. One thing I would like to see us do is to be careful not to too narrowly focus the funding. The things that Dr. Stupp is describing, I think he has pointed out, rely on discoveries from many different areas, and we don't know exactly which of those areas the solutions are going to come from.

I think what we want to do is encourage, as several people have said, teams of investigators who bring expertise from a lot of different areas to be working together, to be communicating effectively—not just working in the same physical space, but communicating, so they can bring all of these ideas together.

That is why a number of us have developed funding mechanisms and new programs that may not specifically focus on nanotechnology, but focus on solving important problems in biomedicine. That said, sometimes those targeted on a medical problem funding approaches can tend to—what you end up funding might be the most obvious next step toward solving a problem. We have to be really, really vigilant about keeping an open mind to leaps forward.

So that is, I think, one of the big challenges for the agencies, is how to balance these various needs, where we have people who—your question implied, I have the spinal injury now, or my daugh-

ter has a spinal injury now. I want to see a solution to that. We have to balance the very obvious near-term research with the things that may not come out for 10 years.

So it is challenging. I mean, obviously, more money is always great.

The CHAIRMAN. Well, do you think there is a structure in place at various NSF, NIH energy that is allowing for that sort of more global view, or is there something that needs more attention?

Dr. SCHLOSS. I think there are things in place, and we are also very aware that it needs more work.

Ms. DEHMER. I am going to agree with everybody. More seriously, I think what we are seeing is an evolution in the way science is done. When I was in school and when my colleagues were in school, we very rigidly fell into a chemistry department or a physics department or a material science or a biology department. The entire science structure of the Nation, and that includes the universities, the Federal laboratories, and the funding agencies, have to recognize that the problems are no longer defined by these tidy departmental names.

We have seen an evolution, no question about it. Sam is tenured in how many departments?

Mr. STUPP. Three.

Ms. DEHMER. Three. And what are they?

Mr. STUPP. Chemistry, medicine, and material science.

Ms. DEHMER. And we are going to be seeing more of those kinds of things. We are going to be seeing more students cross-train, speaking a language that they didn't speak in individual departments.

This is happening. Science is a pull that drags universities and Federal laboratories and funding agencies along. But in addition, the institutions and the funding agencies have to recognize what is happening and be a push, as well. It is happening. It will happen naturally, but everybody has to recognize that it needs nurturing.

The CHAIRMAN. I think Mr. Lizotte's point also is—and certainly Dr. Stupp's point—is that you can't do it without human capital coming up.

Mr. STUPP. Right.

The CHAIRMAN. Is this technology so advanced in its need for academic background that it makes it impossible, for example, for us to educate average workers, people who are coming through the system through a technical college system, to be contributors to the manufacturing side, or does it gradate out like other sciences?

Mr. STUPP. Well, I think that certainly we will have to educate workers on the manufacturing side, because once nanotechnology is implemented in many products, there will be certain procedures that have to be used. Clearly, that kind of—that group of individuals is not going to be the one making discoveries.

The CHAIRMAN. Right.

Mr. STUPP. So yes, there will be need for education at many different levels as the new technologies get implemented. But I think the most important one right now, in 2003, if we think about how we move forward, is to ask ourselves if we are doing everything we can to encourage—to make science an exciting career for young people. I mean, we need to ask that question very seriously.

I think the NSF, for example, does a lot of great things, but they don't have very much money. I mean, they spread themselves very thin and sometimes they are not effective because the resources aren't there.

The CHAIRMAN. Of course, a big element of that is economic return——

Mr. STUPP. Sure.

The CHAIRMAN. —which drives a capitalist society and draws people in. How far are we from Mr. Lizotte being able to execute on your ideas and initiatives in the nano area?

Mr. STUPP. Well, I think the nano area very much needs the start-up company model to move forward, and I think you are beginning to see this culture develop. It is very difficult right now, with some exceptions, to think about the right R&D programs in the traditional large companies of this country. I think these technologies need to move out of the laboratory into very small start-up companies that then slowly receive more and more investment and then eventually are acquired, perhaps, by the larger ones, and then products will be developed that way.

I think the start-up company culture is very important in nanotechnology and we should do everything we can to promote it. It also creates employment. It is very exciting employment for our Ph.D. students, for example, because they are not excited about going to the large—I don't want to use specific names of companies, but we all know which ones those are—they are not excited about those jobs because they know they are going to be there solving problems about existing products and they find that boring and not challenging. Twenty, 30 years ago, they went to those companies to do research and to introduce innovation and produce new products. That opportunity really isn't there for them anymore.

So the start-up company takes a bright Ph.D., entrepreneurial students and keeps them on that mold, and that has a very, very positive impact. So it is a source of employment and a source of wealth, because eventually real development takes place in those start-up companies.

The CHAIRMAN. And Mr. Lizotte made some good suggestions there. Did you have a comment?

Mr. LIZOTTE. Yes, I have a comment in regards to—as just a perspective. In the micro world, it was easy for me to transfer into, back in the mid-1980s, in from a macro education into the micro world very easily because there was the equipment was already in place. All we were adapting was the existing infrastructure in the semiconductor and microelectronics industry, and that had 60 years worth of development in the equipment end and the device end.

I think we are at the—my belief, we are at this same situation as these discoveries that are happening, and sorry for this terminology, and maybe at a test tube level or chemistry level, where the thing is, is that the problem is those tools don't exist. You don't have the equipment in place. So what is happening is you are making discoveries, but then you are saying, okay, well, how do I scale this up and make it profitable? How do I make it into a product and such? And that is the problem.

Back when I came into this marketplace, there was a full established discipline, so I could read and I could train and I could work on that equipment and come up to speed very rapidly and make my own discoveries over the years. In this case, there is no equipment. It is you have got a discovery and you are struggling now with how am I going to scale this up, and I see that as a big issue because the new people coming in that might have some micro background don't have any equipment to jump on and focus on the manufacturing end of it. So I think it is going to be difficult, the translation of this stuff back into industry. Maybe in the bio area, which there is a lot of equipment out there in the bio area, but nanotechnology as applied to maybe all the other markets, like materials and stuff of that nature, I think it is going to be a hard time to ramp up and bring into the marketplace.

Mr. STUPP. And that is exactly where I think the—why the start-up companies are so important.

The CHAIRMAN. Doctor, you were going to make a point, Dr. Schloss?

Dr. SCHLOSS. No, it is past.

The CHAIRMAN. OK. Unfortunately, we are going to have a vote here in a minute, but let me ask one more question. To what extent are we going to get down the road here 3 years and you are going to have that capability of actually saying to somebody, well, we can cure something very significant, whether it is spinal or cartilage or whatever, and we run into an ethics problem? To what extent is that a potential, and if it is a potential, how should we try to anticipate it and avoid it?

Mr. STUPP. Your question is about, are we going to run into an ethical problem.

The CHAIRMAN. Right.

Mr. STUPP. It is not clear to me that there would be an ethical problem. I think the only problem that I can see would be related to the cost of the procedures and whether the population at large would be able to afford them. I mean, they will initially be relatively expensive procedures, and so I think affordability might be the issue.

The CHAIRMAN. Well, that is the issue throughout medicine today already.

Mr. STUPP. Exactly. But at the same time, if you have, let us say, joint disease, or if you have a spinal cord injury, the cost to the government of an individual being afflicted with joint or spinal cord disease is enormous. The cost of the new procedures that nanotechnology will bring will be minute compared to what we currently spend. So there will be a need to balance those two, but——

The CHAIRMAN. You don't see stem cell——

Mr. STUPP. Right. OK. The stem cell——

The CHAIRMAN. —a policy question here?

Mr. STUPP. OK. I would like to answer this way. Regenerative medicine procedures, advanced ones which are based on nanotechnology, will be possible with or without stem cells. Now, so there will be advances that will not require stem cells. They will be based entirely on nanotechnology.

There will be others that will require stem cells, and, in fact, many of them will require combinations of the two. So I think the

best solutions in the long run will be those that utilize nanotechnology and also look to stem cell biology. The combination of the two, I think will be the most effective.

The CHAIRMAN. You were going to say something, Dr. Schloss?

Dr. SCHLOSS. No, I really agree, a very good answer.

The CHAIRMAN. Are there any other points folks want to make on any of this?

Mr. LIZOTTE. Just one thing. I know there is a lot of debate and there was a lot of stuff in regards to this nanotechnology and a lot of books have been written and a lot of science fiction not involved in biotechnology. I have never feared technology. I always say that there are a lot of things that potentially can kill us out there.

I have been dealing with nano particles and stuff, debris from processes I have worked on for the last 15 years and there are safeguards and infrastructure in there in which to alleviate any of those concerns of small particles being ingested by humans and this, that, and the other thing.

You are always going to have situations where somebody does something wrong, but I think a lot of this technology is so beyond the groups that might use things like this for things that are maybe not so useful in society, but my feeling is a lot of this stuff is science fiction.

The CHAIRMAN. I agree with that. I don't see that as—I think that threat, although it is represented, there are so many other things that are very simple to do——

Mr. LIZOTTE. Right.

The CHAIRMAN. —that it would be unusual for somebody to pursue this.

Mr. STUPP. Senator Gregg, if I could just say one more thing, I think there is enormous hype about the dangers of nanotechnology. In fact, my community is trying very hard to eliminate that because the hype and the problem is really people that have, for some reason, and it is very difficult to understand where this exactly came from, where did it come from, but there is an enormous amount of hype about the dangers of nanotechnology. They are definitely not based on fact.

The CHAIRMAN. I think that is a problem the technology world has that we continue to see, whether it is genetically modified foods, which significantly improve production and reduce poverty and reduce hunger being stopped by people who think they are doing good, to science like this. We have to—I think as long as we are transparent about it——

Mr. LIZOTTE. Right.

The CHAIRMAN. —and aggressive in being transparent on science, that the average person is going to appreciate the benefits over any threat.

Mr. STUPP. That is correct.

The CHAIRMAN. The key is for us that are in the public policy arena and for you who are in the science arena to be constantly pushing transparency so that people can't make up conspiracy theories——

Mr. LIZOTTE. That is right.

The CHAIRMAN. —based on some information that they think is being hidden from them. And so that is why this hearing is, I think, useful and will be covered.

I congratulate you on the science you are doing. I honestly feel, and I think Mr. Lizotte made the point excellently, that we are not as a nation going to be compete with China in basic manufacturing. We are going to compete clearly in our capability of adding value, and where we are really going to be adding value is in breakthrough science activity, and this is clearly one of them and you folks are on the cutting edge, so you hold our future, not only from a science standpoint, but potentially from an economic standpoint, in your hands.

So please keep up the good work, and our committee is here to try to be supportive and helpful, and if you think there are things you need from the Congress, tell us. We want to react.

[The prepared statements of Senators Enzi and Murray follow:]

PREPARED STATEMENT OF SENATOR ENZI

Mr. Chairman, the application of technological advances in today's healthcare is one of the key contributors to the longer and healthier lives that most of us enjoy. Today's surgical techniques, for instance, make those of a generation ago look positively primitive. The current trend toward less invasive surgery allows people to recover from surgeries more quickly, which gets them back to productive pursuits more quickly, which is good for them, our economy and our society.

The application of nanotechnology in medicine has the same potential to move today's healthcare forward by leaps and bounds. Nanotechnology, however, is not the process of making current technologies smaller—it is the science of building completely new technologies at the molecular level.

Molecular devices will give us the ability to attack diseases and conditions cell by cell. Imagine if we were able to fight cancer, for instance, by targeting specific cells, instead of attacking broad areas of tissue. The possibilities are limitless.

In May, I visited Ireland with the U.S.-Ireland Alliance. During the trip, Congressman Xavier Becerra and I visited the Nanotechnology Center at Trinity College in Dublin and learned about some interesting areas of research.

One of these areas is nanofluidics—the engineering of fluid-carrying systems at ultra-small dimensions. Trinity College's physics and clinical medicine departments are collaborating in research on advanced nanofluidics instrumentation for applications in medical diagnostics and pharmaceutical industry.

From its research, the group at Trinity College has started a spin-off company that will be located for the time being in the "Innovation Centre" of the college. The company, known as Allegro Technologies, is specializing in the development of advanced instrumentation for high-throughput screening for applications that pharmaceutical company could use in the development of new drugs.

Interestingly, Trinity College screens its proposal for internal funding in two ways. The first is through traditional "peer review" to determine the most promising possibilities for advancing our col-

lective knowledge base. The second is through attempting to determine the potential business applicability of the research. By putting each proposal through both of these rounds of scrutiny, Trinity College demonstrates that it values basic research, but especially the type of basic research that can lead to product breakthroughs.

As we look at nanotechnology in medicine, we ought to ensure that both basic and applied research receive adequate attention. Traditionally, the National Institutes of Health and other federal agencies have funded business-oriented applied research through their Small Business Innovation Research (SBIR) programs. I understand that we are already funding applied nanotechnology research through SBIR grants to small businesses, and I support this, because our nation's risk-taking small businesses will probably develop many, if not most, of the major breakthroughs in medical nanotechnology.

I commend Chairman Gregg for convening this roundtable discussion, and I look forwarding to working with him and my fellow Committee members to make sure that the federal government plays an appropriate role in supporting the development of nanotechnology and its application in medicine and healthcare.

PREPARED STATEMENT OF SENATOR MURRAY

Mr. Chairman: I appreciate your efforts in putting together this HELP Committee roundtable to discuss the emerging opportunities presented through nanotechnology. The health care and job creation potentials for this field are truly exciting.

This innovative new technology provides new hope and possibilities for how we treat heart disease.

As all of my colleagues know, cardiovascular disease is the number one killer of men and women in this country. And in many cases, it is a silent killer.

Devices that offer the possibility of destroying cancer cells without surgery could both improve—and save—lives.

Federal support for developing this new technology must be comprehensive, coordinated and innovative.

We need to enhance and grow existing biomedical technology and infrastructure.

We need to ensure that federal agencies are "partners with the research community"—rather than competing for bureaucratic and regulatory turf.

To achieve new technology breakthroughs we must increase our support—particularly through appropriations to the research community.

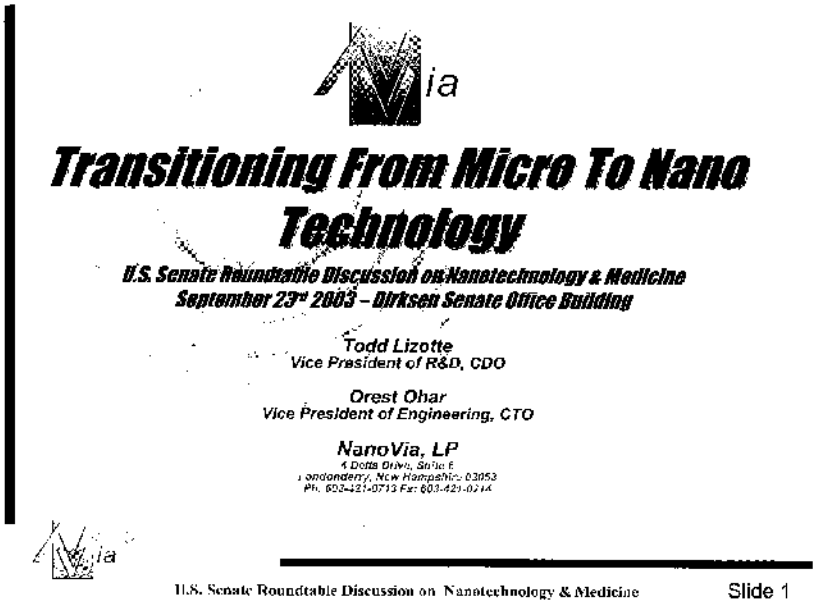
This is a huge public undertaking, but it will have huge rewards for health care and for high wage family jobs.

I appreciate the involvement of all of today's participants in this roundtable and thank them for their leadership in this area.

The CHAIRMAN. Thank you. We appreciate your coming by.

[Additional material follows.]

ADDITIONAL MATERIAL

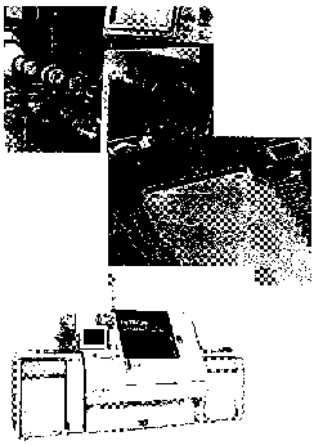


Agenda

- Introduction
- Transitioning From Micro To Nano Technology
- Homeland Security & Defense
- Traditional Markets
- Closing

Introduction

NanoVia -- Londonderry, NH



General Info

- Formed July 1999
- Focused On Emerging Technology For USA Competitive Advantage Within Microelectronics Packaging & Micro Systems Markets
- Product / Technology: Micro Machining, Micro Engineering, Nano Particle / Fluid Delivery and Diffractive/Holographic Optics

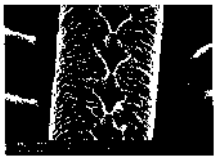
Products / Services

- Semiconductor and Microelectronics Manufacturing Systems (Licensing & Components)
- Medical Device Product Development Services
- Homeland Security and Defense Product Development

Transitioning From Micro To Nano Technology

Why should the USA be involved in Micro / Nano Technology

- **New Market Development And Growth in USA**
  - R&D, Component and Product opportunities with Micro
  - Medical Device & Diagnostics, Microwave and High value Added Products Still Competitively Built in USA (Key Markets)
- **Micro is the new macro for USA manufacturing**
  - Requires Skill and Multi-Discipline Education (USA Best At It)
  - Requires new capital equipment development (USA)
  - Broad based applications for military and homeland security an opportunity to fulfill national security needs and develop domestic manufacturing



Transitioning From Micro To Nano Technology

Technology Leap Opportunities: Micro To Nano

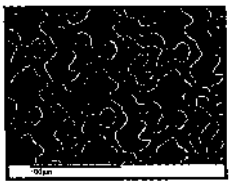
- USA Micro/Nano Market Entry Barriers For Foreign Competitors
  - Need For Highly Trained Skilled Workforce
  - USA is the Market for New Technology
- New Capital Equipment Requirements
  - Micro- Machining / Nano-Assembly / Testing Equipment
  - Process Equipment / Metrology (Microscopes)
- USA Companies Hold Significant Market Share
  - Medical Device and Diagnostics
  - Microelectronic IC Chips
  - Communications Devices

Homeland Security and Defense

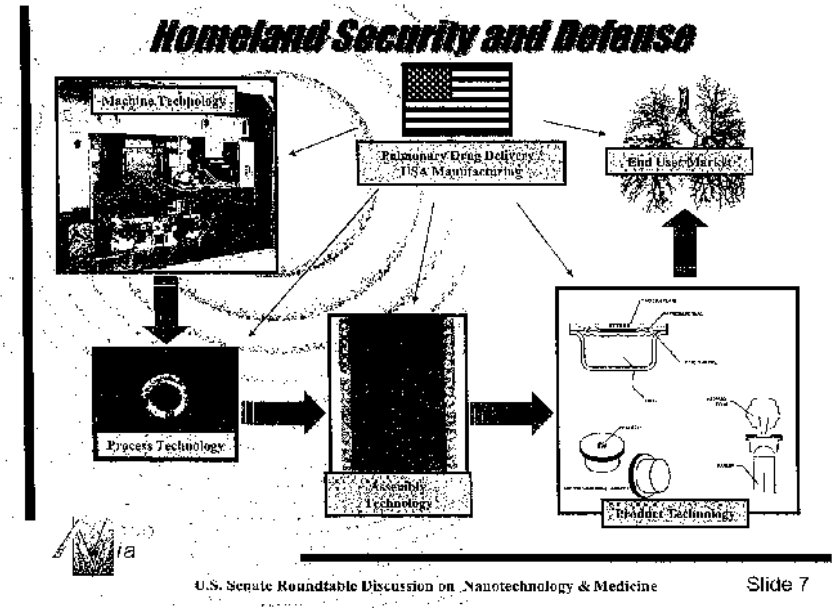
NanoVia Specific Focus

- **Passive Military Vehicle ID Tagging**
  - Retro-Reflective Device To ID Friend From Foe On A Battlefield
- **Single Dose Military Pulmonary Drug Delivery Device**
  - Atomizing Device For Pulmonary Drug Delivery On A Battlefield (Inhale To Deep Lung/ Chemical & Bio Warfare)
    - Sub-Micron Particle Generation / Disposable Device
- **Anti-Counterfeit Holographic ID Device For Passport, Resident Alien or Military Security ID Card Applications**
  - Encoded Hologram Technology To Make Counterfeiting Of Government ID Nearly Impossible For Terrorist Organizations
    - Encode Personal Info Or Specific ID Code Or Multi Wavelength Go / No Go ID.

Pulmonary Drug Atomizing Nozzle



Encoded Hologram / Micro & Nano Structures

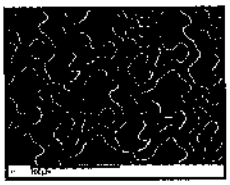

Homeland Security and Defense
Machine Technology
Pulmonary Drug Delivery
USA Manufacturing
End User Market
Process Technology
Assembly
Technology
Product Technology
U.S. Senate Roundtable Discussion on Nanotechnology & Medicine
Slide 7

Traditional Markets

NanoVia Markets

- **Microelectronics Packaging (Chip Packaging)**
  - Micro Hole Drilling
- **Single Dose Commercial Pulmonary Drug Delivery Device (Third World Medical Applications)**
  - Micro / Sub-Micro Hole Drilling
- **Holographic / Diffractive Optics (Telecom)**
  - Micro / Sub-Micro Structures
- **Fluid Metering**
  - Inkjet
  - Bio Analysis
  - Micro Extrusion Dies (Micro / Nano Fiber)

Pulmonary Drug Atomizing Nozzle

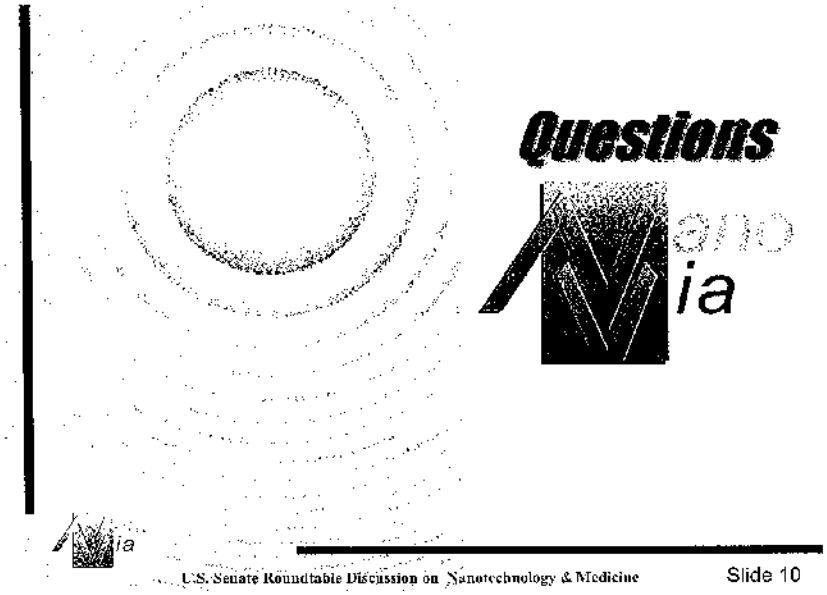


Encoded Hologram / Micro & Nano Structure

Closing

Government Role (Small Business) Micro to Nano Technology

- **Entrepreneurial Grants** (Small Business Entrepreneurial Grants)
  - Fund Companies Who Already Have A Product Prototype
    - Market Pilot Funding (Fund Product Development)
    - Market Intro (Fund Marketing / Business Development)
    - Scale Up (Pilot Manufacturing / Equipment / Raw Materials)
- **Multi-Industry (Multi-Region) Alliance Grants**
  - Grant Program Which Rewards Small Business Alliances Across Industries and Regions
  - Proposals Are From Alliances (Companies Who Will Work Together To Manufacture The Product)
    - Link Product Developer & All Manufacturing Companies Involved in The Manufacture, Marketing and Distributing of the Product.
    - Offers Companies an Opportunity to enter markets they never would have thought about. Transition old traditional market US manufacturers into new competitive markets.

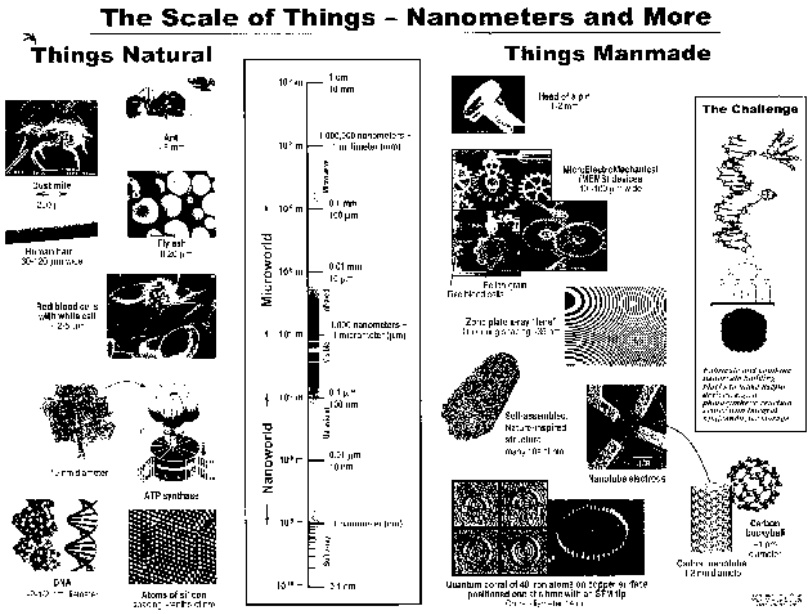

Questions
and
Nia
Nia
U.S. Senate Roundtable Discussion on Nanotechnology & Medicine
Slide 10

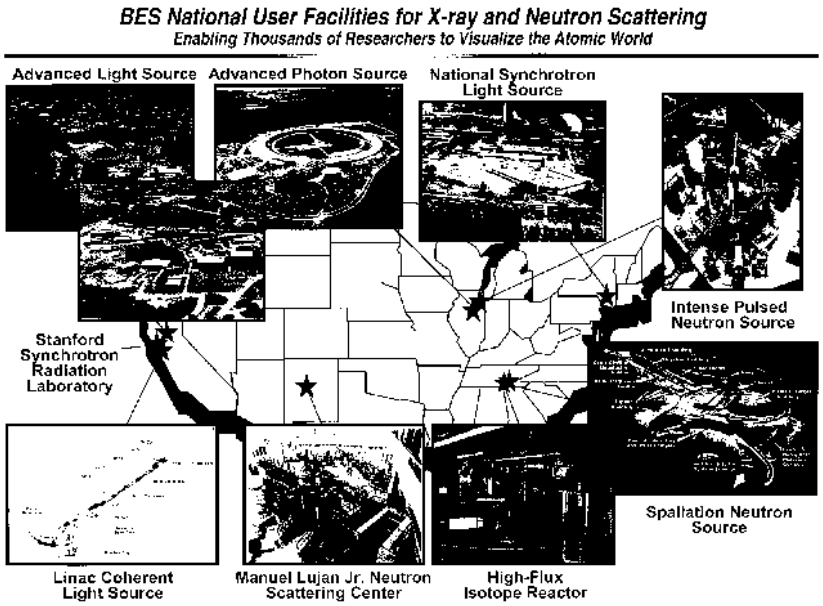
Office of Basic Energy Sciences
Office of Science
U.S. Department of Energy

Nanoscale Science and Technology in DOE's Office of Science

Presentation to:
Senate Roundtable Discussion on Nanotechnology and the Future of Medicine
U.S. Senator Judd Gregg
Chairman, Committee on Health, Education, Labor, and Pensions

Dr. Patricia M. Dehmer
Director, Office of Basic Energy Sciences (BES)
Office of Science
U.S. Department of Energy
23 September 2003


The Scale of Things – Nanometers and More
Things Natural
Things Manmade
The Challenge
Microworld
Nanoworld
ATP synthase
DNA
Nanotube electrodes


BES National User Facilities for X-ray and Neutron Scattering
Enabling Thousands of Researchers to Visualize the Atomic World
Advanced Light Source
Advanced Photon Source
National Synchrotron Light Source
Intense Pulsed Neutron Source
Stanford Synchrotron Radiation Laboratory
Spallation Neutron Source
Linac Coherent Light Source
Manuel Lujan Jr. Neutron Scattering Center
High-Flux Isotope Reactor

BES National User Facilities for Nanoscale Science

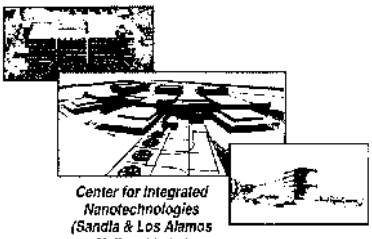
Facilities (under Construction) for the Synthesis, Characterization, and Study of Nanoscale Materials

Center for Functional Nanomaterials (Brookhaven National Laboratory)

Center for Nanoscale Materials (Argonne National Laboratory)

Molecular Foundry (Lawrence Berkeley National Laboratory)

Center for Nanoscale Materials Sciences (Oak Ridge National Laboratory)



Center for Integrated Nanotechnologies (Sandia & Los Alamos National Labs)

DOE Nanoscience Research is at the Intersection of the Bio & Physical Sciences

Example: Biomolecular materials – harnessing Nature's strategies in search of new materials and processes for innovative energy technologies

Biomineralization

Probing cellular processes: Single-molecule imaging and spectroscopics

Biosynthesis of Polymers

Biological Strategies to New Materials

Living Cells in Hybrid Materials Systems

BIOMOLECULAR MATERIALS

Hybrid Structures

Artificial cells

Cell based sensors

Energy transducing membranes/processes

Bio/Inorganic interface

Biomolecular Functional Systems

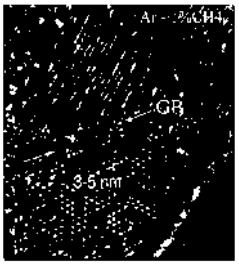
Pores, gates and channels

Artificial enzymes

Motors, switches

Fundamental Research Repeatedly Produces Surprises

Example: Ultrananocrystalline diamond (UNCD) – a versatile material with multiple applications



WHAT? Diamond film with 3-5 nm grain sizes and many outstanding properties:

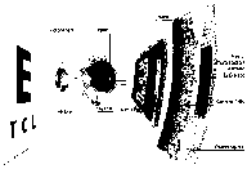
- Hard as natural diamond
- Low coefficient of friction
- Electrical conductivity can be varied by many orders of magnitude
- High field emission from micropoints
- Chemically inert
- Bioinert and biocompatible

WHERE? Developed at Argonne National Lab

BLUE RIBBONS? Yes. The inventors of UNCD won an R&D100 Award in 2003.

Electron field emission devices

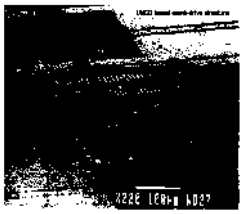
Artificial retina project



Participants:
5 DOE Labs (ANL, LANL, LLNL, ORNL, SNL)
2 Universities (USC, NCSU)
Private Company (Second Sight)

Hard, wear-resistant coatings

MEMS and NEMS devices



NIH Nanoscience and Nanotechnology Research

Jeffery A. Schloss, Ph.D.
Program Director,
Technology Development Coordination
National Human Genome Research Institute, NIH

Senate Roundtable
September 23, 2003

BECON

Nanoscience and nanotechnology refer to
research and development
at the atomic, molecular, or macromolecular levels,
at a scale of about 1 – 100 nm,
providing a fundamental understanding of
phenomena and materials at this scale and
creating and using structures, devices and systems
that have novel properties and functions
because of their small size.

Unique opportunities

BECON

1. Nanotechnology operates at the same scale as biological processes, offering an entirely unique vantage point from which to view and interact with the fundamental biology of life.
   - Most other technologies require the study of large numbers of molecules purified away from the cells and tissues in which they actually function; nanotechnology will offer ways to study, quantitatively, how individual molecules and assemblies of molecules work inside of cells.
   - Those studies at the nanoscale will enable understanding of the *design* of biological systems and processes.
   - That knowledge of component and system design is needed for, and will emerge from, quantitative modeling of biology.
   - The design information will change the way we think about biology and medicine. Moreover, it will have implications for materials and systems design that have nothing to do with biology ("biomimetics").

Unique opportunities - 2

BECON

2. Materials, devices and tools currently emerging from other disciplines provide opportunities to approach the study of biology and disease mechanisms, and the diagnosis and treatment of disease, in powerful new ways:

- miniaturization (but that's only the beginning…)
- sensitivity
- selectivity
- new concepts

NANOTECHNOLOGY RESEARCH AT NIH

BECON

Nanotechnology Research at the NIH
is coordinated through the
NIH Bioengineering Consortium
BECON

NIH BIOENGINEERING CONSORTIUM (BECON)

BECON

BECON MEMBERS

NIH-OER	NCRR	NIAMS	NIEHS
NIH-CSR	NEI	NIBIB	NIGMS
NIH-OIR	NHGRI	NICHD	NIMH
NIH-CC	NHLBI	NIDA	NINDS
NIH-ORS	NIA	NIDCD	NINR
NIH-CIT	NIAAA	NIDCR	NLM
NCI	NIAID	NIDDK	*DOE NSF NIST*

NIH BIOENGINEERING CONSORTIUM (BECON)

BECON

BECON Symposia: Guiding the Science, Guiding the Programs

Bioengineering: Building the Future of Biology and Medicine	February 27-28, 1998
Biomedical Imaging: Visualizing the Future of Biology and Medicine	June 25-26, 1999
Nanoscience and Nanotechnology: Shaping Biomedical Research	June 25-26, 2000
Reparative Medicine: Growing Tissues and Organs	June 25-26, 2001
Sensors in Biological Research and Medicine	June 24-25, 2002
Catalyzing Team Science	June 23-24, 2003

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

NIH supports nanoscience and nanotechnology research in the context of many programs.

While in some of those programs/projects, the focus may be on the nano-research *per se*, in other cases the nano-research may be a component of a larger project with broader goals....

Several examples are provide here, to demonstrate support for the breadth of potential applications of nanotechnology for understanding, diagnosis and treatment of disease.

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

Program announcements issued through BECON:

- Nanoscience and Nanotechnology in Biology and Medicine
- Bioengineering Nanotechnology Initiative (SBIR)
- Exploratory/Developmental Bioengineering Research Grants
- Bioengineering Research Grants
- Bioengineering Research Partnerships
- Mentored Quantitative Research Career Development (K25)

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

Basic Research, Instrument Development

Single Molecule Detection and Manipulation

- http://grants.nih.gov/grants/guide/pa-files/PA-01-049.html
- http://grants.nih.gov/grants/guide/pa-files/PA-01-050.html

Technology Development for Biomedical Applications

- http://grants.nih.gov/grants/guide/pa-files/PAR-03-075.html

Sensors

Innovative Technologies for the Molecular Analysis of Cancer

- http://grants.nih.gov/grants/guide/pa-files/PAR-01-104.html

Technologies for Saliva/Oral Fluid-Based Diagnostics

- http://grants.nih.gov/grants/guide/rfa-files/RFA-DE-02-002.html

Tissue Engineering

Functional Tissue Engineering of Musculoskeletal Tissues

- http://grants.nih.gov/grants/guide/pa-files/PA-02-014

Novel Approaches to Corneal Tissue Engineering

- http://grants.nih.gov/grants/guide/pa-files/PA-02-053.html

Disease and Syndrome Research

Cutting-Edge Basic Research Awards (CEBRA)

- http://grants.nih.gov/grants/guide/pa-files/PAR-03-017.html

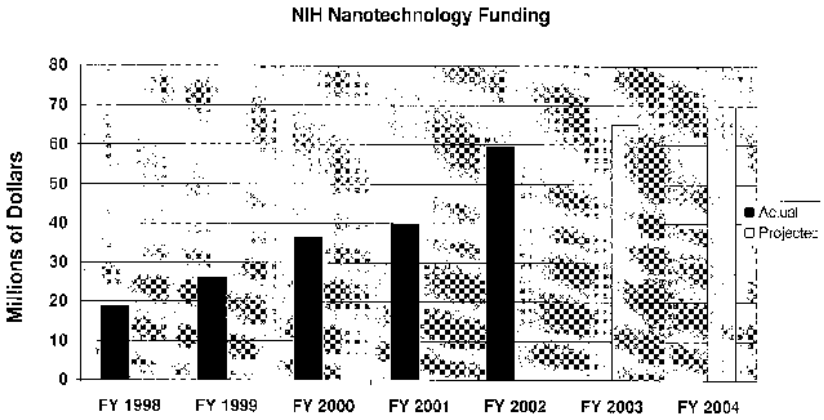
Diagnostics & Therapeutics

Novel Technologies for *in vivo* Imaging

- PAR-03-124 and -125 http://cancer.gov/bip/

Development of Novel Drug and Gene Delivery Systems and Devices

- http://grants.nih.gov/grants/guide/rfa-files/RFA-EB-03-011.html


NIH Nanotechnology Funding
Millions of Dollars
80
70
60
50
40
30
20
10
0
FY 1998
FY 1999
FY 2000
FY 2001
FY 2002
FY 2003
FY 2004
Actual
Projected

NANOTECHNOLOGY RESEARCH AT NIH

BECON

NIH goals for NNI

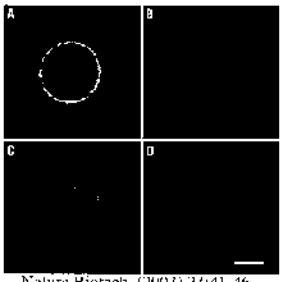
are exemplified in the

Grand Challenge for Healthcare

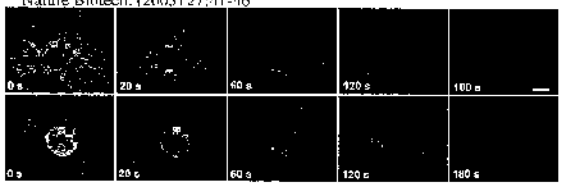
National Nanotechnology Initiative (NNI) Grand Challenge for Healthcare

BECON

- Detecting Disease *Before* Health Has Deteriorated
  - Imaging
  - Sensors
- Implants to Replace Worn or Damaged Body Parts
  - Controlling interactions of synthetic and inorganic materials with the body, for effective integration
- Delivery Of Therapeutics
  - Particle Size
  - Targeting
- Research Tool correlates of the above



Nature Biotech. (2003) 21:41-46



QUANTUM DOT CORP.

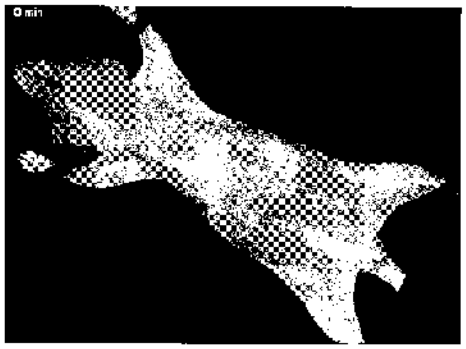
Marcel Bruchez, Ph.D.

Semiconductor quantum dots are being developed for use as probes for intracellular structures. In this study, they were used to label the breast cancer marker Her2 on the surface of fixed and live cancer cells, to stain actin and microtubule fibers in the cytoplasm, and to detect nuclear antigens inside the nucleus. Quantum dots offer several advantages over the organic dyes typically used for comparable studies.

QUANTUMDOT

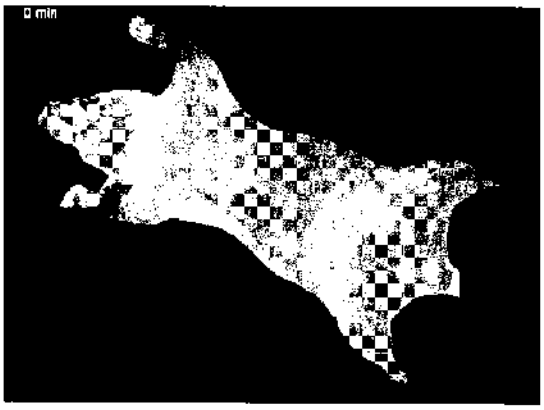
NATIONAL CANCER INSTITUTE

CARNEGIE-MELLON UNIVERSITY
Molecular Biosensor and Imaging Center
Alan S. Waggoner, Ph.D.



Timelapse: Mouse injected with methoxy-PEG700-Qdots

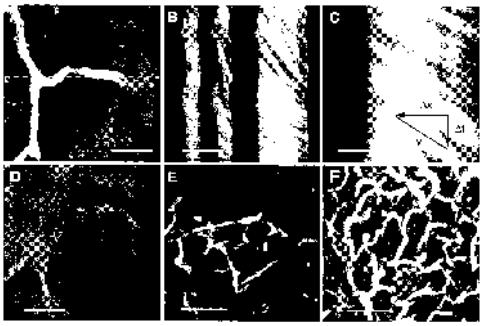
Carnegie Mellon



Timelapse: Mouse injected with methoxy-PEG5000-Qdots

CORNELL UNIVERSITY
Watt W. Webb, Sc.D.

QUANTUM DOT CORP.
Marcel Bruchez, Ph.D.



Semiconductor quantum dots were imaged by multiphoton microscopy through the skin of living mice. Blood flow velocity and heart rate (from undulation of the capillary wall) could be determined through the skin.

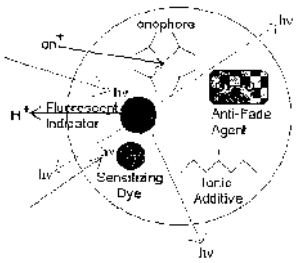
No adverse effect on the mice was observed (the mice are being maintained to investigate long-term Qdot toxicity).

Larson, D.R., et al. Science (2003) 300: 434-1436.

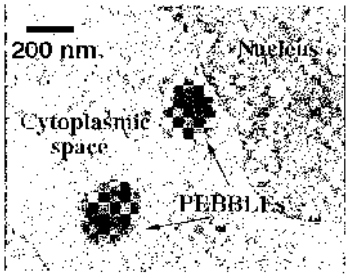
UNIVERSITY OF MICHIGAN

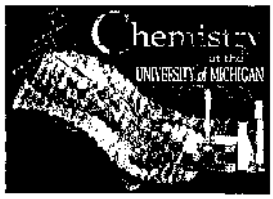
Raoul Kopelman, Ph.D.

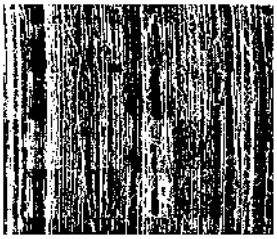
The objective is to produce optical nanosensors for direct, real-time chemical imaging of cellular membranes and intracellular processes. These sensors will monitor pH, calcium, magnesium, sodium, potassium, chloride, oxygen, nitrite, nitric oxide, carbon dioxide and glucose.



PEBBLE (schematic composite) liquid polymer





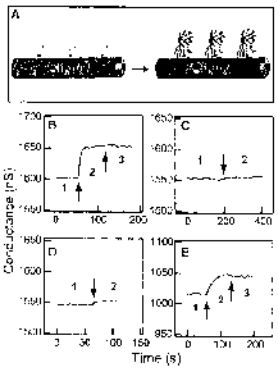


NASA AMES RESEARCH CENTER

Meyya Meyyappan, Ph.D.

NASA Ames Research Center

Carbon nanotubes (CNT) exhibit unique electronic and extraordinary mechanical properties. Ames has grown CNT, only 1 nm in diameter in the form of films and aligned bundles, and is currently making an effort to grow vertical tubes of controlled length for sensor development. The tip of the nanotubes will be functionalized with appropriate probe molecules for diagnostics. A prototype catheter will be developed which would permit detection of specific oligonucleotide sequences that serve as molecular signatures of cancer cells.



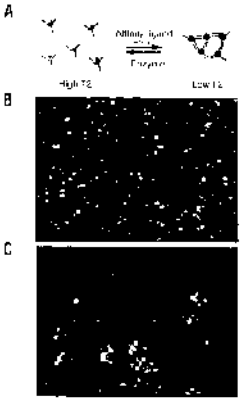
Real-time detection of protein binding: biotin-modified SiNW and subsequent binding of streptavidin (drawn approximately to scale). (B) region 2 corresponds to the addition of 250 nM streptavidin, (E) 25 pM streptavidin.

Y. Cui, Qingqiao Wei, Hongkun Park, Charles M. Lieber.
Science (2001) 293:1289-1292.

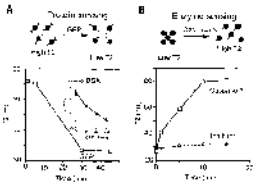
NANOSYS, INC.

Robert Daniels
Chunming Niu

Nanoscale materials such as nanotubes and nanowires (20 nm diameter) can act as field effect transistors (FETs) at room temperature. NanoChemFET works because the conductive properties of nanowires are modulated by charges on the analyte molecule that act like a gate voltage in a conventional field effect transistor. Biosensors based on FETs would be sensitive, specific, and quantitative; they would not require complex instrumentation such as is typically used for fluorescence detection, and analytes need not be labeled. Two SBIR grants support development of FETs for detecting specific nucleic acid sequences and proteins.

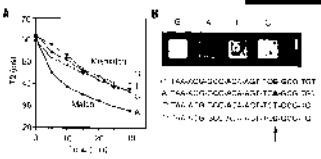


Nature Biotech. (2002) 20:8:16-820

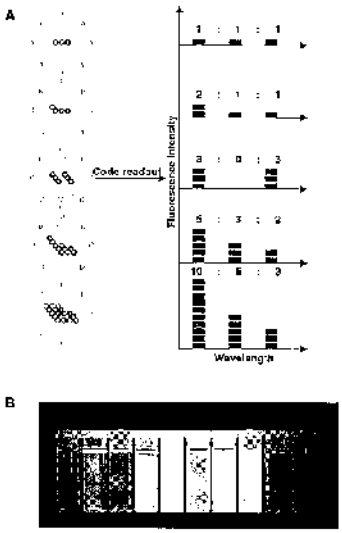


MASS. GENERAL HOSPITAL

Ralph Weissleder, M.D.

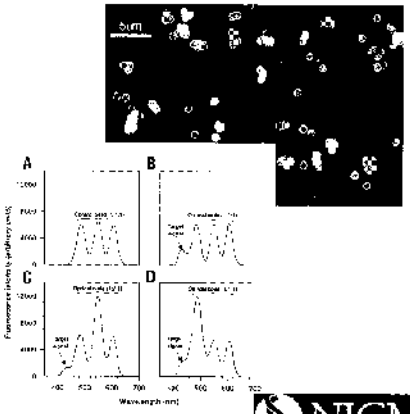


Molecular relaxation switches are being developed as probes of molecular interactions. Superparamagnetic nanoparticles assemble into complexes in the presence of binding targets, and complexes disassemble in the presence of enzymes. The signal may be detected by magnetic resonance imaging in turbid media and in whole-cell lysates, and may be useful for *in vivo* imaging.

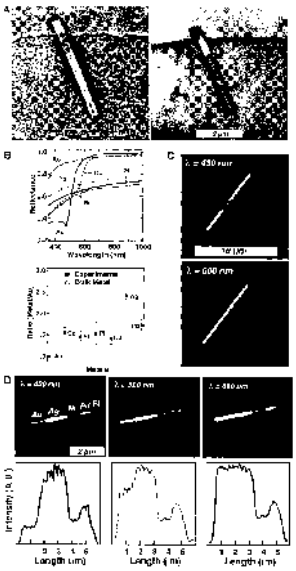


Nature Biotechnology (2001) 19:631-635

GEORGIA TECH
Department of Chemistry
Shuming Nie, Ph.D.

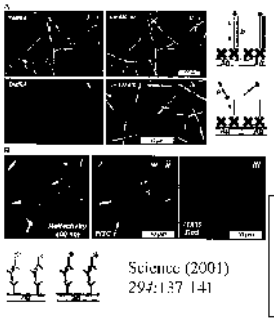


NIGMS



PENNSYLVANIA STATE UNIV.
Christine D. Keating, Ph.D.

SURROMED, INC.
Michael J. Natan, Ph.D.



PENNSTATE

SurroMed

NIST ATP award to develop high multiplex SNP screening using Nanobarcodes™ with Calida Genomics

Science (2001) 294:137-141

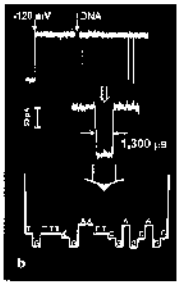
Submicron metallic barcodes for high throughput DNA and protein assays.

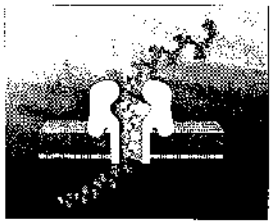
UNIV. OF CALIFORNIA SANTA CRUZ

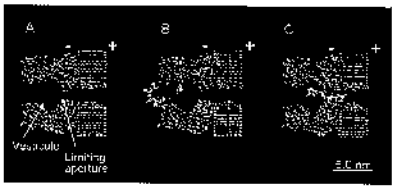
Department of Chemistry & Biochemistry
David W. Deamer, Ph.D.

UC SANTA CRUZ

Single-stranded nucleic acid molecules passing through a nanometer-sized pore modulate the ionic conductance across the membrane. This observation may one day lead to a device for single molecule DNA sequencing.

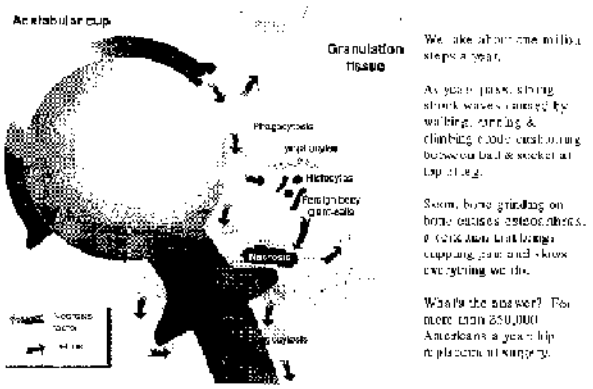






NATIONAL HUMAN GENOME RESEARCH INSTITUTE

Total Hip Replacement - Osteolysis



We take about one million steps a year.

As years pass, strong shock waves caused by walking, running & climbing cause crushing between ball & socket at hip joint.

Soon, bone grinding on bone causes osteoarthritis. A condition that brings crippling pain and stops everything we do.

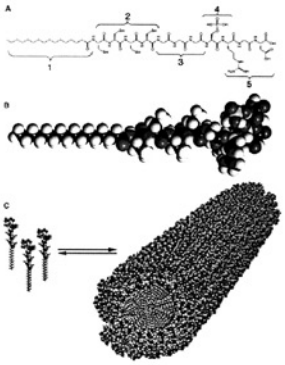
What's the answer? For more than 350,000 Americans a year: hip replacement surgery.

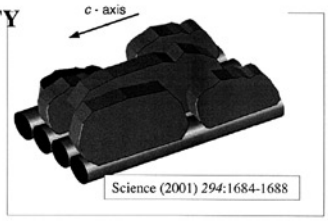
Provided by Dr. Tony Tomsia, Lawrence Berkeley National Laboratory (LBNL)

NORTHWESTERN UNIVERSITY

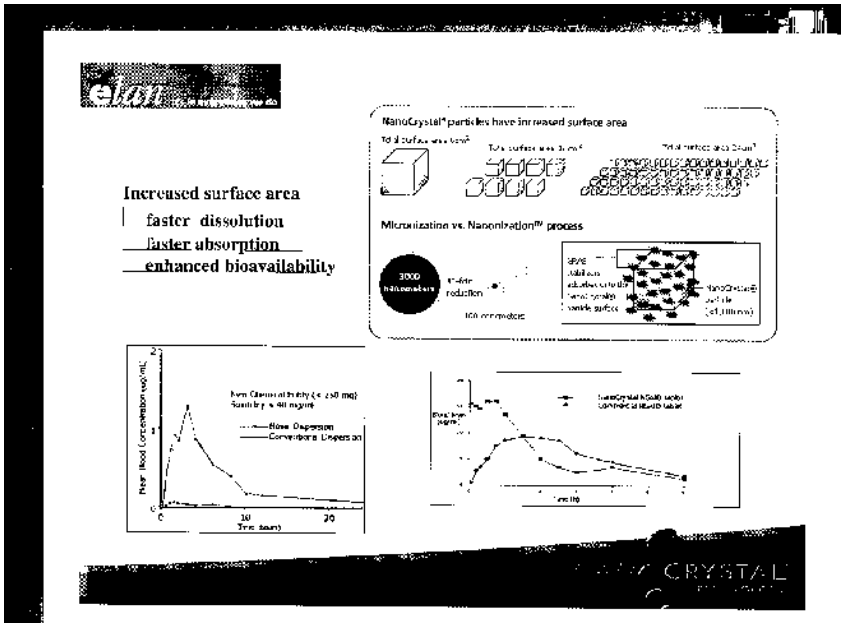
Samuel Stupp, Ph.D.

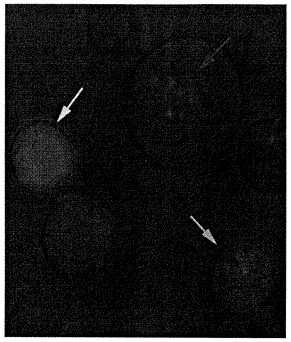
NORTHWESTERN
UNIVERSITY





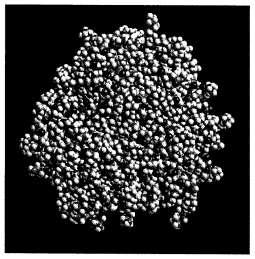
pH-induced self-assembly of a peptide-amphiphile makes a nanostructured scaffold (micelle) reminiscent of extracellular matrix. The structural integrity of the nanofibers is controlled by reversible cross-linking. The alignment of crystals of hydroxyapatite, directed by the nanofibers, forms a composite material that mimics the alignment of hydroxyapatite on collagen fibrils in bone.


Increased surface area
faster dissolution
faster absorption
enhanced bioavailability
NanoCrystal® particles have increased surface area
Microniza tion vs. Nanonization™ process
reduction
Time (min)
CRYSTAL

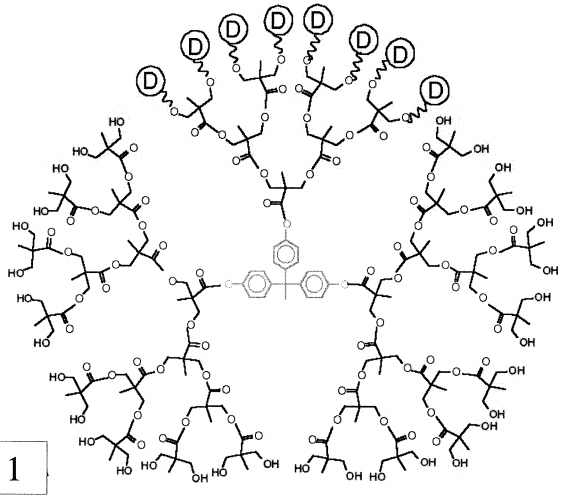


UNIVERSITY OF MICHIGAN

James Baker, M.D.



Multifunctional nano-devices based on dendritic polymer components will be developed that target neoplastic cells and sense the earliest signatures of cancer. The dendritic nano-devices will be designed to support the specific release of a therapeutic agent within a tumor, and analyze the effect of the therapeutic identifying evidence of residual disease.

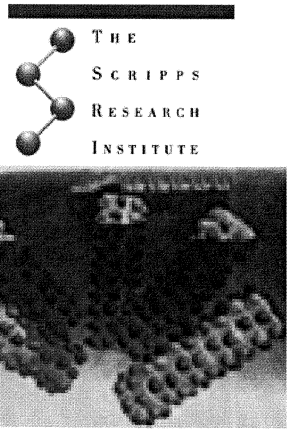


1

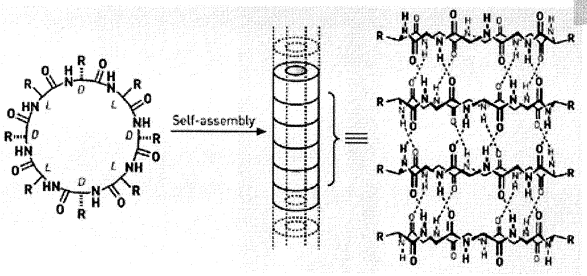
Dendrimer structure, from Jean Frechet, U.C. Berkeley

SCRIPPS RESEARCH INSTITUTE

M. Reza Ghadiri, Ph.D.



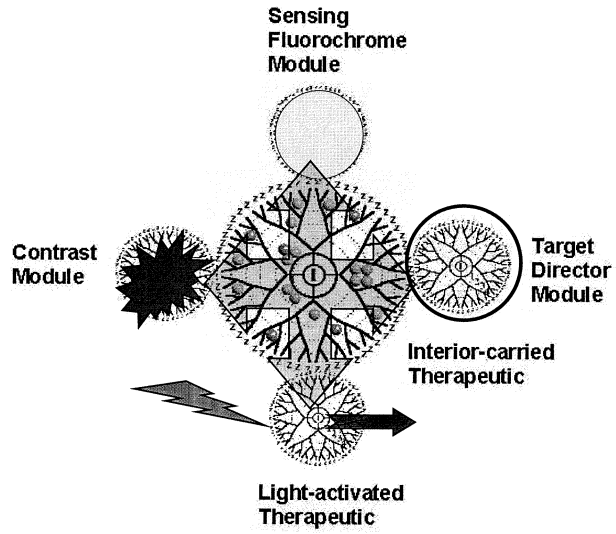
A new class of antibacterial peptides is being developed. Nanotubes are formed by self-assembly of cyclic peptides composed of alternating D- and L-amino acids. With appropriate design, the nanotubes insert themselves into bacterial, but not mammalian, cell membranes. Pores are created, resulting in bacterial cell death.



Figures are from C&E News, August 6, 2001

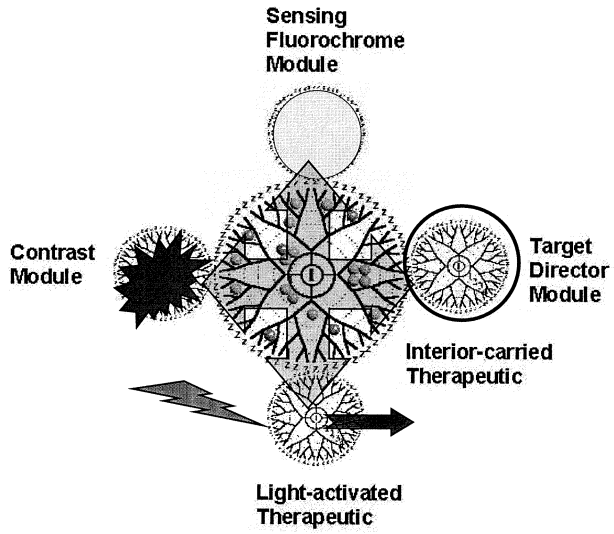
UNIVERSITY OF MICHIGAN

James Baker, M.D.



UNIVERSITY OF MICHIGAN

James Baker, M.D.



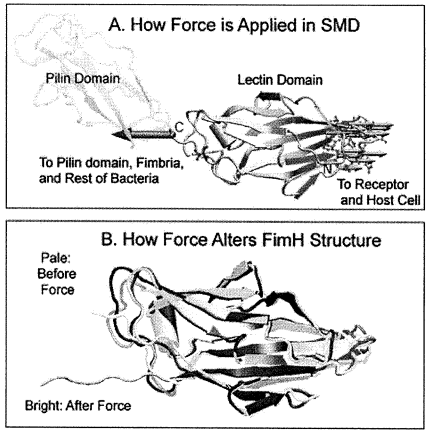
UNIVERSITY OF WASHINGTON

Center of Excellence in Genomic Science
Viola Vogel, Ph.D., Deirdre Meldrum, Ph.D.

Elucidating nature's design principles

Steered Molecular Dynamics simulation of change in protein structure when force is applied to a bacterial cell bound to an erythrocyte. This study provides "insights into the structural mechanisms by which proteins can act as force sensors and undergo a functional switch when subjected to mechanical force *in vivo*. This information … has the potential to be exploited for medical and technological applications."

W. Thomas, et al., Cell, Vol 109, 913-923, June 2002



NIH BIOENGINEERING CONSORTIUM (BECON)

BECON

- Initiated in February 1997 by Office of the Director, NIH
- Operates out of the National Institute of Biomedical Imaging and Bioengineering
- Aimed at facilitating development of bioengineering and fostering intra-NIH and inter-agency cooperation
- Multi-agency membership. Members consist of senior-level representatives from NIH institutes, offices and centers and other federal agencies

Biomedical Engineering At The NIH - Netscape

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Bioengineering Consortium

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NIH Bioengineering Consortium (BECON)

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Welcome to the BECON Web Site - Your Source of Information about Bioengineering at the NIH

BECON - The Bioengineering Consortium (BECON) is the focus of bioengineering activities at the NIH. The Consortium consists of senior-level representatives from all of the NIH institutes, centers, and divisions plus representatives of other Federal agencies concerned with biomedical research

NIH's mission of improving the quality of the nation's health by increasing biological knowledge and facilitating the development of novel devices and drugs.

This Web Site - This Web site contains information about the structure and

What's New?

- Registration Now Open For BECON 2003 Symposium
- Chairs Named for BECON 2003 Symposium on Team Science

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Your portal to bioengineering grants & programs at NIH

http://www.becon.nih.gov

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

Nanoscience and Nanotechnology in Biology and Medicine

- i) create & use structures, devices & systems that have novel properties and functions because of their small size, to achieve a fundamental understanding of biological processes or for disease detection, therapy, or prevention; ii) conceive, fabricate and test devices to detect and analyze nanoscale entities of relevance to biomedicine; iii) study biological systems at the nanoscale to develop nanotechnologies and nanostructured materials for use in biomedicine.
- Encourages team approach to nanotechnology research
- R01 (research project) & R21 (exploratory/developmental) if little preliminary data and potential for groundbreaking impact. Up to 3 years, up to $125,000 per year direct cost
- Review panels dedicated to this program announcement
- Application Receipt: February 18 and August 18, through 2006
- http://grants.nih.gov/grants/guide/pa-files/PAR-03-045

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

Bioengineering Nanotechnology Initiative (SBIR)

- Nanotechnology is emerging as a field critical for enabling essential breakthroughs that may have tremendous potential for affecting biomedicine.
- Encourages team approach to nanotechnology research
- Phase I may request up to two years, $200,000 per year
- Phase II may request up to three years, $400,000 per year
- Applications Receipt per SBIR:
  April 1, August 1 and December 1
- Competes with other SBIR applications
- http://grants.nih.gov/grants/guide/pa-files/PA-02-125

BIOENGINEERING RESEARCH SUPPORT AT NIH

BECON

Bioengineering Research Grants

- For basic and applied multi-disciplinary research that addresses important biological or medical research problems.
- Hypothesis-driven, discovery-driven, developmental, or design-directed research.
- Multi-disciplinary research performed in a single laboratory or by a small number of investigators that applies an integrative, systems approach to develop knowledge and/or methods to

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Saltzman, W Mark | Yale University | Micro-And Nano-Engineering Of Biomineralized Materials | DE014097 | 5 years | NIDCR

Abstract: Biomaterials have a long and successful history in dental and bone restoration, but the current technology is imperfect. Three-dimensional, biomineralized templates are a necessary component of bone and dental tissue engineering strategies, but methods do not yet exist for controlling the formation of biomineralized substrates with chemical and physical features that promote cell integration and function. We will first fabricate two-dimensional substrates in which macromolecules with functional groups that appear during tooth and bone formation will be micropatterned to regulate calcium phosphate crystal nucleation and growth. A constant composition method will be used to mineralize the patterned surfaces with specific chemical composition and crystalline phase. In addition, three-dimensional matrices with micropatterns will be fabricated using natural ECM proteins or synthetic polymers in a silicon mold. The patterned hydrogel matrices will be mineralized in a controlled manner using a modified constant composition method and microfluidics. Mineralized structures will be extensively characterized for chemistry, crystal structure, and topography. The controlled microstructures will be used to study the interaction between cells and the extracellular environment. Experiments will focus on the effect of the mineralized material on cell behavior; the influence of chemistry and geometry on the attachment, migration, and specific functions of cells will be studied. Together, these studies will provide new insight on the interactions between cells and substrates that occur during biomineralization. Since precisely designed synthetic materials will be produced and characterized to meet the study objectives, this project will also lead to new approaches for engineering of dental and orthopedic tissue.

NIH BIOENGINEERING CONSORTIUM (BECON)

BECON

BIOENGINEERING RESEARCH AREAS

- Behavioral science
- Biomechanics
- Bioprocessing
- Bioelectrics, ion channels, and organ function
- Clinical medicine, therapeutics and drug delivery
- Combinatorial approaches to chemistry, materials, genes, and therapeutics
- Functional genomics including microarray technology, integrated systems, and analytical tools
- Imaging, molecular imaging, and image-guided methods
- Nanotechnology and microtechnology
- Informatics, databases, and computational methods
- Computational modeling and simulation
- Medical implants, biomembranes, sensors and devices
- Optics
- Complex biological systems
- Organ culture systems and organogenesis
- Rehabilitation and prostheses
- Cell and tissue engineering and biomaterials
- Tissue regeneration
- Integrative physiology
- Drug bioavailability
- Telemedicine
- Computer-assisted diagnosis and procedures

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

Examples of Nanoscience/Nanotechnology-related awards under Bioengineering Research Grants

Paul Campagnola, Univ. of Connecticut Health Center, R01 GM60703

Multiphoton Biomedical Nanofabrication

To develop a new method to direct 3D assembly of active biomolecules and synthetic polymers by crosslinking using highly controlled multiphoton illumination, for application in biosensors, micro-machines, drug delivery, and tissue engineering.

Jan Hoh, Johns Hopkins Univ., R01 GM64020

Nanofabrication of High Performance AFM Cantilevers

To develop AFM cantilevers (and a detector for their characterization and use) with resonance frequency 10-1000x better than currently available, to allow faster scanning, higher temporal resolution of force measurement, and higher sensitivity.

BIOENGINEERING RESEARCH SUPPORT AT NIH

BECON

Bioengineering Research Partnerships

- For basic and applied research by a multi-disciplinary team applying an integrative, systems approach to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to

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Bookmarks Location: http://www.becon1.nih.gov/Funded/BRPFY02.pdf What's Related

31. **Principal Investigator:** **Mcknight, Timothy** **Affiliation:** UT-BATTELLE, LLC-OAK RIDGE NATIONAL LAB
Project Title: Nano Arrays for Real-Time Probing Within Living Cells
Grant Number: 1-R01-EB-433-1-A1 **Funding Organization:** NIBIB
Abstract:

This project will exploit the recent development of rigid, vertically aligned, carbon nanofiber arrays to provide nanoscale probes for mapping intra and extracellular molecular events in and around living cells in real time with extremely high spatial resolution (< 50 nm probing areas). Devices will be fabricated and characterized to determine the performance of nanoscale arrays as independently addressable electrochemical molecular probes. Characterizations will be performed using a set of standard analytes that have been routinely used for characterization of carbon-based electrode systems (year 1). Probe response to hydrogen peroxide and superoxide anion will then be characterized (year 1 into year 2). Strategies and methods will then be develop for coupling nanofiber arrays around individual and groups of living cells (year 2). Electrochemical analysis techniques will be applied at individual elements of carbon nanofiber arrays to spatially and temporally map the activity of peroxide around and ultimately within individual cell locales (year 3). This research will be structured around development of these methodologies using microfluidic-based cell and analyte handling strategies, thereby promoting future high-throughput screening applications, such as clinical diagnostics of cell and tissue specimens and pharmaceutical exploration and discovery. This effort will be conducted by various organizational groups within the Oak Ridge National Laboratory. The Interdisciplinary team involved with this effort features mechanical and electrical engineers with experience in microfluide systems/semiconductor/and nanoscale fabrication, a biochemist and biologist with expertise in cell culture and single cell monitoring, analytical chemists, and a biophysicist, with expertise in cell signaling and environmental response. This effort will directly address BRP thrust areas including nanotechnology and microtechnology, functional genomics/microarray technology/gene expression analysis, cell and molecular imaging, and complex biological systems.

BIOENGINEERING RESEARCH SUPPORT AT NIH

BECON

Bioengineering Research Partnerships

- For basic and applied research by a multi-disciplinary team applying an integrative, systems approach to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to

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NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

Examples of Nanoscience/Nanotechnology-related awards under Bioengineering Research Partnerships

Shimon Weiss, LBNL/UCLA, R01 RR14891
Development of Q-Dots as Biological Probes
5 years, $1.1M/yr, cost-shared by NCRR, NCI, NIGMS

William Shain, Wadsworth Center, NY, R01 NS40977
Brain Prosthesis: Tissue Compatibility and Integration
Technology advances in prosthesis insertion, design, and pharmacological delivery will be used to control [early and prolonged biological] responses. Prostheses will be made using nanofabrication techniques.

H. Lee Sweeney, Univ. of Pennsylvania, R01 AR47292
Bioengineering Research Partnership - Muscular Dystrophy
Uses AFM for characterization of dystrophin interaction with other proteins.

BIOENGINEERING RESEARCH SUPPORT AT NIH

BECON

Exploratory/Developmental Bioengineering Research Grants (EBRG)

- To support innovative, high risk/high impact bioengineering research in new areas that are lacking preliminary testing or development.
- For basic and applied multi-disciplinary research that addresses important biological or medical research problems.
- Hypothesis-driven, discovery-driven, developmental, or design-directed research.
- R21 mechanism.
- Up to $275,000 direct costs over 2 years.
- Applications Receipt: February 1, June 1, and October 1
- http://grants.nih.gov/grants/guide/pa-files/PA-03-058.html

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

BECON

Administrative Supplements for Quantitative Physical Measurements at the Nanoscale

- Supplements to current NIH grants that are studying, at a molecular level, biological or disease processes, or diagnostic or treatment modalities.
- To add capabilities to enable analyses of biological nanostructures, assemblies and nanomachines using quantitative physical parameters, such as force, stoichiometry, kinetics, energy utilization and transduction, etc.
- Ultimate goal is to lead to knowledge of the design principles of biology.
- Supplement Application Receipt: August 1, 2003
- http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-051.html

NANOTECHNOLOGY RESEARCH SUPPORT AT NIH

Basic Research, Instrument Development

Single Molecule Detection and Manipulation

- For basic research on detection and manipulation of single molecules to provide fundamentally new information about biological processes for understanding cellular function; real time measurements of single molecules in living cells
- NIGMS, NIDCD, NHGRI
- http://grants.nih.gov/grants/guide/pa-files/PA-01-049.html
- http://grants.nih.gov/grants/guide/pa-files/PA-01-050.html

Technology Development for Biomedical Applications

- To develop innovative (1) new and improved instruments or devices, (2) new methodologies using existing instruments, or (3) software related to instrumentation.
- NCRR, NHGRI, NIBIB, NIEHS
- http://grants.nih.gov/grants/guide/pa-files/PAR-03-075.html

[Whereupon, at 11:27 a.m., the committee was adjourned.]

○