NATIONAL PRESS CLUB LUNCHEON WITH FRANCIS S. COLLINS, M.D.

SUBJECT: THE NATIONAL INSTITUTES OF HEALTH

MODERATOR: ALAN BJERGA, PRESIDENT, NATIONAL PRESS CLUB

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ALAN BJERGA: (Sounds gavel.) Good afternoon, and welcome to the National Press Club. My name is Alan Bjerga. I'm a reporter for Bloomberg News and President of the National Press Club. We're the world's leading professional organization for journalists, and are committed to our profession's future through our programming and by fostering a free press worldwide. For more information about the Press Club, please visit our website at www.press.org. To donate to our programs, please visit www.press.org/library.

On behalf of our members worldwide, I'd like to welcome our speaker and attendees at today's event, which includes guests of our speaker, as well as working journalists. I'd also like to welcome our C-SPAN and Public Radio audiences. After the speech concludes, I will ask as many questions from our audience as time permits.

I'd now like to introduce our head table guests. From your right, Mary Wooley, president of Research! America; Barbara Culliton, president of the Culliton Group and former editor-in-chief of Genome News Network; Dr. Raynard Kington, Principal Deputy Director of the National Institutes of Health, and a guest of the speaker; Susan Heavey, a health reporter for Reuters; John Burklow, director of the NIH Office of Communications and Public Liaison; Andrew Schneider, associate director and editor of Kiplinger Washington Editors, and chairman of the NPC Speakers Committee and organizer of today's event.

Skipping over our speaker, Doris Margolis, president of Editorial Associates, and National Press Club member who organized today's luncheon with fellow member, Ira

Allen of the U.S. Food and Drug Administration; Dr. Kathy Hudson, NIH Chief of Staff; Keith Hill, editor/writer with BNA and Treasurer of the National Press Club; Dr. Patricia Berg of George Washington University Medical School, director of one of the center's cancer labs and health writer for Weiner Public News; and Rick Borchelt, communications director for the Office of the Chief Scientist, U.S. Department of Agriculture. (Applause)

Our guest today has had a career of many scientific achievements, capped by his leadership of the National Institutes of Health, the world's largest research enterprise with a budget of more than $30 billion. Dr. Francis Collins was appointed Director of the NIH by President Obama last year, a recipient of the U.S. Medal of Science, the highest honor bestowed on scientists by the U.S. government, as well as the Presidential Medal of Freedom. Dr. Collins headed the National Human Genome Research Institute from 1993 to 2008. There, he led the government's project to map the genetic code of human beings, which landed him on the cover of *Time* magazine.

He was born in Stanton, Virginia, the son of a drama professor and a playwright. He received a chemistry degree from the University of Virginia, a Ph.D. from Yale, and a medical degree from the University of North Carolina. Before joining NIH, he was a professor at the University of Michigan.

In addition to his achievements with the human genome, Dr. Collins's own research laboratory has discovered a number of important genes. He also has a longstanding interest in the interface between science and faith, and has written two books on the topic. A third book, due early next year, will be about personalized medicine.

Although he is one of the leaders in the world of science, Dr. Collins is known in other circles as a devoted rider of Harley-Davidson motorcycles, and a rock guitarist, having appeared recently in a *GQ* feature on "Rock Stars of Science," and on the "Colbert Report" where he took off his glasses, shook out his hair, all for the higher cause of promoting biomedical research. (Laughter) So, Dr. Collins, welcome to the National Press Club and rock on. (Applause)

DR. COLLINS: Well, thank you for, shall we say, a very lively introduction, Alan. Great to be here at the Press Club and to have a chance to say something about medical research and the exciting future that we see just ahead as new opportunities to understand how life works in a very comprehensive way, and to apply that to the prevention and treatment of disease are looming ahead of us in ways that we couldn't have imagined even a few years ago.

I want to thank the members of my staff that are here, already introduced. Again, thanks to Raynard Kington who has ably served as acting director of the NIH for the time in between when Dr. Elias Zerhouni was the director and when I arrived last August and now serves as the principal deputy. And John Burklow, who has been such a capable assistant and wise advisor as far as communication strategies. And Dr. Kathy Hudson, the

Chief of Staff who I recruited from her previous role as the head of the Genetics and Public Policy Center.

The NIH mission is actually encapsulated in a very brief sentence. People look at mission statements and sometimes wonder, “Who wrote that?” Well, I don't know who wrote this one, but it actually says pretty well what the National Institutes of Health is all about. Science in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. So it's two parts to that. The fundamental, basic science, and the applications. And we are very serious about both of those and find ourselves at really exciting times right now in being able to move the ball forward.

I hope you have seen a brochure that was distributed. If not, this is what it looks like, and I think there's some copies around outside if you didn't pick one up. This is a new description of what NIH does called, “Turning Discovery into Health.” I'll just mention a few of the things that are pointed to in this brochure as far as ways in which our medical research supported by NIH, which is the largest supporter of biomedical research in the world, have already made substantial differences in human health.

If you look at longevity, for instance, over the last 20 or 30 years, the average life span has been increasing by about one year every six years. That's pretty impressive. If we got to one year every one year, then we’d all live forever, but we're not quite there yet. But positive is good. Now, we do worry, of course, with the epidemic of obesity that that curve might flatten out and maybe even start to go the wrong way, and that's a major agenda item at NIH as well.

But if you look at the statistics so far, the evidence that our medical research is leading to longer lives is very compelling. And you can draw a direct line from biomedical research that NIH supports to the observations that have led to that increase in life span. Similarly with disability, if you go back 30 years, 26 percent of individuals over 65 were disabled from some major life functions. That is now less than 20 percent, so we've made a lot of progress in that area, although obviously we’d like to push it even further.

And this has been done at a pretty amazing cost in terms of the investment and the return on that investment. Take heart disease, for instance. Deaths from heart disease in the last 40 years have fallen by 60 percent, and that has been at the investment of about $4 per American per year in biomedical research, about the cost of a latte, as long as it’s not a Vente latte. That's a pretty good deal. And in fact, you can make those same arguments about other investments in cancer and diabetes and so on. And you can see around us the results of that in terms of the kinds of advances that make it possible for people to get through difficult times. Just in the last month, of course, we've seen two major figures in past administrations with heart problems, President Clinton and Vice President Cheney. Both of those afflicted with circumstances that in the past, at a minimum, would have led to a hospitalization of many weeks, and at a maximum, of course, might not have been survivable. And it seems like, okay well, it’s another one of

those things, needs another stent, let's take care of it. We almost take that for granted. All of that comes out of NIH research.

Look at HIV/AIDS, where we are now. When I was a starting out assistant professor at the University of Michigan in the 1980s, and HIV/AIDS was first being discovered and described initially much of it by Tony Fauci at NIH, the average life span for somebody after a diagnosis of having HIV/AIDS was about 15 months. Today, for someone who's 20 years old, turns up HIV positive for the first time, that life expectancy for that person, because of anti retroviral therapies that are now available, is about 70 years. So we have converted what was a rapidly fatal disease in to a chronic, treatable disease. Obviously, we need to go further with that and come up with better means of prevention with vaccines and other approaches. But it is amazing to contemplate how far we have come with a disease that was such a death sentence only about 20 years ago.

Cochlear implants, sort of an interesting example as well. It is certainly the case that a child who is born with congenital deafness can, in fact, live a highly productive life and many of those kids have been able to do so. But now with early screening to be sure whether children can hear or not, those children are picked up early. The cochlear implants developed within NIH research are now highly successful, and something like 60,000 people now have those. That basically then makes it possible, if instituted early for that child to develop normal language. The cost of the cochlear implant, well yes, it's about $60,000 per patient. But if you add up the additional costs for education that are needed by a deaf child, those add up to about a million dollars. And so there you see the economics as well as the benevolent side of this are very strongly in favor of what's now possible.

Speaking of economic arguments, I wanted to say a word or two about that, given that we are, after all, at a time where there's much concern about our economy and how we're going to pull ourselves out of a difficult situation, both here in this nation and worldwide. Economists agree, looking back over our history since World War II, that more than half of the economic growth in the United States came from investments in science and technology. I don't know if that's widely appreciated, but that's generally agreed upon by economic analysis.

So if we are, in fact, in need of getting our economy jumpstarted again, this would be a pretty good place to make those investments. And in fact, that's just what's happened. The Recovery Act, which of course has now been in place for about a year included $10 billion that went to the National Institutes of Health to be spent in a two year period in fiscal year '09 and fiscal year '10. That was an enormous influx of resources and of course at NIH, there was a great challenge to figure out how to use that wisely in a short period of time.

The staff rose to the occasion, developed new ideas about proposals that we'd love to see, put out what we call requests for applications to see who was out there that had some science they'd like to propose. Assembled 15,000 reviewers to look at the

grants that came in. And over the course of just a few months, did the reviews, did a second level of review and then made decisions about which grants to fund.

The outpouring of ideas was spectacular. When I arrived in August, I had a chance to read through some of the grant applications that were likely to get funded, but maybe were a little bit on the cusp of whether we could afford it or not. And they were fantastically interesting and innovative. It's clear we have a great engine of discovery out there that needs to be revved up.

And so out of that, we funded some 13,000 grants, 2,000 of those were people who'd never gotten a grant from NIH before. So we're bringing in new disciplines, new investigators, institutions, more than 20 of them, that had never been funded by NIH. Some of them small businesses, also supported by Recovery Act grants.

And out of that, we estimate in the course of this two year period, 50,000 jobs will be created or retained. High tech jobs, high paying jobs, jobs that contribute to our economy in special ways. And this is all distributed across the country, in all 50 states. Because 85 percent of what NIH does is given out in grants to universities and small businesses and other institutions across this great country. So we are, I think, a very effective engine of economic recovery.

There is, of course, a challenge for us trying to manage science in this way, because science is not a hundred yard dash, it's a marathon and a two year cycle time is generally too short for a project to get fully explored. And so we are facing now, as the Recovery Act's two year period, will come to close in another year, how will we make sure that we keep that momentum going? We're very fortunate that we have a president who believes in the value of science, to contribute to our nation in solving problems and stimulating the economy. And so when the president's budget was rolled out on February 1st, if you saw the details there, you would notice that science actually did quite well, even in the face of flat discretionary budget limits. The National Institutes of Health in that budget proposal receives an extra $1 billion, which is about a 3.2 percent increase over the previous year. And we will certainly be able to use that in many exciting ways.

So, I want to tell you what some of those exciting ways might be. I was initially approached about the possibility of becoming NIH director several months before it was announced or confirmed by the Senate. There's a long process that goes on there where the FBI delves into what you really did in sixth grade. And I told them my life was pretty boring, and I guess they must have agreed. Because ultimately, the nod came through. But over all of those weeks of waiting for that, there was an opportunity to think about what would really be a useful way for the NIH director to try to steer this amazing ship called the National Institutes of Health with all of its promise and all of its complexity, all of its 325,000 grantees, scientists who work on our grants, all of the ways in which we can nurture science in particular directions.

And I came up with a series of five themes which I had the chance to discuss with some other big thinkers in the community and which seem to have settled out pretty well.

And I want to mention those, but I also, as I do so, want to mention the fact that just yesterday we funded seven new cross cutting innovative projects as part of what's called the NIH Common Fund. And I want to show you how those fit together with those themes.

The Common Fund is a part of the NIH budget, which was actually just formalized four years ago in the NIH Reauthorization Act, which has now grown to a half a billion dollars, and which is supposed to be utilized for projects that none of our 27 institutes and centers would be likely to be able to fund on their own. Those institutes and centers are wonderful organizations of talented and visionary scientists, but they have specific missions. There's the Cancer Institute, and the Heart, Lung and Blood Institute, the Diabetes Institute, and so on.

When you encounter a scientific opportunity that actually does not easily fit into one of those diseases, how does that get supported? Well, the Common Fund is the answer to that. Elias Zerhouni was the one who advocated strongly for the need for this, and I am the beneficiary of the fact that he was successful, because the Common Fund now gives the NIH director a chance to do some bold things that might otherwise have only been achieved by a lot of tin cupping, which is not always so easy to succeed in tight budget times.

So the Common Fund did, in fact, make it possible yesterday to announce the seven new bold proposals, which you might have seen a little bit about today, or even yesterday evening. But I'll mention them as I go through here. But let me talk about these five themes, the themes that I see as particularly exciting opportunities that cut across diseases, cut across basic and applied science.

The first of those is the ability to apply new right throughput, bold technologies to look in a comprehensive way how the cell actually does what it does, how the organism does what it does, and how sometimes that goes wrong and disease occurs. And I'm talking about several things. Genomics is certainly one of them, the field that I've had the great pleasure of working in in my previous life as the Genome Institute director, that allows you then to look at all the DNA in a cell and all of the RNA that represents the expressed part, and pretty soon all the proteins, although we're still kind of working on the ability to be comprehensive there.

But it’s also about imaging approaches, it’s about special approaches that involve very small scale efforts, nanotechnology. It’s about computational biology. All of those have reached a point where they're ready to be applied in large scale fashion to disease applications that we couldn’t have really done, even a few years ago. Let me give you a couple of examples; cancer. Cancer is a disease of DNA, and yet we have not had the ability comprehensively to see where are all the glitches in a cancer cell that cause that good cell to go bad? We've had abilities to look at candidate genes, which is kind of like the guy who lost his keys at night on the street and only looked under the lamp post because that's where he could see. We were limited in the same way.

Now, we can light up the whole street by having the tools to survey the entire genome in a cancer cell and ask, “What's wrong there?” And there are prodigiously exciting things coming out of that. We in the cancer genome atlas, which is an NIH effort, have already applied this for brain tumors, glioblastoma multiforme, the most severe form of brain tumor. In the paper just published last month, it’s clear that that has completely taken this monolithic idea that brain tumors are just one thing and broken it down into four very distinct subsets that are biologically very different, and different in terms of their likely prognosis and their response to therapy. And this is the kind of thing you dream of because up until now, all brain tumors are pretty much considered the same, treated the same way, and the outlook has been pretty dismal.

Not only have we learned to break this down into subsets, but we've discovered new targets for drug therapy that we didn't know were part of the way in which a cancer cell operates and those also will give us new ideas to revolutionize therapeutics in the coming years.

That's a great example of how we could now take high throughput approach and apply it to a disease where we desperately need that information. And we can now take what we've done for brain tumor and apply it to the 20 most common cancers, and that is going to happen over just the next two years. Basically, this amounts to doing 20,000 human genome projects in the next two years, which is pretty breathtaking for me to stand up with a straight face and tell you we're going to do that. Because after all, I was a bit involved in the first human genome, which took about 13 years and cost about $300 million. And now, I can tell you we can do a genome for a few thousand. And soon, we’ll be to the thousand dollar genome, probably in the next four or five years.

Other applications of this kind of high throughput approach would include things like autism where we desperately need to understand what are the causes of this disease which is terribly distressing to those families in which it has occurred, and seems to be increasing in its incidence without a clear understanding of why that would be. Clearly, there's a mix here of heredity and environment and we need to go as hard as we can to understand what those factors are in both instances.

The microbiome, an interesting approach, also being taken to disease. You may not want to think about it, especially right after a nice lunch, but if we counted up the number of microbes that live on you and in you, and compared that number of cells to the cells that are actually your own human cells, they've got us outnumbered. And we don’t know much about them, actually. We kind of hope that they're there with good purpose and being symbiotic and synergistic and not making us sick. But sometimes, I'm sure, we're going to discover, with better tools, that they are. And the tools that we can now apply will allow us to discover things about what's there that we could never have determined by standard microbiology because most of these microbes cannot be grown in the laboratory. But they have DNA, so we can find them by that particular signature.

Well, those are a few examples of the high throughput approaches that I think are going to be quite exciting. The projects I mentioned a minute ago, seven new ones

coming from the Common Fund, there are three that fit into this theme. One is an approach to systems biology, to try to understand how turning down one particular gene might have a similar effect to adding one particular drug. It's an idea of taking a collection of cells and hitting them with all kinds of perturbogens (sic), that's a new word for today, I bet. A perturbogen is something that is going to make the cell react. And if you look at those patterns and look at the readouts of what you're able to assess, you're going to find connections that you didn't know were there about systems biology.

Another program is develop better protein reagents to be able to sample one particular protein out of hundreds of thousands, or millions. These are often monoclonal antibodies, but we don't have a good inventory of those that are high quality, and we need to generate those and make them available at low cost for investigators who depend on these heavily for research. So this is a systematic approach to providing a research tool.

A third one that fits into this approach is the knockout mouse effort. We already are funding the effort to take the 20,000 protein coding genes in the mouse and knock them out one at a time using a technology that allows you to do that in embryonic stem cells in the mouse. And we'll have that inventory of stem cells, but we won't really know unless we do the next step, what's the consequence? Okay, you knocked out this gene, nobody knows much about it. You got it there in the cell, but let's make a mouse and see what the mouse looks like. So that is also going to be part of this in a large international collaboration involving Europe and Canada, especially.

So you can see this first theme of high throughput technologies is ripe for all of this, and we're going to infuse this with other energies as much as we can with new projects that come along through the Common Fund.

The second theme, and one that's particularly relevant to what's being talked about in Washington a lot these days is healthcare reform and the need to supply a scientific evidence base for decisions that may need to be made about what works and what doesn't. NIH has been doing that kind of research for a long time. I mean, that's what a lot of clinical trials are about, is to figure out whether something works. A particularly strong area of interest right now is what's called comparative effectiveness research, usually just abbreviated CER, where you now there is more than one approach to a particular kind of problem and you're not sure which one is better. And so let's do a clinical study and try to find that out. NIH has been supporting those studies for many years, but it is now very much a high priority to pick out areas where we need that information and provide it to those who are trying to make decisions about our healthcare system.

It's timely, in fact, for me to tell you that there is an announcement just today from the neurology institute about a very powerful example of comparative effectiveness research. What they did was to try to assess what is the right treatment for somebody who has narrowing of the carotid artery in the neck and who is, therefore, at a risk for stroke? And that gets picked up in a regular exam, or it may even involve a little glimmer of a

risk from somebody who's had a TIA, a transient ischemic attack. And then the question is, "Oh, what do you do?" And the standard treatment has been surgery to go in there and actually pull the plaque out of that artery, what's called a carotid endarterectomy. But more recently, people have been using stents, the same kind of stents that you use in heart disease are now being applied to the carotid artery. Well, is that as good, do we know?

So NIH sponsored a large, controlled trial randomizing people to one or the other. And the answer is it's just about the same as far as the success rate. But the stents are much less invasive. It does look as if there's a little difference between younger patients and older patients, and doctors will need to take that into account. But this is really useful information. Well, that's the kind of thing that we are doing to assist the healthcare reform discussions. Personalized medicine is there as well, and a better focus on prevention and trying to figure out what works in that regard.

Heath economics is in there, trying to understand what motivates providers in terms of the decisions they make about care? Maybe NIH could do something more to try to test out various incentives that might be useful in bending the cost curve.

Again, the seven new Common Fund proposals that came out yesterday, I should just mention one of those, is directly relevant to this. And that is a new research program on the science of behavior change. How is it that people make decisions about altering their health behaviors? Because we may generate all this information about effective prevention measures, but if we don't know how to convey it in a way that people absorb it and act on it, then the resources are going to be wasted. And there is some evidence there that there are better ways to do that, but we need a lot more research, and this new RFA is going to achieve that.

The third theme of my five is global health. We are at a time where global health research has much more potential than it has had, perhaps, in all of history because we've learned a lot about those pathogens that cause diseases in low income countries. And we have a chance, therefore, to develop new strategies, new drugs, new vaccines, new diagnostics. And I would like to see NIH, which already invests $600 million a year, even bump that up a bit because of the opportunity here. And I think the mandate that we have as a country with resources to reach out and perhaps this is a particularly good time to remember that that kind of outreach is also a very good, effective means of diplomacy, that this is soft power or smart power instead of hard power.

We can focus not only on AIDS, tuberculosis and malaria, but also on some of the neglected tropical diseases that haven't gotten much attention. And we will need to focus on the non-communicable diseases like diabetes and hypertension which are the fastest growing cause of morbidity and mortality in the developing world. Maybe that was not widely known by most of you, but that is the fact. And we've done relatively little to prepare for that.

We also need, I think, in our global health agenda, to be sure that we are encouraging the building of capacity in those countries where the problems occur instead

of continuing to go forward at a time where somehow we in the developed world are providing the tools and then just handing them over. It's the time to build research capacity in sub Saharan Africa, in other places.

In that regard, one of the announcements yesterday was that we decided to contribute to an initiative which actually comes through PEPFAR, the President's Emergency Plan for AIDS Relief, to provide tools for better medical and research education at institutions in sub Saharan Africa. But we put some strings on it to say it was not just, then, about aids, TB and malaria. It also should be about non-communicable diseases. And we're happy to have a chance to be part of that effort.

Well, those are three of the themes; high throughput, healthcare reform, global health. The fourth one, and one that I think is particularly exciting right now to talk about is what I would call translational medicine, bringing the basic science discoveries into the clinic. There are several components of this that are at exciting junctures. One that one could mention is the ability to discover such plasticity among cell types, that we could actually take one of your skin cells and convince it to become a neuron. Or, an islet cell for your pancreas, if that's what you happen to need. And this is the magic of what Shinya Yamanaka taught us all about three years ago, of induced pluripotent stem cells, or IPS cells. And I don't think anybody was prepared for this. I remember reading that paper, I was supposed to be on vacation and I snuck off in a corner and read this paper. And I literally got cold chills, just because of the way in which this had changed forever our understanding of what you might be able to do in terms of changing one cell type into another.

It turns out just four genes inserted into that skin cell can convince it to go back in time and become pluripotent. And then you can take that pluripotent cell, and with a variety of cocktails, convince it to go down pathways towards cells that you might need if you had Parkinson's Disease or diabetes or a spinal cord injury. The opportunity there for therapeutics is particularly exciting because these are your cells. So if this were to be applied in the therapeutic arena, you wouldn't expect transplant rejection problems, or the need to give you strong immunosuppressives.

Many steps have to be taken before this could become a reality because the safety concerns are quite real. But I don't know anybody who's not pretty excited about pushing this forward as a translational opportunity of a major sort. We did, in fact, announce yesterday that we would be putting substantial new resources into the creation of a center for IPS cell research on the intramural campus of NIH up here in Bethesda because of the close connection to the clinical center, which should allow us to move things into this kind of translational opportunity at the earliest phase, as soon as it looks like it's safe.

Not only stem cells, though, are exciting to look at, but also an approach to developing therapeutics that had depended upon so-called small molecules. Small molecule's a funny term, but we seem to be stuck with it. So what do I mean by that? You can think of them as shapes. They're organic chemistry compounds, that's what drugs are. They are mostly small molecules. But we don't know for most situations what

kind of a shape you need in order to try to treat that disease. And there's a whole science about how to do that that's largely been the province of the private sector.

But as we look around and see how many diseases are not getting any kind of therapeutic effort made on them because they tend to be uncommon and so there's not much of an economic incentive, it has seemed that it's time to get academic investigators more involved in at least the front end of this pipeline to be able to make a contribution that might ultimately help a lot of people. After all, there are 25 million people in this country who suffer from rare diseases. Collectively, that's a lot of people. And the science has gotten to the point where we could imagine academic investigators playing a very useful role.

So what's the step you have to take? Well, first you have to know a target. You have to study disease well enough to know what would be the vulnerable Achilles heel to be able to correct a cell that's gone wrong. That's a lot of what basic science has been doing. Once you identify that target, then you have to figure out how to take that knowledge and turn it into an assay. And by an assay, I mean something that you could test hundreds of thousands of times in the presence of 100,000 or more different compounds, and figure out, is there something in your library of chemical shapes that actually works against that target? And there's a whole science, and kind of an art to that as well.

We have now made that possible. We have also made it possible for academic investigators to actually do that kind of screen with high throughput centers; four of them in the country, one of them right up here in Rockville, that allow you to do that in a matter of two or three days, and to get out of that some very promising starting points as far as what could become drug development. And in the course of the last five years, NIH investigators have found 128 such compounds directed against more than several dozen targets. Now after that, you want to take those promising compounds into the next step, which is ominously called the valley of death, because that's where projects often go to die because the problem there is a very high failure rate. Your compound might look good in a cell based assay. You give it to an animal and everything goes wrong. So you have a lot of work to do in that circumstance. But we are starting into that space as well.

Then once you have reached the point where you have a compound that looks promising in animals, then you go to the FDA and you ask for permission to give that to patients in a clinical trial. You run the clinical trials. If all goes well, you go back to the FDA and say, "Will you approve this for general use?" That long pipeline, which often stretches out over a decade or more and is terribly expensive has been, as I said, primarily the province of the private sector. But we're not going to see progress at the level that we all hope to if we leave it only in that area.

And again, if we could come up with a new model for a partnership between NIH funded investigators and biotech and pharma, this could be very exciting. So what's the model? The model is that NIH investigators, now empowered by these capabilities and these technologies, can start things down that pipeline and as soon as they get to a point

where they've already de-risked a project and it looks like there's something pretty promising and a company says, “Okay, now I'm interested,” then we license it out and the company can take that and carry it through with the appropriate profit motive because now the economic advantages look pretty acceptable.

Similarly, there may be compounds out there that actually companies have carried pretty far along and then abandoned for one reason or the other. We could bring them back into this public pipeline and see what we could do with them, repurpose them for some other applications.

This whole pipeline, a reengineering, is an enormously exciting opportunity. I don’t think I've encountered very many people who after they've seen the potential here don’t get excited about it. And that includes people in academia and people in the private sector. Five years ago, I don't think we could have done this. Now we can.

To facilitate that, just two days ago we announced a much tighter relationship between the FDA and the NIH. Peggy Hamburg and Secretary Sebelius came out to NIH, the three of us announced a Leadership Council that will bring together the senior leadership of NIH and FDA to focus on ways to streamline the process of evaluating new possible therapeutics. And also, agreed to support a whole new set of scientific projects on what's called regulatory science to try to get a better handle on how exactly we should be reviewing protocols for rare diseases or unusual applications. And that, indeed, is also a very exciting opportunity.

Well, I should draw to a close and let you ask questions. Let me point out, though, one more theme of my five. If you were counting, we've only made it to four. The fifth theme is really to empower and invigorate the research community, because that's our most important resource. We may have great ideas and great science projects, but if nobody does them, they just sit there.

And that means we need to come up with new and better ways to inspire innovation, and there's a lot of ideas that we're putting into place right now about that to make sure that scientists are given a green light to be bold and to take risks and propose things that are out of the box. We need to be sure that we're supporting early stage investigators because there's been a bit of a graying of our research community, and we need to be sure that individuals who are just joining this get a chance to get started and get supported.

But there's one other aspect of this that I just wanted to conclude with because it is a concern of mine, and it is perhaps not a concern that has routinely come from NIH, but I think we now have to take it on very seriously. The future of biomedical research is in danger because of something we're not doing, we're not doing a good job of cultivating the next generation of scientists. In fact, I think it’s fair to say we're doing a pretty terrible job. Let me share with you some depressing statistics. Today, 15 year olds in the U.S. rank 29th in science achievement among students from 57 countries, 29th. Almost half of our 12th graders score below basic in science. And here's a disturbing one. A survey of

students found that 84 percent say they would rather clean their room, eat their vegetables or go to the dentist than do their math homework. (Laughter) That doesn't sound like a good thing for our future.

Forty years ago when I was in high school, we had the best high school graduation in the world. By 2006, we had slipped to 18th place. So why does this matter? I'm not saying that all of our high school students need to become scientists, although I would love it if a few of them did. But clearly the workforce needs people with quantitative skills in science and math. And all of us as consumers are going to need to be increasingly able to deal with information of a scientific and mathematical sort if we're going to make good decisions about ourselves and our families.

So what to do about this has been a major challenge. We can do little things, and we can do grand things. In April, I'm going to do a little thing. I'm going to go to observe national lab day, which is now an across the U.S. priority and spend a day in a D.C. public school with high school biology students. And I hope to share with them the awe and wonder of what it means to be a scientist and to make a discovery or have a chance to see the human genome emerge for the first time, or figure out what causes a rare disease like progeria, the disease that causes children to age at seven times the normal rate, which is a major function of my lab's efforts right now to try to understand.

I'm also going to encourage the thousands of scientists out here in Bethesda, and the tens of thousands of NIH funded researchers to do the same; to get involved in national lab day, which means they simply make themselves available and go to a school and make a relationship with a teacher and a class, not just as a one-day shot, but actually something that could be built on over time.

After all, in the 1960s after Sputnik, our nation became passionate about scientific education and technology and engineering and math and this helped us to win the space race and also prepared us for a challenging future in terms of the ability to make the right decisions, and stimulated our economy for decades. But we have really slipped in that regard. So how do we do the big things? Well, I hope you've looked at the initiatives that the President and the Secretary of Education have been putting forward, because I think those are really appropriate ways to try to get this turned around.

The Race to the Top, which Arnie Duncan is presiding over, is an example. The Educate to Innovate Program the President announced to try to give teachers an opportunity for better science training and math training. Those are as well. And the governors are getting into the act. They're working together to develop and implement common math and science standards. So as the NIH director, I guess I wanted to come here today in my closing moments and say this is going to be a priority for the National Institutes of Health.

If we are going to capitalize on these phenomenal scientific opportunities that now lie just ahead of us, we have to have the talented, new entries into our scientific workforce that are waiting to get excited the way that I was. I got excited about science in

10th grade. And when I talk to scientists who are currently successful in their area, 90 percent of them say it was that teacher that taught me biology or physics or chemistry that got me to realize this is something I want to do. And I fear we don't have enough of those experiences happening, and we have to do something about it, and we have to do it quickly.

Well, I've gone on probably longer than I should have, which is a chronic problem for me, and you've been very understanding and listened quite faithfully and graciously. And I would now like to stop and take whatever questions our moderator has sorted through and try to do my best to answer them. Thank you very much. (Applause)

MR. BJERGA: Well, thank you very much for your time, and our audience has eaten its vegetables, and it has no homework when this is done. And so they're very excited about the questions they have for you. The first one, Dr. Arnold Relman, the Editor Emeritus of the *New England Journal of Medicine*, has said that "if the money America now spends on healthcare were to be spent intelligently, efficiently and honestly, it would give every man, woman and child here the best medical care without costing America a penny more than today." Is he right?

DR. COLLINS: Well, let me declare my lack of expertise in healthcare economics, but I suspect he's right, given the way in which our healthcare system reinforces the kind of spending on healthcare that makes not really much sense. If you all have followed some of the recent writings on this topic from people like Atul Gawande, you will see that an awful lot of our expenditures don't actually do that much to improve healthcare, but actually are often counterproductive. So Relman who, of course, is pretty much of an expert, I think has hit the nail on the head.

MR. BJERGA: There are, of course, many questions about healthcare reform. Several of them took the form of what is your prescription for healthcare reform? What role, if any, have you played in crafting the pending legislation? And how important is it that a bill be passed this year?

DR. COLLINS: Well, let me remind you that I'm a member of the executive branch appointed by the President and hoping to keep my job as long as the President is in place, so I should be careful to remind you that I'm therefore not in a position to help write bills in the legislative branch. NIH does get asked for technical advice when bills are being written, and certainly we have been consulted as the process was going forward by both the Senate and the House about some of the specific provisions that affect us and that we think we could be helpful with.

One of those is about comparative effectiveness research that I talked about. That is an area of interest in both the House and the Senate versions. What it will look like when we do get our healthcare reform, if we do, is not yet possible to determine. Basically, the inspiration to do more of this and to make sure that it's connected with decision making downstream about how medical care is actually practiced makes a lot of sense. So I think our role at NIH is to be a cheerleader for a better healthcare system that

results in better outcomes and lower costs, and also to provide the evidence that makes it possible for decision makers to know when they're deciding what to do and whether to actually support a particular approach. Does it work or not? We're in the business of knowing whether things work.

MR. BJERGA: To use a phrase that you taught us all today, do you at times find the tone and progress of the healthcare debate to be a perturbogen to you? (Laughter)

DR. COLLINS: Well, doesn't everybody? This has been such an amazing ride over the past many months that it certainly has been hard to keep up with in terms of all of the particular provisions of particular versions. I don't know how many people had a chance to watch the back and forth yesterday. It was pretty interesting in terms of the positions being taken and certainly, again, as a presidential appointee, I am proud to serve a president who seems to have a pretty good command of the details of the healthcare system. So yeah, maybe it's a perturbogen, but for a purpose. So when we perturb a cell, we hope to learn something. I hope we're all learning something by being perturbed.

MR. BJERGA: Please rate the effectiveness of the press in disseminating information about health, science and research. How do you believe it could be improved?

DR. COLLINS: Should I talk about specific reporters? No, I don't want to do that. (Laughter) You know, I think for the most part, the press does a good job of reporting what science is all about. And obviously particularly now, with the stresses on the media, my hat is really off to those who write stories in the face of limited resources, ridiculously short deadlines and try to convey what has happened in a balanced fashion.

And I know that reporters are always struggling with pressures that come down on them that indicate if something is bad, it's really bad. Otherwise, you don't get into that particular issue. And if it's good, well, you've just cured cancer. And I think we all in the scientific community struggle with those same tendencies when we're trying to talk about a new scientific effort to try to be absolutely clear about what it is and what it is not. When it goes well, it can be enormously interesting to the public and enormously compelling to read. And science is well served.

I will mention one very positive example, if you all read Amy Harmon's three pieces this past week in the *New York Times* about the development of a drug for cancer that really brought into that a lot of human stories, but a lot of really important science to get your mind around. That's a great example. And, of course, it doesn't hurt that she was given enough space to put it on the front page for three days in a row, which I'm sure a lo of reporters would love to have. But when you win the Pulitzer Prize, I guess that does help a bit.

There are certainly, though, examples of where everything goes wrong. Maybe the scientist was a little bit too glowing about what they had discovered. The reporter actually hated science in high school, was one of those people who would rather go to the

dentist. And the outcome of that kind of interchange can be garbled enough as to be almost unrecognizable. Fortunately, I don't think that happens all that often.

MR. BJERGA: In your address, you talked about the science of behavior change. And we have a question in that area. With research showing that approximately 50 percent of premature deaths in the United States are directly attributable to social and behavioral determinants, such as healthcare disparities, personal life choices regarding exercise, alcohol consumption, tobacco smoking, et al., what do you see as opportunities on the horizon for NIH to leverage social and behavioral basic research findings to reduce this percentage?

DR. COLLINS: Well, I think they're substantial. And let me say, when I was director of the Genome Institute, the only branch that was founded de novo in the last ten years in that institute was the social and behavioral research branch. You might wonder, what's that doing in a genome institute? Well, if you think about it, a clear need that if you're going to make all these discoveries about information that might help people know what they're at risk for, where you have interventions to offer to reduce that risk but you don't know how to get people to actually act upon those, you're not going to get very far.

Certainly we've, I think, learned a bit, but not nearly enough, about interventions for smoking, about addictions. If we are going to see prevention successful for all of those things, we have to have more data. That was why we included this science of behavior change as part of the seven new initiatives. That's why we have a new program at NIH called Op Net, which is a focus on behavioral, basic behavioral, and social science research which is also new at NIH. There is an office at NIH, the Office of Behavioral and Social Science Research that reports directly through one other division to me. And I think this is an area that's going to be a priority. If we really want to understand how to influence health behaviors, we need better data.

MR. BJERGA: Please share some of your insights about the benefits of religion and of music in healing and helping improve an individual's health?

DR. COLLINS: Well, I don't know how much rigorous data there has been about music. Certainly, those who are music lovers and who've gone through a trying medical experience would be likely to tell you that's been a source of comfort to them. Whether we have double blind trials-- Now how would you do that? Okay, you're going to get to listen to music, and you're going to get to listen to music, but it isn't really. There's a little issue there in terms of the placebo effect.

Certainly in terms of religion, there have been lots of studies there. It seems that people who do have a religious part of their life, if you look at their overall health status, it seems to be on the average somewhat better than those who do not. But those are large population averages and certainly don't tell you about the individual in a very explicit way.

MR. BJERGA: How is your research playing into Michelle Obama's initiative to end childhood obesity within a generation?

DR. COLLINS: Well, we were delighted to see the First Lady step out with this priority and it's certainly much needed. I think we mentioned that we're all concerned that the improvements in health that have happened over the last few decades might be erased if we don't get control of this epidemic of obesity. It's not unusual now for pediatricians to see adult onset type II diabetes in kids who are eight or nine years old, unheard of a few years ago. And certainly very much connected with the obesity problem. So this is a public health matter of very extreme importance. And to have the First Lady with all of her credibility identify this as something that needs a national program and a national attention is welcome indeed.

NIH has been working on the obesity problem. We have a trans-NIH obesity task force. Secretary Sebelius has recently impaneled a trans-HHS obesity task force that we have a significant role in as well. And there's a lot that goes into this in terms of healthy behaviors, again, in terms of figuring out how to alter environments, in terms of the built environment and the availability of soft drinks and unhealthy foods in schools. And just in terms of public education, getting things like calorie counts put on menus. All of these things could help, but none of them is a perfect solution.

We do also work on whether there are ways in terms of pharmacology to be able to assist in the dealing with obesity, although we would much rather, I think, have people arrive at healthy weights without the need for that. There are certainly going to be instances where that doesn't work, and there's a lot of effort, therefore, being made to understand what are the molecular pathways involved in appetite control, and are there actually safe ways to interfere with that that might assist people who are struggling with obesity that's not yielded to other things.

NIH also has a program called We Can, which is specifically devoted to childhood obesity. The Heart, Lung and Blood Institute has led that and it has now more than a thousand community efforts, again, talking about many of the things I just mentioned as far as what one can do in the community to decrease the risks of obesity. And that is something that we, I think, can be linked up very nicely with Michelle Obama's announcement.

MR. BJERGA: How far can personalized medicine, such as gene therapy and other approaches, go toward relieving and preventing suffering in the years to come? What limits will it have?

DR. COLLINS: Well, the death rate will still be one per person, I fear. And we might be able to come up with ways to prevent diseases like cancer and diabetes and heart disease a lot of the time. But some people will still drive their Harley motorcycles into trees and we'll have to take care of them. I'm thinking about my own risks here as I'm saying that.

Personalized medicine has great promise in terms of giving people individualized information to enable them to practice prevention in more effective way. Right now, the one size fits all approach hasn't worked very well. Part of that is because we don't reimburse for it, but a lot of it is just because people ignore it. It doesn't sound like it's relevant to them. Given information about yourself, and I've gone through the experience of having my DNA tested to see what the results were, and it was interesting and it did have an impact. I'm 20 pounds lighter than I was last summer after finding out my diabetes risk. This is a way, I think, to give people a chance to have information that all of us might want to have if it's something you could do something about, recognizing that is an important part of it. Maybe people aren't so interested about things they can't do something for.

Gene therapy, for its part, is making strides after 20 years of a rollercoaster experience with some real success stories. But I think we're quite a ways away from seeing how gene therapy will apply in a broader scale. Clearly, as we talk about these advances, you can point to individuals where personalized medicine or gene therapy have had dramatic consequences, but most of us aren't there yet. And the question is what's the trajectory going to be to get there? And a lot of that will depend on the robustness of the research that we do, and the willingness of the public to participate in it. And, if we have a medical care system where once we know what the right answers are, we can actually implement it.

MR. BJERGA: How do you feel about the patenting of genes, especially in respect of their impact on biotech and new drug development?

DR. COLLINS: Well, NIH has a longstanding, and I think very thoughtful, policy about patenting of genes. It's a set of guidelines, let me be clear about that. Obviously, the Bayh-Dole Act made it possible for investigators at NIH, supports at universities, if they make a discovery, the university can apply for a patent and the university becomes the patent holder. And NIH gives out that opportunity. But we did, I think, many years ago begin to worry about whether our patenting system was doing what it was supposed to in some instances, which is to benefit the public. That's why we have patents. That's why Benjamin Franklin came up with this plan, was not actually to make inventors rich, but to try to provide an incentive for an inventor to develop their invention to the point of making a product that the public could use, and not therefore having some other competitor come in and take the market away the second day it was out there.

Are genes in a good category for that? Well, a gene that's been discovered as a means of developing a therapeutic might fit that pretty well because you do have a long path, as we talked about, to get to the point of having a product, and to have a limited monopoly is probably a fair trade for getting that product out there. For diagnostics, on the other hand, the case, in the view of most of us, much less compelling. Diagnostic tests do not require the same level of investment over many years, and hundreds of millions of dollars. And so NIH's position is that while patents on genes for diagnostics are legal, and that's actually now somewhat under question with a suit that's been brought by the

ACLU about the BRCA1 gene, but at least as long as they are legal, NIH would say you ought to not license them exclusively for diagnostics because then you've created an unnecessary monopoly.

But for therapeutics, if the case is good, you might go along with a license that's exclusive. I hope you get the sense here, it's partly about patenting, but it's partly about licensing, and the two are not the same. And we need to think about both.

MR. BJERGA: Illumina recently announced the $10,000 one-week genome, and they also announced the sale of over 100 instruments to a genomic center in China. Are you concerned about losing the lead in genomic knowledge?

DR. COLLINS: Well, that announcement did cause some ripples across the scientific community because this powerful new instrument, which brought down the cost and increased the throughput by another significant factor was certainly greeted by many people with excitement. And yes, China announced they had bought 128 of these machines, making their total capacity for DNA sequencing now higher than the United States, or any other country.

If this is going to be applied for discoveries that are then made broadly available, everybody will cheer. If, on the other hand, there is an intention to try to take what has been up until now a general ethic that DNA sequencing information ought to be made immediately accessible in the public domain and bring it more behind a curtain, then that might be a cause of some concern. That is still not entirely clear. What are they going to do with all these machines? You could sequence a lot of people's DNA and a lot of species. I have good friends in China. They assure me that we should not be alarmed about this. And in fact, a wonderful partnership that has existed in the international community around DNA sequencing will continue and will be, I think, a very good influence on what happens next.

MR. BJERGA: We're almost ready for our last question, but there are just a couple items we need to take care of here. First of all, a note on our future speakers. On Friday, we have former Massachusetts Governor Mitt Romney, who will be talking about the case for American greatness. On Monday, we're going to have the head of the EPA, Lisa Jackson, speaking on environmental issues. And on Tuesday, we're going to have the U.S. trade representative in to talk about those issues.

So with that, we are going to also have the second very important part of this program, which is the presentation of the National Press Club mug. (Applause) I would also like to thank you all for coming here today. For more information about getting a transcript of today's program, or more information about joining the National Press Club, please go to www.press.org. I would also like to thank the staff from especially our library and catering offices for working with this program today. Thank you very much for attending this luncheon at the National Press Club. Our meeting is adjourned.

And one last question. So, we have someone from the NIH who has the question for you, are you going to the NIH Philharmonic this weekend? Second question is are you still playing in a band? And if so, what role in therapy does it play in your life?

DR. COLLINS: I'm going to Boston this weekend for a scientific presentation, so I'm afraid I'll miss the philharmonic, but I'm sure it will be wonderful. I hope I said that right. And yes, I am still in the rock and roll band. We are called The Directors, because there are some directors involved. We do ‘60s rock and roll, and we sometimes rewrite the lyrics to make them more scientifically relevant, and we always make sure to lock the doors before we start so nobody can leave. And yeah, our phone doesn’t ring very often. But if you have a bar mitzvah or a wedding where people are having a lot to drink, we would probably be just right for you.

MR. BJERGA: Thank you, Dr. Collins. (Applause)

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