

THE BROOKINGS INSTITUTION
THE LIAISON CAPITOL HILL

PHDS, POLICIES AND PATENTS: INNOVATION AND AMERICA'S
FUTURE

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PARTICIPANTS:

Welcome:

ROBERT E. RUBIN
Co-Chair, Council on Foreign Relations
Former U.S. Treasury Secretary

PANEL DISCUSSION: THE STATE OF SCIENTIFIC AMERICA

Moderator:

ANN KELLAN
Science Correspondent, Cable News Network

Panelists:

ANGELA BELCHER
Professor of Materials Science Engineering and Biological Engineering,
MIT

FRANCIS S. COLLINS
Director, National Institutes of Health

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PROCEEDINGS

MR. RUBIN: Good morning. I'm Bob Rubin. Let me welcome all of you on behalf of my colleagues at the Hamilton Project for today's discussion of PhDs, Policies, and Patents: Innovation and America's Future.

We began the Hamilton Project about six years ago. It's an extraordinary combination of policy analysts, academics, and business people. Our purpose was to put forth proposals and catalyze discussions in policy areas that are key to our economic future. The idea was not to propose or endorse individual ideas, but, rather, to help foster seriousness and purpose with respect to discussion of economic issues in the public domain and also action in our government. And we have consistently held that economic policy should serve multiple purposes -- growth, broad-based participation in that growth, and economic security for all -- and that these purposes can be mutually reinforced.

Serious policy engagement, serious policy involvement is more needed today than ever before, given the challenges facing our economy in both the short term and the long term and the often dismaying nature of our public discourse.

Clearly, today's economic difficulties, the likelihood that they will continue for quite some time, and the hardship that is being suffered by far too many Americans call for a tense commitment and serious action by policymakers, and that was a project that has convened policy deliberations to focus on the shorter-term situation. We've had discussions of a stimulus, mortgage relief, and a whole host of other subjects. But our primary focus has remained long-term economic policy.

We believe that our country has enormous strengths -- our cultural dynamism, our willingness to take entrepreneurial risk, flexible labor capital markets, the rule of law, and so much else -- and that with that we should be able to succeed in the global economy that's undergoing change of historic dimensions, but realizing that potential requires that we meet usually consequential challenges. And in order to do that we have to have a willingness to work across party and ideological lines, to base decisions on facts and analysis, and to make politically tough decisions to establish sound, long-term fiscal conditions; to provide strong public investment in the areas that are critical for economic growth, education, infrastructure, basic research, and so much else; and to reform our policy in non-budgetary areas, like education, health care, energy, and the like. Within that framework, America has long had a culture and an economic system that has spurred innovation and scientific advance that in turn created vast new industries, enormous numbers of jobs, and a powerful competitive position in the global economy.

Today's conference was stimulated by many concerning indicators that our innovative edge could not be taken for granted but needs to be supported and nourished by public policy. But just three of many examples: Four out of the five most powerful supercomputers in the world are now not in the United States; broadband coverage in Korea is substantially greater than the United States; and according to a recent survey, of the 20 communications companies in the world with the largest number of patents, only 35 percent are located in our country.

Today's conference will focus on possible future areas: innovation

in scientific advance, policies and regulatory regimes to foster innovation and creativity, obstacles to these activities in the regulatory area, and translating innovation into job creation and economic growth in the United States.

Let me now outline our program and briefly introduce our panel and speakers. As you can see from having looked at the program at your seats, this is a truly remarkable group of individuals. I will not introduce each one. Their resumes are in your materials, but it is an extraordinary group of people to discuss these very important subjects.

Our first panel, entitled "The State of Scientific America," will explore the question of what innovations and scientific developments may emerge over the years and decades ahead ranging from life sciences to depressing natural gas to whatever else the panelists may desire to raise, and then that question of how these innovations can be turned into economic activity, growth, and jobs in our country.

The moderator of the first panel will be Ann Kellan, former science correspondent, CNN. She'll be joined by two extraordinary panelists -- Angela Belcher, professor of materials science engineering and biological engineering at MIT, and Francis Collins, director of the National Institutes of Health.

The second panel, entitled "Obstacles and Opportunities for American Science and Innovation," will focus on policies and regulatory approaches that are conducive to innovation and scientific development and also policy and regulatory obstacles. The moderator is Michael Greenstone, director of the Hamilton Project, professor of economics at MIT. He'll be joined by four panelists, highly experienced in these matters: Tim Bresnahan, professor of

technology and the economy, Stanford University; Aneesh Chopra, chief technology officer of the United States; Tyler Cowen, professor of economics, George Mason University; and Glenn Hutchins, co-founder, chief executive officer of the private equity firm Silver Lake and member of the Advisory Council of the Hamilton Project.

The third segment of today's discussion will be remarks on the administration's regulatory review process by Cass Sunstein, administrator of the Office of Information and Regulatory Affairs. He'll be introduced by Roger Altman, founder and chairman of the board of Evercore Partners, former deputy secretary of the Treasury, member of the Advisory Council of the Hamilton Project.

The final portion of our program is titled, "A Path Forward -- The Future of Innovation in the United States." The moderator will be Greg Ip, U.S. Economics editor, *The Economist*. Two outstanding panelists will be Eric Lander, founding director of the Broad Institute of the Massachusetts Institute of Technology at Harvard University and co-chair of the President's Advisory Board on Science and Technology; and Lawrence H. Summers, Charles W. Eliot University professor of Harvard University, former assistant to the President for economic policy, former Secretary of the Treasury, and member of the Advisory Council of the Hamilton Project.

Finally, this is really a truly extraordinary program for giving us all of us the opportunity to listen to and be engaged with this extraordinary group of people.

Let me thank three people: Michael Greenstone, director of the

Hamilton Project; Karen Anderson, the managing director of the Hamilton Project; and Adam Looney, policy director of the Hamilton Project and senior fellow of the Brookings Institution.

With that, it is my pleasure to turn the podium over to the moderator of our first panel, Ann Kellan. Ann.

MS. KELLAN: Hello and welcome. I'm fortunate to be here and honored to be sitting with these wonderful leaders in the field of science and technology in medicine. And it's interesting because I was a host of a show called *The Next Big Thing*, so I think it led me here today. We're going to check out what's the next big thing, and I just want to open the questioning to Francis Collins, who is the director of the National Institutes of Health.

You also played a significant role in the Human Genome Project, and I think, you know, back then when we were covering it, we were wondering what is it going to lead to? What's going to be next? And what do you say has emerged and will emerge as the possible next big thing that we should focus on?

MR. COLLINS: So, it's been now 10 years since the publication of the draft sequence of the human genome in 2001, and so there's been a decade-long experience here, and there have been a fair amount of reflections upon how far we have come in those 10 years. I would say for researchers, this has utterly transformed the way that we ask and try to answer questions about human biology. Graduate students have a hard time imagining how actually people did anything worthwhile in studying human biology without this information. It is so much a minute-to-minute, hour-to-hour experience of simply going to the web, clicking with your mouse, and pulling down information about our instruction

book; and increasingly, layered on top of that, is phenomenally interesting information also of a comprehensive sort that allows you to look at all the variations in the human genome. There's now this Thousand Genomes Project, which is laying out that in the greatest detail so far information about what genes are expressed in which tissues, information about the epigenome -- that is, the various ways in which the DNA is marked by various proteins to determine whether it's going to be on or off in a given circumstance -- and all the networks that are emerging from that that we are increasingly able to understand.

So, as anybody who is interested in human biology or medicine, we have moved into an entirely new territory that is radically different than what we had prior to the availability of this information. And the fact that the information has been made immediately accessible, which was a cardinal principle of the public Human Genome Project, putting the information out there even prior to publication, has also become an ethic of the field of genomic science, has spilled out into lots of other datasets, and that is further enhancing and empowering the pace at which one can begin to answer these questions.

I think the difference it's made, put in one way, is that we used to have to approach questions about human biology with a rather narrow focus if we had any chance of making any progress, which meant you often had to have a hunch about what the answer was going to be. Now, the genome has a bounded set of information, and we've been able to derive an awful lot of the details about that information already. So, you can ask comprehensive questions: What are all the variations in the genome that play a role in the risk of diabetes? What are all of the components of the human immune system? What are all of the proteins

present in a given cell? Not saying we can fully answer all of those questions now, but we have the tools to get there.

Now, in terms of medical implication, there were some I think slightly cynical comments coming forward in the past few months about, well, you know, why haven't we seen a total revolution in medicine already? Where are all those benefits that were promised 10 years ago? I think anyone who was proposing that having the instruction book in a language that we understood quite poorly 10 years ago was going to result in a vast array of new diagnostics and therapeutics haven't been paying much attention to all of the steps that are necessary to get you from that fundamental information to its implication in the clinic. But we are getting there.

My predictions I think 10 years ago were about on the pace that I thought we would be. Certainly we have derived information that is, in many instances, useful for making diagnostic predictions about who is at highest risk for breast cancer, colon cancer, a few other diseases. We've learned how to make predictions about which drugs are going to work in which doses for which people for a substantial number of drugs that are already in use.

An example in the cancer arena: A woman who has breast cancer diagnosed today who has a tumor that's smaller than 2 centimeters and whose lymph nodes are negative and whose estrogen receptor is positive faces the question -- and this is a lot of women in the U.S. -- should they have been cured by surgery and radiation, or is it necessary also to offer chemotherapy? In the past, most women went ahead with the chemotherapy because of the slight improvement in outcome. But, clearly, most of them were already cured by the

surgery and radiation. Now, with a method that allows you to look at the gene expression in the cancer itself, you can make a very accurate prediction about whether that is a cancer that needs the chemotherapy or whether it's essentially a very low likelihood to recur, and about 50,000 women will take advantage of that test this year and that will save our health care system about \$100 million in terms of chemotherapy that will not have to be administered because it won't be considered necessary.

So, there are definite implications already. But most of the promise of genomics for really revolutionizing our health care system lies somewhat ahead, and perhaps we'll talk about that -- what are the steps that we need to go through to take this fundamental information about the molecular basis of disease -- which is pouring out of laboratories, and translate that into really targeted, effective therapeutics for cancer, for diabetes, for heart disease. We can see the path forward there, but it is a long, complicated path. It is fraught with high risks of failure, and it requires I think right now some special attention to ways to try to speed that up, to look at that whole process the way an engineer would and see whether there are ways we could move the ability to develop clinical benefits forward at a maximally productive pace, even in the face of difficult economic times.

MS. KELLAN: So, one benefit we have seen is something that Angela Belcher has worked on, and who would have thought, right? Who would have thought you could grow batteries in a Petri dish? And what is the connection between the Human Genome Project and growing batteries in a Petri dish?

Angela, why don't you explain a little bit about what you're doing and what's the connection?

MS. BELCHER: There definitely is.

So, what we've really been interested in over the last several years is trying to understand how nature makes materials, how nature is incredible at making hard materials. One example is like the abalone shell here. This is a biocomposite material. It's 98 percent by mass calcium carbonate, 2 percent by mass protein. But it's a really exquisite structure, and it's built in the ocean using nontoxic materials and doesn't add toxic materials back into the environment, and it's self-assembled.

Well, how does it do it? It has the genetic information that says this is how to build this great material under environmentally friendly conditions. And so I thought that was really fascinating and said, well, what if you could give kinetic information to a battery or a solar cell or a catalyst so that you could build advance materials with the same kind of control using environmentally friendly processing? And so basically what it is, is how do you find a DNA sequence that codes for a high-power battery? How do you find a DNA sequence that codes for the ability to assemble a solar cell? And that really comes from doing a billion experiments at a time, to be able to have a billion different DNA sequences and look for one that can do something you want it to be able to do.

Well, that's pretty complicated, especially for me as a material scientist. And a lot of the advancements that have come along with the Human Genome Project are being able to have DNA sequenced cheaply and inexpensively, being able to make it cheaply and inexpensively, and taking some

of the really difficult procedures, to be able to have libraries of a billion possibilities of DNA, and give it to my group which are engineers and allow us to take advantage of all that technology that's already been developed and say, okay, we're going to take this DNA and we're not going to use it for necessarily human health, although we have programs in that. We're going to use it to see if we can find one sequence out of a billion that will make a new catalyst material for converting methane to ethylene for energy, and we'll find one sequence out of a billion that can build us a better solar cell.

And so, you know, we -- I'm not that good of a biologist. I could not have done that without all that the groundwork that was laid to be able to take this technology and make it basically not that difficult for us in my lab to work on, and it's been very, very fun. And you can find a DNA sequence that can code for a protein that can improve the efficiency of your solar cell in about three weeks.

MS. KELLAN: So, what is your innovation? I mean, where are you seeing this going?

MS. BELCHER: Well, I would say I've never been accused of focusing. (Laughter) So, that's one of my favorite things about being an engineer right now, being a scientist-engineer right now. There are so many opportunities. All you have to do is look around and pick one. Do you want to pick health care? Do you want to pick energy? Do you want to pick the environment? Do you want to pick water? All of those are science and engineering opportunities. And in my group we focus on energy quite a bit -- energy storage, batteries. We focus on solar. We do new catalyst discovery from temporary reactions for energy. We work in cancer as well. We look for

new diagnostic probes for early detection of cancer. And we also look at CO₂ sequestrations and storage. So, you see that's a huge -- you know, pick just one of them. But I'm a material scientist, and so everything to me is a material. So, whether it's a material for energy or material for health care, it's still how the atoms are arranged and put together that makes a difference.

MS. KELLAN: And so are you seeing future benefits as far as all of us sitting in this room? Are we going to get that battery that's going to last forever? Are we going to get the --

MS. BELCHER: I've got a battery here.

MS. KELLAN: Okay.

MS. BELCHER: (Laughter) This is a small coin cell battery. This is a biologically assembled battery. You can use it to light an LED in this case. It's a high-powered battery. Through genetic engineering, we engineered organisms to make it higher and higher powered as a function of time. It got better. We first built a battery that was okay, and then a little bit better through genetic engineering, and we got it to be very, very good, and this one actually went to the White House for an example of environmentally friendly clean energy. We've done the same with solar cells.

And I've spun out a couple of companies, including one that has a product that just came out a couple of weeks ago, a touch screen for this cell phone that's made with environmentally friendly processing. Usually touch screens and your smart devices are made from indium tin oxide -- a transparent electrode material -- but indium is a volatile, expensive, and geopolitical element. And over 50 percent of the indium comes from China, so that the company that I

founded, the technology was really -- it's called Cambrios Technologies -- the technology was really developed in the company, has found a replacement for it, that a solution-based process, roll-to-roll printing that doesn't use materials -- uses materials that are much more abundant and much more environmentally friendly. And this is our first product that's now out after several years of development.

MS. KELLAN: So, what does it take to get an invention, a bright idea to market? Maybe you could touch on that. You know, you get this moment of ah-ha, I have an idea. Is it a pain in the neck in this country to get it to fruition or are we paving a good path for our inventors?

MR. COLLINS: Well, I think it depends a bit on the field in terms of just how readily available the path is. If you're a university-based investigator, like Professor Belcher, you have MIT there to assist you in figuring out when you have an idea just how you would go about obtaining a patent if it seems appropriate to do so, and then what kind of licensing arrangement might be most beneficial in terms of getting your invention actually moved into a space where it will be developed into a product that the public can benefit from.

I think at the moment there is both good news and bad news. The good news is there's a lot of innovation in our universities, in our companies in terms of coming up with potential major advances that are going to be beneficial to the public, to the environment. The bad news is that capital is harder to find right now than it has been at times in the past, and I think that has slowed down the process of taking some of these exciting new inventions and moving them forward. Unless you've got something that clearly is going to result in profit in the

fairly short term, it's harder these days to find investors who are willing to put the money into it.

I assume that you would agree with that from your own experience.

MS. BELCHER: I definitely do. And from an academic standpoint, MIT's been very supportive in helping negotiate -- or how to do the patents and trying to make contact with the industries or helping start companies that might either license this technology or develop the technology. But in both the companies that I founded, the technology was very, very young when it went into the company. And so in that case, you know, it's very high risk, and in the terms -- in the case of Cambrios, it's been eight years. The idea was a pretty young idea and it was developed, and now we have products, but it really -- we have mostly venture capital money, and it took the investors believing that we'd actually come to product. And so, you know, think about what it would be like if they didn't stick with us because, you know, we have this -- we can make enough of this transferrant conductor for the whole world in our manufacturing plant. And so it could have big implications in electronics as well as in, you know, geopolitical issues. And so it really took people staying with us and believing in us, and so that was absolutely key.

MR. COLLINS: If that was happening today, would you have the same success in convincing people that this was maybe 8, 10, 12 years down the road? Would you be able to start a company of this sort? Or would it be tougher or the same?

MS. BELCHER: I do think it would be tougher.

MR. COLLINS: Yeah?

MS. BELCHER: My newest company I started since then is a company in catalysis. It's Siluria Technologies and it's been going faster because -- a little bit -- we have more experience in it, but it's looking at a very big market, gas to liquids for transportation as well as special chemicals. There's a lot of interest in it because the possibilities are so huge. But we'll -- that's just a couple years old, so we'll wait and see.

But I think it's tricky, and I think it's really hard for young faculty members coming in to a university that has this idea, to know whether this idea is worth pursuing, and understanding what the path is like to get from basic science idea to company to commercialization. And it's a tricky path.

MS. KELLAN: Do they have to see the whole picture to lay it out for people now or do -- is basic science still supported?

MS. BELCHER: Oh, I said -- I'd say that it's on a very individualized basis. We're lucky at MIT to have quite a bit of mentoring. But it's a risk.

MR. COLLINS: You know, my concern is that we have young scientists who never had the chance to get into this environment to be able to pursue such inventive ideas just because of funding constraints. It is difficult these days, particularly for early-stage investigators, to get started. If you look at NIH -- and of course we're the major funder of biomedical research in the world -- over the last 40 years the likelihood if you sent a grant to NIH as an early-stage investigator or an experienced investigator, it was about one in three that that grant would get funded. That was the availability of the funds versus the

requests for them. Some might have argued that we'd have done better if we could have funded one in two, but one in three was kind of the experience. But in the last few years, since 2003, since the budgets have basically flattened out and now, actually this year, seen a real decrease in real dollars, that success rate has gradually been trimmed back. It's now about one in five and it's headed to one in six probably this year. And that means that a lot of early-stage investigators who are trying to get started, who are oftentimes the engine of these bright, creative ideas, are simply having difficulty getting their laboratories going because they depend upon that grant support offer, a starting point.

We at NIH try to do everything we can, especially with early-stage investigators, to give them a special leg up. They compete against each other and not against the more established investigators. We have done everything we can to try to free up enough funds to be able to support as many new applications even if it means that some of the continuing applications are being cut back. But still that means five out of six of these new proposals in which there are lots of kernels of innovation that are going to make a difference both for health and for our economy are going begging in the current circumstance. It is a difficult time to try to encourage this sort of innovation when the pressures are so strong.

MS. KELLAN: So, the ramifications are that things don't get invented. You don't get the cure for diseases that you're hoping. I mean, is that --

MR. COLLINS: I'm sure we are missing out on opportunities that could be supported if we were in a more favorable environment because it's very

hard to assess when you look at a proposal whether, in fact, this is going to be a successful new innovation. Sometimes it's the wacky science that you most don't want to miss supporting, and yet wacky science at a time where you're only funding one out of six grants may be a difficult one for our peer review process to identify and say, yeah, we're going to do that even though it means not doing some very solid, established science that's in the same pool. We have at NIH, and NSF has similar efforts, programs that focus specifically on high-risk, high-reward kinds of proposals to be sure that those are considered welcome and that they come in and compete against each other. But still the resources are limited to be able to do as much of that as we would like.

MS. KELLAN: You kept seeing the same thing?

MS. BELCHER: I have a visual thing. I'd like to follow up on that, which is that the generation of sciences and engineering graduate students and postdocs and young faculty that are entering academia right now and probably industry as well are a different kind of scientist and engineer. They do have a very innovative mind.

MR. COLLINS: Yep.

MS. BELCHER: And they come from interdisciplinary training for the first time. They may have a bachelor's degree in biology and a PhD in physics or in engineering, and they have a different way of looking at the world. Now, if they're going through the purity process, it makes it very, very difficult. But if I'm sick, I want someone thinking about the world from a different direction to help figure out how to solve it. It's that combination of different disciplines I think that can really push these forward. And those are the most fun kind of

students to educate. We need to think about that in the grant process. My degrees are all in different fields, and when I wrote my first grant proposal my first day, you know, in my job, I got the review back that said I was insane.

MS. KELLAN: Insane? (Laughter)

MS. BELCHER: Yes, insane. And, you know, I think it's not like that anymore because now it's more of the norm to be educated in different disciplines, and it's actually very celebrated, that we really need to figure out how to keep facilitating that so those young investigators make it more into the mainstream funding, so that they can have the radical ideas that, you know, change the way, you know, we treat disease or the way that we make new materials or solve problems.

MS. KELLAN: Why did they say you were insane?

MS. BELCHER: Because I said that we were going to use genetic control to build semiconductors. Yeah.

MS. KELLAN: The ultimate multidisciplinary approach to -- yeah, they said no way could you do that.

MS. BELCHER: And it's worked out okay for me.

MR. COLLINS: Apparently so.

MS. KELLAN: So, that person -- well, you are working in a multidisciplinary area world now because of what you're doing.

MS. BELCHER: It is, but it's not so unusual. I'm also really lucky to be in a new institute, MIT. The campus is half engineers and half cancer biologists working together. And when I was asked to be in it, I was, like, oh, I don't know, I love my space where I am now, and I don't want to move, but now

I'm in an office suite with three cancer biologists and myself. And --

MS. KELLAN: How's that working?

MS. BELCHER: It is so fantastic. You know, I can say I don't know anything about cancer politics. I don't. And I get expert tutoring in what's important. And we had a conversation just this week where we were sitting down and going back and forth about an engineering idea and a science idea -- well, okay, let's do it -- and it's this idea of we would have never run into each other on campus, but now we're in the same office suite. And, you know, it's just -- it's really fantastic, and I'm learning how to use their instrumentation and they're learning how to use our instrumentation. We're learning how to speak a similar language. So, it's actually -- it's very fun.

MS. KELLAN: It is a language barrier, too, somewhat.

MS. BELCHER: It's a language barrier and it's a style barrier, as well, because a lot -- you know, people will go -- say that they work on hypothesis-driven research, and I don't really know what that is. I want to know what the problem is and how can I solve the problem.

MR. O'HANLON: As an engineer.

MS. BELCHER: Yeah. That's the way that I look at it, and so what's the problem? What needs to be fixed? And, so, you know, if you take those combinations and put it together, you know, it really is a whole new world.

MR. COLLINS: That's interesting. We have -- in the biology field there, of course, has been much of a focus on hypothesis-driven research. Some of us are beginning to think that we ought to think about sometimes whether there's a problem with hypothesis-limited research because you are,

in fact, narrowing your focus down to a small possibility of what the answer might be as opposed to asking a comprehensive question about a problem, as you've just said. And I think the field of genomics has certainly stimulated that kind of thinking. Again, it's the ability to ask comprehensive questions. If you can decide what the question is and you have the tools to approach it, well, the hypothesis I guess is that you have the ability to answer the question. And that's not a bad hypothesis to drive yourself forward in a very exciting way.

I really like what you said about the interdisciplinary aspect of what you do, and the Cancer Center at MIT is a nice experiment, and there are many others of that sort that are really wonderful to watch in my own research lab at NIH. The people that I depend most on are the ones who came out of physics, came out of engineering, or particularly came out of computer science, because computational approaches are so critical these days for our ability to sift through massive datasets and mine those nuggets of truth out of them to tell us something about diabetes or heart disease or cancer.

I want to point to another area that right now at NIH we think is particular ripe for this sort of engineering attitude, and that is this process of how we go from these fundamental discoveries about the molecular basis of disease and develop diagnostic tools and therapeutics, whether they're biologics or small molecules. If you look at that process, it is not a particularly pretty picture in terms of the way it has been conducted for the last 20 years or so. The average time to go from that insight about a possible target for therapy and having that therapy approved is about 15 years. The failure rate is about 98 percent. And that means the costs, when you add up all the failures, are exorbitant in order to

get one success.

An engineer would look at that and go, oh, there's something wrong here. This pipeline needs attention, and not in a way that would be fixed by a series of one-offs where you simply look at one project at a time, but what are the steps involved and why are they so prone to failure? And I think there's a real opportunity right now to bring this kind of interdisciplinary approach to that in a partnership with the private sector, who also are very frustrated by the inefficiencies of the steps, and with the FDA, which is a critical partner because they're watching over this to decide whether what you've developed is ultimately safe and effective.

Why do we do, for instance, testing of drugs? Before you ever give that small molecule to a patient for the first time, you have to decide whether it might be toxic. So, how do we do that? Kind of the same way we've done it for a long time: we try it in a bacterial system; you try it in small animals and large animals. It is tried, but it's not all that true because clearly this fails in some instances to predict toxicity. Clearly, it probably over-predicts toxicity in other instances and really promising drugs never make it into clinical trials because a mouse had some problem when they first saw this little molecule.

Why, at this point, don't we try to get closer in a safe way to human patients? We now have this incredible proliferation of information about how to culture human cells from embryonic stem cells to turning them into liver cells or heart cells or kidney cells. We can even build three-dimensional organoids made out of those cells that are increasingly good representations of what goes on in vivo. Might we, if we organized this the way an engineer would,

set up a system that would be more predictive and actually probably faster and cheaper to do this simplest test of preclinical toxicology to assess whether it's safe to go forward with that first patient application? That's just one example. There are multiple other things that we could be doing more systematically that would speed up this process, but it hasn't been really possible to have that kind of focus until now. The science wasn't quite ready, maybe the dynamics weren't quite there.

The interdisciplinary aspect that you've talked about between scientific disciplines also needs to now apply across sectors where academia and government and the private sector can get together in a new way to tackle this problem. And I think the enthusiasm for that is very high right now. We at NIH are hoping to set up this fall the National Center for Advancing Translational Sciences to be a hub for that kind of activity. And I'm pretty excited about that as a way to take even in a limited-resource situation the kind of innovative attitude and bring it to a problem, which is going to be critical for the future of medical advances.

MS. KELLAN: Is the educational system supporting that do you think?

MR. COLLINS: Well, we have an issue, I think, in terms of our education system in this country if you're referring to do we have a pipeline --

MS. KELLAN: Right.

MR. COLLINS: -- of bright, capable scientists coming into the field? We clearly -- everybody would agree by every measure -- have a K-12 system that is not encouraging a lot of bright minds to see science as something

exciting because it's not presented in that way. We clearly are losing people along the way after that. We clearly have a workforce that is not as diverse as our population. That means we're losing some very bright minds from groups that are not traditionally represented in science. And we can't continue to count on the fact that our scientific leadership is going to come from other countries. We've had a great opportunity in the past to recruit such bright minds from all over the world, and many of them have stayed and become central to our own national success. But they are increasingly not staying. The opportunities to go back to home country in places like China and India are getting very strong, and we have not particularly been friendly to many of those individuals in terms of our visa policies, and I think we're headed for a real potential problem here just in terms of scientific talent.

On top of that, we do have this sort of university system for training, which, while it's getting better in some universities, is still very much based on the old model of this department and that department, and you're in this one, so you don't talk to that one. And we really need to break down a lot of those barriers for our educational process if we're going to have the kind of scientists that Angela is talking about that she loves having in her own domain, who are not really afraid to jump from one discipline to the other and they actually find it rather exhilarating.

MS. KELLAN: Do you care to comment on that? I know you have a --

MS. BELCHER: So, I'm very passionate about that. I love education and what we can do because, you know, children love to play with

LEGOs. They love discovery. They love the nature in the world around them. How do we keep them involved in that? And I think that it really is getting the hands-on experience. How do you address projects that aren't -- okay, we're just going to learn math, but we're going to learn math and how it relates to the environment --

MS. KELLAN: Right.

MS. BELCHER: -- how it relates to solar. Young kids right now are so aware of energy. They're aware of the environment. They're aware of so many issues that I didn't think about when I was a child. And I also think that they naturally want to make a difference and naturally want to go into recycling. They naturally want to make the world a better place. Well, how do we incorporate that into the elementary school levels, which is just a part of their everyday life, and enforce that they can invent new approaches, that of course science and math and engineering are critical components of education, and they're fun? I mean, I love my job. I can't imagine anything more fun than what I do and having kids know that, what it's like to be an engineer, what it's like to be a scientist and what we get to invent and discover and do I think is key. I don't know what the answer is for that. I mean, I have my own piece of trying to do that, as so many universities and principle investigators do, but, you know, I think it's the ability to capture the imagination.

MS. KELLAN: And as far as where do you see in, like, 10 years what you're working on now, obviously they're going to have to pick up the baton and take it, but where do you see them taking it? What's going to happen next with what -- where do you hope this leads for you?

MS. BELCHER: Well, you know, as a professor, you see that the generation that just graduates and leaves is already better than you. So, you know, they're the ones that were in the lab actually making the things, making discoveries, and doing the devices. And then they go out into industry and they go out and start companies. They go out and start their own academic labs and try to push things in different directions.

I personally, for -- I'm going to say in two main areas right now, which are materials for energy and materials for cancer, those are areas that I look around and think that we have the ability to make an impact because I'm not going to work on anything that doesn't have an impact. It may be scientifically interesting. It may be fun. But ultimately, I want to make something that makes a difference, makes people's lives better. And, you know, I think that my students and the undergraduates share the same idea. And so it's great, you train these fantastically brilliant young people and they go out and take their ideas in their own directions and see what problems they're interested in and continue to become better.

MS. KELLAN: But do you have a vision, like, where you want to see everybody using cell phones with green touch pads or --

MS. BELCHER: I want to see environmentally friendly materials. Going back to this, you know, the abalone doesn't make materials that are toxic to its environment. He uses room temperature and pressure. What a wonderful manufacturing idea: Let's don't pollute our environment, but, at the same time, make high-quality good materials. That's my vision. My vision is to be able to do clean processing and not things that are just kind of cute experiments in the lab.

I want something that you can hold in your hand that makes a difference.

And so what I do is you do a combination of genetics, a billion possibilities of biology, mix that with a combination of many, many different possibilities of chemistry. Mix those two ideas together and see what comes out, and then integrate with that heighten (inaudible) screening, and that's how we're developing new catalysts that people have been working on for 30 years and haven't made that much progress. Well, it's not because we took one material at a time to try to figure it out.

MR. COLLINS: Right.

MS. BELCHER: It needs the power of biology, billions of experiments, the power of chemistry, mix them together and you get new combinations that have never been made before. And so we can only touch on a couple of different kinds of applications, but, you know, that's just one example. But the idea is kind of better living through biology or understanding natural systems, you know, cheaper. You don't need billion-dollar fab labs. It can be solution processed, things that are recyclable or don't go back into the environment. That's the vision and we can go lots of places with that.

MS. KELLAN: Yeah, lots of places. I think we're going to be handing out cards, so if you have any questions you can jot them down and I'll try to go through some of the cards for the last 10 minutes of the session.

One other comment on --

MR. COLLINS: Well, you're asking where fields might go.

MS. KELLAN: Yeah.

MR. COLLINS: I'm a physician. The reason I got so excited

about genomics is the promise that it holds for taking medicine from where it's been to where it needs to go, and certainly over the next 10 or 20 years we're going to see remarkable advances of that sort.

MS. KELLAN: Are we going to get a cure for cancer?

MR. COLLINS: Hah. Remember, cancer is hundreds of diseases.

MS. KELLAN: I know.

MR. COLLINS: We will get some cures for cancers. Will we get a cure for ever single one? Well, let's hope so, but I know we will make remarkable progress.

I mean, a lot of this is build on technology, and I think that's another lesson here that science and technology are more tightly interwoven than ever. The things that Angela has been talking about would not have been possible without these technological advances. Medicine is going to be built upon these advances as well. Just look at DNA sequencing when that first genome cost us about \$400 million. Currently, the sequence of your genome or mine could be done for about \$8,000, and that is headed clearly downward. There are no laws of physics going to stop this curve from continuing to outstrip Moore's Law and probably will be in the thousand-dollar genome range in the next three or four years.

MS. KELLAN: So, we're talking personalized medicine?

MR. COLLINS: That absolutely will be a likely consequence in some instances. People are already taking advantage of that information.

By the way, I can't help since we're also talking about economics,

there was a recent analysis done by Battelle. Look at that first 10 years of having the genome sequence and ask what was the economic benefit of that \$400 million investment? Turns out it was about \$796 billion that were gained in economic growth in that 10-year period. If you add up everything we spent on the Genome Project, not just the sequence of the genome, but all the other work that went along with that, you still come up with a return on investment of 141 to 1, which is not so bad. (Laughter) And, again, at a time where resources are tight and people are trying to figure out what are the investments that are going to really encourage our economy, that's the sort of thing that I think is worth paying attention to.

NIH supports 487,900 jobs right now, and all of those are states and districts all over the country. The economic growth from our investments in 2010 was \$68 billion. The return just on the average grant is over twofold in one year for local economic goods and services. So, I hope there's enough legitimacy there for us to say that this is not only about advancing human health.

This is also a great opportunity to rebuild our economy and support our global competitiveness. But in 10, 20 years, if we are successful in retaining the best and brightest of this generation -- and I am worried about that, to be honest -- we should have the opportunity to be able to understand, at a very detailed level, why do people get cancer, heart disease, diabetes, or how diagnostics that will allow us to identify at a very early stage when something has gone wrong. And we'll have a wide variety of menu opportunities for interventions that should be much more powerful and less toxic than what we have now.

But that is a long, slow process. This is not a hundred-yard dash. This is a marathon. And unless people are willing to sort of recognize that and train for it and go through it, then there will always be cries of, "Where's the beef?" because it is a long, slow process. But, boy, what an exciting time to be a scientist. People come to me occasionally and say, hmm, I think I missed all the exciting stuff because I wasn't there when you sequenced the human genome. And I'm like no, no, no, no, the good stuff is what we can do now because we have this fundamental information and we can really start to figure out what's going on.

Imagine having a computer model of a cell that captures all of the components and makes accurate predictions about what happens with an external influence applied to that cell or makes a prediction if you mutated this particular protein in a certain way what would happen. That's a ways off, but it would be a pretty exciting thing to contemplate being part of putting together. All of those ideas, which 20 years ago would have seemed really, as you were described, insane because they were too broad, too interdisciplinary, are now achievable with the right talent and the right resources.

MS. KELLAN: That's interesting. And jobs in your sector, do you see a growth of job potential?

MS. BELCHER: I think so, for sure. I think with, you know, manufacturing materials --

MS. KELLAN: Right.

MS. BELCHER: -- and manufacturing materials and keeping it in the United States something that we're all interested in. And in both my

companies we're very focused on making new materials and developing jobs. And in Siluria where we're looking at natural gas to liquid fuels, you know, the new process that we've developed could have a huge impact on many different areas of job growth from oil and gas to the chemical industry, and to me that's very exciting to be a part of. Not only are you making something that could give you a cleaner source of energy and a lower carbon footprint, but creating jobs, and it's kind of a dream come true.

MS. KELLAN: Natural gas to liquid fuel using a --

MS. BELCHER: Yes. Well, so, this is the idea of how do you take our very abundant resource of natural gas and also methane that comes from renewable sources? You have methane, which is a molecule carbon with four hydrogens on it, it's a pretty inert molecule. It's very happy being methane by itself. Well, how do you use that as a building block to make longer chains to grow something like ethylene, which is two carbons. Put those together in a really specific way. And so what we've done is we've done catalyst discovery using the a combination of biology -- the billions of possibilities of biology -- chemistry, and high-throughput screening to figure out how to make it just so that you can rearrange that in a very efficient manner. And people have been wanting to do that for a long time.

MS. KELLAN: Is it expensive to do?

MS. BELCHER: Is it expensive? Well --

MS. KELLAN: The initial process I take it is costly.

MS. BELCHER: Well, it's -- the initial process, no, it's actually going to be quite a bit cheaper. We've developed catalysts that are very

effective. Starting a company is always expensive.

MS. KELLAN: Yeah.

MS. BELCHER: But the thing that's exciting to us is that it's compatible with already existing petrochemical industry, and so we're going to take our materials and our plants basically (inaudible) and put them into already existing facilities. And so, when you're getting -- when you're flaming and getting rid of natural gas that won't be used, well, let's use that to make fuel or let's use that to make products -- plastics are part of our everyday lives -- things that would normally be going out to form CO₂. And it really, you know, came about through initial basic science transitioning into a company with really fantastic engineers who said, okay, we're going to get this going. We're going to find out all the combinations until we find a winner. And then -- now interacting with industry.

MS. KELLAN: So, you're there. You're pretty much there doing it.

MS. BELCHER: Oh, we have -- we're very excited about where things stand, yes.

MS. KELLAN: Wow, that's great. Very exciting.

So, if you had a top three things to concentrate on as far as focusing money and interests, do you have something that you would -- should I -
- wow. Maybe we should go to the questions first.

MR. COLLINS: If you can sort a minute.

MS. KELLAN: Yeah, go ahead.

MR. COLLINS: Basically I think one of the things we have to be careful about at NIH is not being overly top-down in prescribing what are the

things that are most ripe for investment because in many ways it's the whole scientific community that provides the best ideas, and that's why our peer review system has to focus primarily on evaluating those and doing so in a rigorous, subjective, but also innovative way. There are some exciting things that you could see we probably need to especially push on: cancer, the ability now to read out all of the DNA mistakes in a cancer cell, and cancer is a disease of the genome. So, we have that opportunity to do this in a comprehensive way, and we're in the middle of that right now. It's breathtaking in the sweep. There'll be a new revelation about this regarding ovarian cancer this week with a publication in *Nature*.

Look at the vaccines. We are probably looking at the possibility of a universal influenza vaccine some time in the next few years by being able to take advantage of structural biology together with some very innovative immunology that brings in genomics in figuring out how to design a vaccine that you only have to take once, maybe a booster shot ever 20 years. But you won't have to have that every-year injection, and perhaps then the 36,000 people that die every year from influenza, that number will go down. Amazing advances that have happened in that kind of field.

Certainly with HIV-AIDS, lots of excitement there in terms of potential both locally and globally for applications. We have to do something about Alzheimer's disease, which if we don't discover ways to slow down or stop that disease is going to create even more havoc than it already does, not to mention horrendous economic costs. And we have new insights into Alzheimer's just in the last year that are pretty exciting in terms of new therapeutic ideas that

hadn't been realized, and the new insights come out of genomics again, studying why people get this disease, what are the risk factors, what pathways must be involved.

So, that's a very short list of what could be a very long list, but I hope you get the sense of the unprecedented opportunities that lie in front of us if we can simply push forward at the maximum speed.

MS. BELCHER: I'd like to add one, which is just education.

MR. COLLINS: Oh, sure.

MS. BELCHER: It's education at the, you know, the PhD level. But I think, more importantly, it's our young people, making sure that they have the opportunity to excel in math and science, both from the educational point of view and the mentors to get them excited about it, and to realize what a difference they can make by choosing a path of math, science, or engineering.

MS. KELLAN: We have a question about that. How can we encourage women to go into engineering and other science fields?

MS. BELCHER: Well, I think it's -- again, it's at the early stages. I think, you don't target girls in high school or women in high school necessarily. You look to elementary school, and that can be done through mentoring and I think encouragement. And I only have, you know, more data from my own institution, but we have a lot of women in engineering, in material science, which is my department. It's sometimes more women undergraduates than men. But the area that we have a problem with is getting more to go on for their PhD or getting more women to go on to academia. And part of that is seen as kind of a lifestyle. I've had students say I don't want your life. (Laughter) And I say, well,

I think my life is pretty good. (Laughter) And I think part of that is through mentoring and education.

And, you know, it's not like we sell ourselves this ivory tower, let's, you know, let's just work on interesting problems. It's let's make a difference in the world. Let's develop solutions. And those are the kinds of things that I think that kids and students will get excited about. It's us being more regular people who want to make a difference in the world, not that are just solving equations and thinking, because it really is about community and interacting with people and about thinking something -- about something bigger than yourself that can make a difference.

MS. KELLAN: And even knowing what the potentials are. I mean, I don't think a lot of kids even know what they can study at a young age. I never knew until I got into reporting science all the different fields there are out there, you know, at a young age. I'm always -- I wish more kids had my job, you know. I think that if I had known what was out there, I probably would have studied it more.

Okay, what is your impression of the job prospects of the interdisciplinary scientists I guess we can call them? Will they be welcome basically into the workforce and --

MR. COLLINS: I think in the forward-looking laboratories and institutions, absolutely. I think this is the area where many of us see the greatest potential for advance is when you bring disciplines together. I think in the past, and maybe still this is true in some institutions, such individuals had a little trouble finding a welcoming home, again, because of the departmental structures

that may have been a little bit mired in the past and not so much in the future. And people who are, say, for instance, computational biologists, didn't feel they were particularly recognized in the computer science department, but in the biology department it was, like, you know, where are your test tubes? So, it's moving forward, though I think by the success of interdisciplinary effort. If you look at the recruitments that are going across now in the top-tier universities in this country, a large number of them talk about how we are looking for somebody who has interdisciplinary skills.

MS. BELCHER: I agree, too, and one of the things I always told young people is that being interdisciplinary is great, but be a real expert in one field and then start integrating other disciplines. So, don't be a little bit about a lot. Really have a depth of understanding in your field, whether it's chemistry, physics, biology. And then add on to it, and that makes you very solid.

MR. COLLINS: Good point.

MS. KELLAN: We're not changing the field, we're just adding more of it.

MS. BELCHER: We're improving the field.

MS. KELLAN: Improving the field, right.

MR. FRANKEL: Yeah, knocking down the barriers.

MS. KELLAN: How do you recognize and promote talent outside of the system, the non-academic genius? That's a tough one. Got any answers for that one?

MR. COLLINS: That sounds like one of those where you'd have to look at them case by case. A non-academic genius, well, in what particular

arena and with what particular dream?

MS. BELCHER: That's a hard one.

MR. COLLINS: It is.

MS. BELCHER: I think that would be hard --

MR. COLLINS: It is. You know, one of the questions that I think we don't have a good fix on is really what is the talent need? What's the supply and the demand equation right now across many fields of science?

I've just recently asked Shirley Tilghman, who's the president of Princeton, to lead a working group for my advisory council about the workforce for biomedical research because, depending on who you talk to, we have way too many PhDs or we don't have nearly enough, and they can't both be right. I think the problem is that we think oftentimes as we're training new PhDs that they all have to become just like us, that is, they have to be, you know, tenured professors at top-tier universities and all other pathways are somehow not quite as impressive or a little secondary or we call them alternative careers, which immediately sends a signal, well, you don't want to be one of those. (Laughter) And yet that's completely wrong. I mean, right now, the way science is going in technology and engineering, there are lots of needs and opportunities for all kinds of interesting pathways that are not the traditional full professor at MIT, and yet we don't do a very good job in exposing graduate students to those options in a way that they get a sense about what might be a really good fit in industry, certainly in teaching and education where we have been talking about we desperately need those creative minds, in reporting, in science policy, all of those areas that are, I think, underserved right now by talented doctoral-level trained

scientists, but which are seen as not quite as somehow fundamentally important careers. They are.

So, what Shirley's trying to do is to build a model with lots of help from people who know how to do this that allows to get a sense of, well, what are we expecting to have as a supply of interested people who want to get into science coming from our country and other countries? And then what are the possible pathways and what are the needs in those pathways? And can we figure out -- because NIH supports an awful lot of this training -- are we doing this right, both in terms of quantity and in terms of quality? Is our training program all across the board here actually well-matched to the needs? I suspect we'll get some interesting answers, and it will require some changes.

MS. KELLAN: Oh, you both have highlighted the enormous potentials through strategic investments in research. Yet AARP is running as across the country pitting spending on Medicare and Social Security against the pickle research. How do we convince Americans and policymakers that this is not a Sophie's choice or is it?

MR. COLLINS: Pickle research, hmm. (Laughter) Well, I think we have economic arguments to bring to bear. So, for instance, longevity. Longevity has improved by about one year every six years in this country, and if you add up what that's added to the economy since 1970, that's estimated to be worth about \$95 trillion.

If you ask what has happened in terms of disabilities, which obviously AARP members -- and, yeah, I'm one, too -- are concerned about, we've reduced disabilities in individuals over 65 years old by 30 percent since

1970 by advances that allow, for instance, people to be more functional even if they have cardiac disease, by joint replacements, all of the things that keep people mobile and able to perform life activities without a major disability. Those are all pretty good returns on investment.

We've seen heart attacks drop by more than 70 percent, strokes by more than 70 percent in the space of the last 40 years. We see cancer now going down for the first time in the last century. For the last 10 years cancer has been going down in incidence by about 1 percent per year. Each drop in cancer of 1 percent saves us \$500 billion in terms of economic situation. That's not bad. When you consider the amount of money we put into research, the return is probably one of the best things that we can possibly do.

So, tell AARP -- and I think they get this. I'm not sure this question is fair to AARP, by the way, because they have actually been quite supportive of research as a means of trying to do things that they care about, such as preventing disability, such as doing something about Alzheimer's disease.

MS. KELLAN: How does the social sciences play a role in innovation and economic growth?

MR. COLLINS: Oh, it's critical. So, just yesterday I spent the day with the Office of Behavioral and Social Science Research, which is part of NIH. They were having a think tank, and they brought in experts from all over the country and some from outside the country to lay out what should be sort of the next agenda here for social sciences as part of biomedical research. A lot of this is trying to understand human behavior because so much of the disease that we

are trying to prevent is based upon behavioral decisions, and we haven't done a very good job of understanding what are those motivators that would result in better outcomes, and this a great time to be able to do that. You can't have personalized medicine, for instance, unless you think about human behavior because otherwise nothing's really going to change. So, it's a fertile field right now for investment.

MS. KELLAN: Okay, Ken. Should graduate students in the sciences be involved in innovations as defined in turning discoveries into economic social good?

MR. COLLINS: You're doing it.

MS. BELCHER: I'm not sure why the question was asked, but, I mean, I think I see much more that the students are looking for technologies that can make a big impact, and a lot of times they are for economic digital, a lot of times they're for countries that couldn't afford better health care or, you know, less expensive ways of getting energy sources to a different part of the world, and that's something that students are very passionate about. At the same time as a professor and a PI of a group, you're always having to, you know, weigh things out in terms of how you provide the best education for your students to go towards, you know, earning your PhD. And so you want to make sure that they're doing the basic science and basic technology.

But, of course, it's great to have the final impact be in technology or in underdeveloped countries or in inexpensive health care, things like that. But we also need to have a lot of things like Engineers Without Borders and other programs we have, something called D-Lab at MIT where the students go and

they work in other countries, either in economics and in engineering and science, where they try to make an impact locally based on technologies that they've either developed in classes or been developed at MIT or other places. And the young people are very passionate about that.

MS. KELLAN: There are a lot of exciting things and challenges ahead. And I thank you two for joining us today, and thank you for listening.

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I, Carleton J. Anderson, III do hereby certify that the forgoing electronic file when originally transmitted was reduced to text at my direction; that said transcript is a true record of the proceedings therein referenced; that I am neither counsel for, related to, nor employed by any of the parties to the action in which these proceedings were taken; and, furthermore, that I am neither a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

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