DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 2011

WEDNESDAY, MAY 5, 2010

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 9:35 a.m., in room SD–124, Dirksen Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin, Pryor, Specter, and Cochran.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF FRANCIS S. COLLINS, M.D., Ph.D., DIRECTOR, NATIONAL INSTITUTES OF HEALTH

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. The Senate Subcommittee on Labor, Health, Human Services, and Education, and Related Agencies appropriations will come to order.

I want to start, first, by welcoming Dr. Francis S. Collins, who, of course, has appeared before this subcommittee many times over the past 20 years. Until now, he always testified as the Director of the National Human Genome Research Institute (NHGRI), today, wearing a much different and bigger hat, as Director of the entire National Institutes of Health (NIH).

The fiscal year 2010 budget for the NHGRI is $516 million. The budget for NIH as a whole is $31 billion. Well, at least that's where it is right now, anyway; we're looking at that. And, of course, the portfolio as NIH Director is much larger than the one that Dr. Collins had at the NHGRI.

But, having known Dr. Collins for all these years, I can't tell you how proud I am, and honored, that he is, now, the Director of the NIH.

I can remember when you first took over at the Genome Project—I think it was called a "project" at that time—1992? 1993? I knew I was close, Dr. Collins. I was close. And to take the project to the complete mapping and sequencing of the human genome was a singular accomplishment. And as I said, watching you during that whole time, and watching you shepherd that thing through,

I'm telling you, you're in the right place at the right time, right now, as Director of NIH.

One of the things that—when you think about the issues that confront NIH today—what role does biomedical research play in healthcare reform? How can we capitalize on the Human Genome Project that we completed? How can we do a better job of translating basic research in the field? How can we encourage some of our brightest young minds to enter this field when we've got tight budgets? So, we need someone who thinks big to head up NIH, and that's why we have Dr. Collins here, because he does think big, and he accomplishes big things.

So, the President's budget for the NIH for 2011 calls for a $1 billion increase more than the 2010 level, a total of $32 billion; it's about a 3.2 percent increase, which I am told is the same as the biomedical inflation rate.

But, fiscal year 2011 will bring with it a very special set of challenges; namely, how to achieve the softest possible landing for NIH after the $10.4 billion that was appropriated in the American Recovery and Reinvestment Act (ARRA). That is one area that I hope to explore with Dr. Collins in our question-and-answer period.

I also want to spend some time discussing one of the questions I raised earlier, how we can more effectively translate basic science into treatments and practices that actually improve people's health.

I know you've heard me say this many times before, Dr. Collins, that there's a reason it's called the National Institutes of Health, not the National Institutes of Basic Research.

But, before we hear from Dr. Collins, I would yield to Senator Cochran for his opening statement.

STATEMENT OF SENATOR THAD COCHRAN

Senator COCHRAN. Mr. Chairman, thank you very much for conducting this hearing, looking at the budget requests for the next fiscal year for the Department; that is, the NIH; specifically, under the generalship of Dr. Collins.

We appreciate very much your fine leadership and good work not only as a researcher, but also to manage and help identify priorities that help this subcommittee decide how much funding we need to place in the different accounts in this bill. It's a very large bill. We wish it could be larger, but the budget constrains us. But, within that budget framework, we have to identify the highest priorities, and your testimony will help us do a better job of that. And so, we appreciate your assistance to the subcommittee and your leadership in your role.

Thank you.

Senator HARKIN. Thank you, Senator Cochran.

I didn't read that before I sat down, I just thought "turning discovery into health." That's one of the things I wanted to talk about.

[The information follows:]

www.nih.gov/about/discovery

Senator HARKIN. Well, Francis S. Collins, M.D., Ph.D., was sworn in as the 16th Director of the NIH in August 2009, after being unanimously confirmed by the Senate. A physician-geneticist noted for his discoveries of diseased genes, his leadership of the

Human Genome Project. Prior to becoming NIH Director, he served as the Director of the NHGRI at NIH. He received his B.S. from the University of Virginia, Ph.D. from Yale, and an M.D. from the University of North Carolina at Chapel Hill.

Well, Dr. Collins, welcome. You're no stranger to this subcommittee. Your statement will be made a part of this record in its entirety, and you can please proceed as you so desire.

SUMMARY STATEMENT OF FRANCIS S. COLLINS

Dr. COLLINS. Well, thank you, Senator. And it is a great pleasure to be here. Good morning to all of you. It's an honor to appear to present the NIH's budget request for fiscal 2010 and to discuss my vision for the future of biomedical research.

I'd like for my written testimony to be included in the record, and I'm going to deviate from it quite a bit this morning in this opening set of remarks.

First of all, I'd certainly like to thank all of you for your steadfast support of NIH's mission: to discover fundamental knowledge about the nature and behavior of living systems, but then to apply that knowledge to fight illness and to reduce the burdens of disability. And this is—of course, we are the National Institutes of Health—I think I've quoted you on that, actually, Senator Harkin—not the National Institute of Basic Science. We are passionate about taking the discoveries that are pouring out of research laboratories, and moving them quickly toward clinical benefits.

Over the course of 15 years as Director of the NHGRI, I must say I was grateful for this subcommittee's strong support. Even at a time, early on, when the scientific community was somewhat divided about whether the Genome Project was worth investing in, this subcommittee was a strong supporter. And you, particularly, Mr. Chairman, were a vocal and articulate visionary for what this project might do. And your vision has been coming true ever since. And I—I'm personally grateful to you for that leadership.

So, I want to introduce you today, instead of going through some specific scientific advances, to some people.

Let's begin with Kate Robbins. Eight years ago, at the age of 44, this nonsmoking mother of two, was diagnosed with lung cancer; specifically, non-small-cell lung cancer. It had already metastasized to her brain. Normally this would be a death sentence. Despite surgery, radiation, chemotherapy, the cancer continued its deadly march, moving into her liver, into her pancreas. Still, she kept on fighting. And in early 2003, she enrolled in a trial of a drug called gefitinib, which is trade name Iressa, which is a new genome-based drug for cancer, based on a molecular understanding of what has gone wrong in certain cases of lung cancer.

Now, after she started the drug, most of her metastases vanished. Look at these CT-scans. This was her original one. In 2002, all of those dark areas are cancer in her liver. Just 6 months later, all but one is gone. And today there is no evidence of cancer in her liver, at all.

Now, why doesn't this work in all cases? In her case, a miraculous recovery. She's 7½ years out, with no sign of cancer in her liver or her lungs or her pancreas.

The disappointing news is that this drug only works in about one-fifth of lung cancer patients. But, we now know why. If your tumor has a specific mutation in a gene called EGFR, this drug is for you. If your tumor does not have that mutation, this drug probably will not work. So, this demonstrates the potential of personalized medicine, which is a major frontier right now for cancer, for heart disease, for virtually all conditions; that we can individualize treatment instead of doing the one-size-fits-all approach.

Well, next I'd like you to meet 9-year-old Corey Haas. This is Corey and his mom and dad. Corey was affected by a disease that was robbing him of his vision, a disease called Leber's congenital amaurosis, which is quite a mouthful, but it leads to progressive vision loss. And by age 7, Corey was legally blind. But, he underwent, in an experimental procedure supported by NIH at the University of Pennsylvania, a gene-therapy approach. Basically, the idea here was to take a normal copy of RPE65 and inject it, in a viral vector, into the back of his eye. And let me show you what happened, in the videos that you can see.

One eye was treated, and then, by patching one eye and looking to see how he would do in being able to follow some arrows on the floor, you can see what the effects were.

So, let's start here. Now, at this point, his treated eye has been blocked, so you're seeing what he's able to see without treatment, trying to follow these little arrows on the floor. And he's basically being asked to follow them, he's saying, "I can't see them." He's frustrated; he's standing there, he really can't see where anything is. They're asking, "Do you want a clue?" He finally says, "I can't see anything."

Now, same day, they now patch the untreated eye so he can see with the eye that's received the gene therapy. And watch what happens. "Okay, follow those arrows, Corey." No mistakes. He even had to climb over an obstacle, there, and go all the way around. And he decided he was doing so well, he wouldn't even stop, he'd just walk outside the door.

And if we had the audio, you would have heard wild applause from the researchers, at that point.

So, isn't that dramatic? And this has been, in Corey, sustained for more than a year, and now the consideration is to treat the other eye.

A third story. This is one that features prevention-oriented research. Now this is about Leslie Cook. She smoked for 25 years, half of her life, a habit that put her at increased risk for heart attack, cancer, and many other diseases. She's a high-powered real estate lawyer; she tried to kick the habit many times. She tried the gum, the patch, you name it; nothing worked for her.

And then she enrolled in a phase II trial of a vaccine against nicotine, called NicVAX. The vaccine spurs the immune system to generate antibodies against nicotine. Those bind to it, preventing it from entering the brain, and therefore no pleasure response occurs after smoking. NicVAX did the trick for Leslie; she has not smoked in 3½ years.

And there is now a phase III trial underway here, supported by the ARRA, to test this in 1,000 smokers at 20 centers. It's the first-ever phase III trial of a smoking cessation vaccine.

So, thanks to the discoveries you have funded——

Senator HARKIN. Working on a broad basis? Now, this is not personalized, it doesn't depend on a certain gene, or——

Dr. COLLINS. No. In this case, the vaccine is actually raised against the nicotine itself, so the antibodies are against the material in the cigarette smoke that gives people a high, and it blocks that effect, and so there's no point in smoking and they have an easier time quitting. It's pretty dramatic. That has not, I think, previously been tried for this purpose.

So, we're mixing immunology and drug addiction in interesting ways. There are efforts underway to do this, also, for other drugs of addiction.

Well, let me quickly conclude, here, by just quickly pointing out to you that these represent just a few of the exciting areas of opportunity. When I first came to this job—and it is an incredible responsibility, of leading the NIH—I scanned the landscape a bit, of biomedical research, to identify areas that seemed ripe for major advances and, in the process of doing so, identified five themes that I thought were particularly ripe for investment. And you have in front of you this publication from Science, published in January, that goes through a description of those five themes, and I think that's been reasonably well received by the scientific community.

One of them is to use the high-throughput technologies that have been invented in the last few years—genomics, nanotechnology, imaging, computational biology—to really tackle questions in a comprehensive way; questions like the causes of cancer or autism or what role microbes play in disease when we can't actually culture them in the laboratory but we can detect their presence by DNA analysis.

A second opportunity, and one that you've mentioned already, Mr. Chairman, the importance of translating the basic science discoveries into new and better treatments, of building a bridge, as you see done here for San Francisco, but a bridge between basic research and drugs and empowering academic investigators to play a larger role in that. And the Cures Acceleration Network (CAN), which is part of the healthcare reform bill, is an important aspect of this that we're very excited about.

I should also say, stem cells fit into here, and I'm happy to tell you there are now 64 human embryonic stem cell lines that are on the NIH registry and approved for Federal funding, followed up on Obama's Executive order from a year ago.

A third area, represented by these banners here, is to reach out with NIH research results and actually have an effect on our healthcare system. And that means personalized medicine research, health disparities research, comparative effectiveness research, behavioral research, and even healthcare economics. We're having a major meeting on that next week.

A fourth area is to recognize that we have both opportunities and perhaps responsibilities to apply our medical research efforts to those in less fortunate parts of the world, and that means a focus on AIDS, tuberculosis, and malaria, but, going beyond that, to neglected tropical diseases and noncommunicable disorders, which are the most rapidly growing cause of morbidity and mortality in the developing world.

And finally, the reinvigoration and empowerment of the research community, which is a challenge, especially at times of stressed budgets, to be sure that we're encouraging young investigators, that we're encouraging innovation, that we're training the next generation, using the Ruth Kirschstein awards. And I should, for a moment here, just say how much we miss Dr. Kirschstein, such a remarkable leader of NIH. We're having a special symposium in her honor, later this month, bringing back many of the people who were supported by those Kirschstein awards, in recognition of the role she's played in so much of what we've done in training.

Also in front of you is this pamphlet. And let me just conclude by saying, if our Nation can be bold enough to act upon these many unprecedented opportunities, we'll be amazed at what tomorrow will bring, and how swiftly we can turn discovery into health, as this title says. The one-size-fits-all approach to medicine will be a thing of the past; we will be using genetic information to personalize our healthcare.

But, if you'll allow me, I see a future in which we will use stem cells to repair spinal cord injuries. We'll bioengineer bones and cartilage to replace wornout joints. We'll use nanotechnology to deliver therapies with exquisite precision. We'll pre-empt heart disease with minimally invasive image-guided procedures, and use an artificial pancreas or other new technologies to manage diabetes better.

I look forward to a universal vaccine for influenza, so that you don't have to get a shot every year for the new strain. I look forward to the possibility, more possible now than ever, of an AIDS vaccine and a malaria vaccine. And I dream of a day when we'll be able to prevent Alzheimer's disease, Parkinson's disease, and many others that rob us, too soon, of family and friends.

PREPARED STATEMENT

As you've heard, the fiscal year 2011 request from this subcommittee is $32.157 billion, an increase of $1 billion. These funds will enable the biomedical research community to pursue a number of substantial opportunities in these major scientific and health opportunity areas.

So, I'm really grateful for the chance to be here this morning. I'm pleased to respond to any questions that you might have.

Thank you very much.

[The statement follows:]

PREPARED STATEMENT OF FRANCIS S. COLLINS

Good morning, Mr. Chairman and distinguished members of the subcommittee: It is a great honor to appear before you today to present the fiscal year 2011 budget request for the National Institutes of Health (NIH), and to discuss my vision for the future of biomedical research.

First, I'd like to thank each of you for your steadfast support of NIH's mission: discovering fundamental knowledge about living systems and then applying that knowledge to fight illness, reduce disability, and extend healthy life. In particular, I want to thank the subcommittee for the fiscal year 2010 budget level of $31 billion, and the $10.4 billion provided to NIH through the American Recovery and Reinvestment Act. I was very grateful for the subcommittee's interest and support over the course of my 15 years as Director of the National Human Genome Research Institute, most notably during our successful effort to sequence the human genome. Now, as steward of NIH's entire research portfolio, I truly believe that the opportunities for us to work together to improve America's health have never been greater.

One of my first actions upon being named NIH Director was to scan the vast landscape of biomedical research for areas ripe for major advances that could yield substantial benefits downstream. I found many of the most exciting opportunities could be grouped under five main themes: taking greater advantage of high-throughput technologies; accelerating translational science, that is, turning discovery into health; helping to reinvent healthcare; focusing more on global health; and reinvigorating the biomedical research community.

The administration's request of $32.1 billion for NIH's biomedical research efforts in fiscal year 2011 would help more researchers take greater advantage of these unprecedented opportunities, all with the aim of helping people live longer, healthier, more rewarding lives. We at NIH are fortunate to have a very solid foundation upon which to build, established by such extraordinary leaders as James Shannon, Nobel laureate Harold Varmus, Elias Zerhouni, and the late and much missed Ruth Kirschstein.

THE RESEARCH MARATHON

In his fiscal year 2009 budget remarks, Dr. Zerhouni warned that our Nation's biomedical research effort is in a race that we cannot afford to lose. I wholeheartedly agree, and want to provide a few more insights about what that race involves.

Science is not a 100-yard dash. It is a marathon—a marathon run by a relay team that includes researchers, patients, industry experts, lawmakers, and the public.

Thanks to discoveries funded through NIH appropriations, we have covered a lot of ground in this marathon. Let us take a moment to look back at a few of the advances made possible by NIH-supported research, and then look ahead to some of our Nation's biggest health challenges and how NIH intends to meet them.

HOW FAR WE'VE COME

U.S. life expectancy has increased dramatically over the past century and still continues to improve, gaining about 1 year of longevity every 6 years since 1990. A baby born today can look forward to an average life span of 77.7 years, almost three decades longer than a baby born in 1900.

Not only are people living longer, they are staying active longer. From 1982 through 2005, the proportion of older people with chronic disabilities dropped by almost one-third, from 27 percent to 19 percent.

Some of the most impressive gains have been made in the area of cardiovascular disease. In the mid-20th century, cardiovascular disease caused half of U.S. deaths, claiming the lives of many people still in their 50s or 60s. Today, the death rate for coronary heart disease is more than 60 percent lower—and the death rate for stroke, 70 percent lower—than in the World War II era.

What fueled these improvements? One major contributor has been the insights from the NIH-funded Framingham Heart Study, which began in the late 1940s and is still going strong. This population-based study, which changed the course of public health by defining the concept of disease risk factors, continues to break new ground with its recent move to add a genetic component to its analyses.

Other factors include NIH-supported research that led to minimally invasive techniques to prevent heart attacks and to highly effective drugs to lower cholesterol, control high blood pressure, and break up artery-clogging blood clots. Science also played a crucial role in formulating approaches to help people make lifestyle changes that promote cardiovascular health, such as eating less fat, exercising more, and quitting smoking.

Many chronic conditions have their roots in the aging process. One such disease, osteoporosis, can lead to life-threatening bone fractures among older people. NIH-funded research has led to new medications and management strategies for osteoporosis that have reduced the hospitalization rate for hip fractures by 16 percent since 1993. Science has also transformed the outlook for people with age-related macular degeneration, a major cause of vision loss among the elderly. Twenty years ago, little could be done to prevent or treat this disorder. Today, because of new treatments and procedures based on NIH research, 750,000 people who would have gone blind over the next 5 years will continue to have useful vision.

Biomedical research also has benefited those at the other end of the age spectrum. NIH-funded research has given hearing to thousands of children who were born profoundly deaf. This hearing is made possible through a cochlear implant, an electronic device that mimics the function of cells in the inner ear. Since the Food and Drug Administration (FDA) approved cochlear implants for pediatric use in 2000, more than 25,000 children have received the devices, enabling many to develop normal language skills and succeed in mainstream classrooms.

Then, there are the infectious diseases—diseases that often know no boundaries when it comes to age, sex, or physical fitness. One of NIH's greatest achievements over the past 30 years has been to lead the global research effort against the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) pandemic. With discovery building upon discovery, researchers first gained fundamental insights about how HIV works, and then went on to develop rapid HIV tests, identify a new class of HIV-fighting drugs, and, finally, figure out how to combine those drugs in life-saving ways in the clinic. As a result, HIV infection has changed from a virtual death sentence into a manageable, chronic disease. Today, HIV-infected people in their 20s who receive combination therapy may expect to live to age 70 or beyond.

HOW FAR WE HAVE TO GO

Although we have accomplished much, and as tempting as it may be for NIH to rest upon its laurels, we all know that biomedical research still has an enormous amount of ground to cover before discovery is turned into health for all Americans.

Consider the challenge posed by cancer. This disease still claims the lives of more than 500,000 Americans annually—about one every minute. But in 2007, for the first time in our Nation's history, the absolute number of cancer deaths in the United States went down. And, over the past 15 years, cancer death rates have dropped 11.4 percent among women and 19.2 percent among men, which translates into some 650,000 lives saved—more than the population of Washington, DC. These are very encouraging milestones, but they are not nearly enough.

NIH-funded research has revolutionized how we think about cancer. A decade or two ago, cancer treatment was mostly reactive, diagnosis was based on the organ involved and treatment depended on broadly aimed therapies that often greatly diminished a patient's quality of life. Today, basic research in cancer biology is moving treatment toward more effective and less toxic therapies tailored to the genetic profile of each patient's cancer.

Among the early success stories in this area is the drug trastuzumab (Herceptin) for breast cancer. An NIH-sponsored clinical trial found that when breast cancer patients whose tumors were genetically matched to trastuzumab received the drug, along with standard chemotherapy, their risk of cancer recurrence fell 40 percent. That improvement is the best ever reported in postsurgical treatment of breast cancer. Studies also have found that the chemotherapy drugs gefitinib (Iressa) and erlotinib (Tarceva) work much better in the subset of lung cancer patients whose tumors have a certain genetic change.

To accelerate the development of more individualized strategies for more types of cancer, NIH has tapped into the promise of high-throughput technologies to launch The Cancer Genome Atlas (TCGA). Over the next few years, TCGA's research team will build comprehensive maps of the key genomic changes in 20 major types and subtypes of cancer. This information, which is being made rapidly available to the worldwide scientific community, will provide a powerful new tool for all those striving to develop better ways to diagnose, treat, and prevent cancer.

Already, TCGA has produced a comprehensive molecular classification system for ovarian cancer and glioblastoma, the most common form of brain cancer. The survey of glioblastoma recently revealed five new molecular subtypes of the disease. In addition, researchers found that responses to aggressive therapies for glioblastoma varied by subtype. The findings hold promise for matching the most appropriate therapies with brain cancer patients and may also lead to therapies directed at the molecular changes underlying each subtype, as has already happened for some types of breast cancer.

Diabetes is another disease that is inflicting much damage on U.S. health. More than 23 million Americans currently have diabetes—nearly 8 percent of the population. Another 57 million have blood sugar levels that indicate they are at serious risk of developing the disease, which is a major cause of kidney failure, stroke, heart disease, lower-limb amputations, and blindness.

For type 2 diabetes, prevention appears to be the name of the game. This form of the disease, which accounts for more than 90 percent of diabetes among adults, often can be averted or delayed by lifestyle factors. The NIH-funded Diabetes Prevention Program (DPP) trial showed that one the most effective ways to lower the risk of type 2 diabetes is through regular exercise and modest weight loss. There is good reason to believe that such efforts may lead to a lifetime of health benefits. A recent follow-up study of DPP participants found the protective effects of weight loss and exercise persist for at least a decade. The United Health Group has recently announced a partnership with Walgreen's and the YMCA to implement the results of this groundbreaking NIH-funded research on a broad scale.

More than one-third of adults in the United States are obese, according to the latest data from the National Health and Nutrition Examination Survey which is conducted by the Centers for Disease Control and Prevention (CDC). And there are signs that the next generation may face an even greater struggle. Over the past 30 years, obesity has more than doubled among U.S. children ages 2 through 5 and nearly tripled among young people over the age of 6. Those statistics translate into tens of millions of Americans who face an increased risk of type 2 diabetes, as well as cardiovascular disease, high blood pressure, certain cancers, osteoarthritis, and other serious health problems associated with excess body fat.

To address America's growing problem with obesity, NIH has launched a variety of initiatives aimed at developing innovative approaches for weight control. One such effort, called the National Collaborative on Childhood Obesity Research, has pulled together experts from four NIH Institutes, the CDC, and the Robert Wood Johnson Foundation. One example of their work is the Trial of Activity for Adolescent Girls, a national study to develop and test school- and community-based interventions to get girls more involved in gym class, organized sports, or recreational activities. Another NIH program, called We Can!, provides families with practical tools for weight control at more than 1,000 community sites nationwide. How to get more people to lose weight is also among the questions being explored by OppNet, a new trans-NIH initiative for basic behavioral and social sciences research.

Meanwhile, other NIH-funded researchers are busy uncovering information about genes and environment that may pave the way for more personalized, targeted strategies for controlling weight and preventing diabetes. For example, in just the past few years, we have identified more than 30 genetic risk factors for type 2 diabetes.

A better understanding of genetic and environmental factors may also help solve a longstanding medical puzzle: the causes of autism. Children with autism spectrum disorders experience a range of problems with language and social interactions, sometimes accompanied by repetitive behaviors or narrow, obsessive interests. Recent studies funded by NIH have associated autism risk with several genes involved in the formation and maintenance of brain cells, but much more work is needed to follow up on these clues.

In fiscal year 2011, NIH will support comprehensive and innovative approaches to piece together the complex factors that contribute to autism spectrum disorders. One ambitious effort will involve sequencing the complete genomes of 300 people with autism and their parents. Other researchers will examine a mother's exposure during pregnancy to identify possible environmental contributions. NIH hopes to use these insights to develop new molecular and behavioral therapies for such disorders, as well as to identify possible strategies for prevention.

Another brain disorder, depression, presents a different set of challenges. Although researchers have made significant progress in understanding the biology of depression, improving treatment, and lessening the social stigma associated with mental illnesses, suicide still claims the lives of twice as many Americans as homicide. And it does not end there—untreated depression also increases the risk of heart disease and substance abuse.

How can medical research reduce depression's tragic toll? One way may be getting people into treatment more quickly. Researchers today are using functional magnetic resonance imaging and other innovative technologies to see how the brains of people with depression differ from those without the disorder. Rapid diagnosis is just part of the equation. Finding the right antidepressant drug for any particular patient currently is a lengthy, trial-and-error process that can take weeks before symptoms are relieved. NIH supports laboratory research aimed at developing quicker-acting antidepressants, as well as genetic studies that will help to match individuals with the drugs most likely to work for them.

In 2008, 143 soldiers died by suicide—the highest rate since the Army began keeping records three decades ago. To address this problem, NIH and the U.S. Army recently partnered to launch the largest study ever of suicide and mental health among military personnel. The Army Study to Assess Risk and Resilience in Service Members will identify risk factors that may inform efforts to develop more effective approaches to suicide prevention.

TRANSFORMING DISCOVERY INTO HEALTH

Whatever the disease, be it depression, diabetes, or something much rarer, NIH's emphasis in fiscal year 2011 and beyond will be on translating basic discoveries into new diagnostic and treatment advances in the clinic.

In the past, some have complained that NIH has been too slow to convert fundamental observations into better ways to diagnose, treat, and prevent disease. Al-

though some of that criticism may have been deserved, most of the delay has stemmed from the lack of good ideas about how to traverse the long and winding road from molecular insight to therapeutic benefit.

That is now changing. For many disorders, there are new opportunities for NIH to shorten and straighten the pathway from discovery to health. This expectation is grounded in several recent developments: the dramatic acceleration of our basic understanding of hundreds of diseases; the establishment of NIH-supported centers that enable academic researchers to use such understanding to screen thousands of chemicals for potential drug candidates; and the emergence of public-private partnerships to aid the movement of drug candidates identified by academic researchers into the commercial development pipeline.

Let me give you one example of how NIH plans to implement this strategy: the Therapeutics for Rare and Neglected Diseases (TRND) program. This effort will bridge the wide gap in time and resources that often exists between basic research discoveries and the human testing of new drugs.

A rare disease is one that affects fewer than 200,000 Americans. However, if all 6,800 rare diseases are considered together, they afflict more than 25 million Americans. Private companies seldom pursue new therapies for these types of diseases because of the high cost of research and low likelihood of recovering their investments. Effective drugs exist for only about 200, or less than 3 percent, of rare diseases. Unlike rare diseases, neglected diseases may be quite common in some parts of the world, especially in developing countries. However, there also is a dire shortage of effective, affordable treatments for many of these major causes of death and disability.

Working in an open environment in which all of the world's top experts on a disease can be involved, TRND will enable certain promising compounds to be taken through the preclinical development phase—a time-consuming, high-risk phase often referred to as "the valley of death" by pharmaceutical firms focused on the bottom line. Besides speeding development of drugs for rare and neglected diseases, TRND will serve as a model for therapeutic development for common diseases, many of which are being resolved into smaller, molecularly distinct subtypes.

NIH will also take other steps to build a more integrated pipeline that connects all of the steps between identification of a potential therapeutic target by a basic researcher and the point when the FDA approves a therapeutic for clinical use. Among the tools at our disposal is the NIH Clinical and Translational Sciences Award program, which currently funds 46 centers and has awardees in 26 States and plans to add even more in fiscal year 2011. This national network is pulling together interdisciplinary clinical research teams to work in unprecedented ways to develop and deliver tangible health benefits. We also need to take advantage of the Nation's largest research hospital, the Mark O. Hatfield Clinical Research Center, located on the NIH campus in Bethesda, Maryland. Just as they blazed a trail for safe and effective human gene therapy, NIH clinical researchers may be well-positioned to move the ball forward for other pioneering approaches, such as those using human embryonic stem cells or induced pluripotent stem cells derived from skin cells.

To make the most of these new opportunities, the NIH and FDA recently forged a landmark partnership with the formation of a Joint Leadership Council. Members of this Leadership Council will work together to ensure that regulatory considerations form an integral component of biomedical research planning, and that the latest science is integrated into the regulatory review process. Such collaboration will advance the development of products to treat, diagnose and prevent disease, as well as enhance the safety, quality, and efficiency of clinical research and medical product approval.

BIOMEDICAL RESEARCH PROPELS U.S. ECONOMY

It is crucial to keep in mind that investing in NIH not only improves America's health and strengthens our Nation's biomedical research potential, it empowers the entire U.S. economy. Consider the following statistics:

—A report issued by Families USA calculated that in 2007, every $1 in NIH funding resulted in an additional $2.11 in economic output in the United States.

—In fiscal year 2007, a typical NIH grant supported the salaries of about 7 high-tech jobs in full or in part.

—The 351,000 jobs resulting from NIH awards paid an average annual wage of more than $52,000 per annum and account for more than $18 billion in wages for fiscal year 2007.

—Long-term, NIH-funded R&D sparks U.S. economic innovation in the high-technology and high value-added pharmaceutical and biotechnology industries. For

example, between 1982 and 2006, one-third of all drugs and nearly 60 percent of promising new molecular entities approved by the FDA cited either an NIH-funded publication or an NIH patent.

—Gains in average U.S. life expectancy from 1970–2000 were worth an estimated $95 trillion.

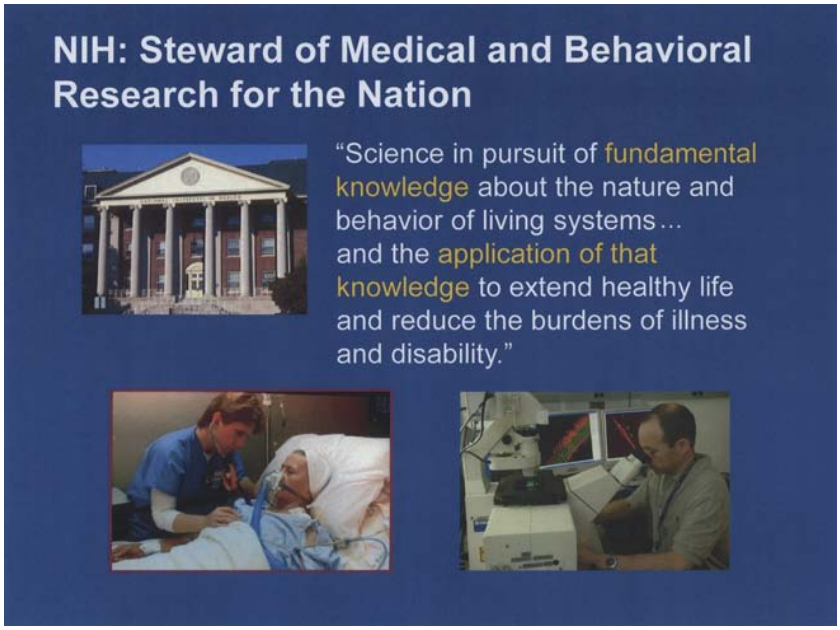
IMAGINE THE FUTURE

If our Nation is bold enough to act today upon the many unprecedented opportunities now offered by biomedical research, we may be amazed at what tomorrow will bring.

In the world I envision just a few decades from now, we will use stem cells to repair spinal cord injuries; bioengineered tissues to replace worn-out joints; genetic information to tailor health outcomes with individualized prescriptions; and nanotechnology to deliver therapies with exquisite precision. I also dream of a day when, in ways yet to be discovered, we will be able to prevent Alzheimer's, Parkinson's, and other diseases that rob us much too soon of family and friends.

Just imagine what such a future would mean for our Nation and all humankind. This is what keeps NIH in the research marathon, and why we ask you to go the distance with us.

Thank you Mr. Chairman.



Kate's Story

- Diagnosed at age 44 with metastatic lung cancer
- Cancer spread after surgery, radiation, and chemotherapy
- Participated in a clinical trial testing Iressa™ (gefitinib), a new genome-based drug for cancer

The NEW ENGLAND JOURNAL of MEDICINE

MAY 20, 2004

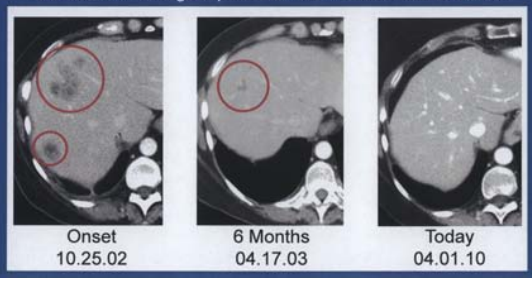
Activating Mutations in the Epidermal Growth Factor Receptor Underlying Responsiveness of Non–Small-Cell Lung Cancer to Gefitinib

Thomas J. Lynch, M.D., Daphne W. Bell, Ph.D., Raffaella Sordella, Ph.D., Sarada Gurubhagavatula, M.D., Ross A. Okimoto, B.S., Brian W. Brannigan, B.A., Patricia L. Harris, M.S., Sara M. Haserlat, B.A., Jeffrey G. Supko, Ph.D., Frank G. Haluska, M.D., Ph.D., David N. Louis, M.D., David C. Christiani, M.D., Jeff Settleman, Ph.D., and Daniel A. Haber, M.D., Ph.D.

Personalized Cancer Treatments

- Kate's metastases shrank; now undetectable in lungs, liver, pancreas
- Why doesn't Iressa work in all cases?
  - Response depends on specific mutation in *EGFR* gene
- Demonstrates the potential of personalized medicine

CT scans showing response of liver metastases to Iressa



Corey's Story

- Leber's congenital amaurosis is caused by a mutation in the *RPE65* gene
- Corey was legally blind by age 7
- Gene therapy procedure was performed in one eye
- Corey's eyesight is returning

Using the untreated eye

Using the treated eye

Leslie's Story

- Tried to stop smoking a number of times
- Four years ago, she enrolled in a NicVAX Phase 2 clinical trial …
  - Stimulates production of antibodies to nicotine
  - Bound nicotine cannot enter brain, subverting rewarding effects
- Leslie's results: "To this day, I haven't smoked a cigarette since. I don't want one."

NicVAX Phase III Trial

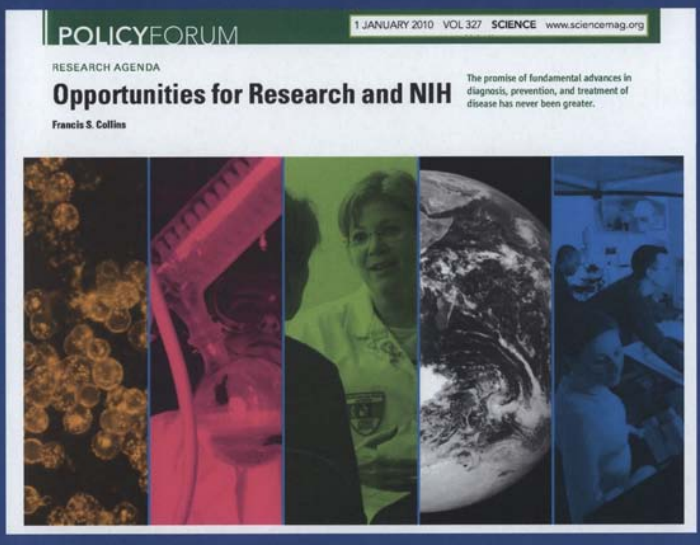
- Involves 1,000 smokers at 20 centers around the U.S.
- NIH Recovery Act funds ($10 million) are helping pay for the trial
  - Vaccine rooted in NIH-funded basic research
  - First-ever phase III trial of a smoking cessation vaccine

CLINICAL TRIALS

CLINICAL PHARMACOLOGY & THERAPEUTICS
2005;78(5):456-67

Safety and immunogenicity of a nicotine conjugate vaccine in current smokers

Dorothy K. Hatsukami, PhD, Stephen Rennard, MD, Douglas Jorenby, PhD, Michael Fiore, MD, MPH, Joseph Koopmeiners, Arjen de Vos, MD, PhD, Gary Horwith, MD, and Paul R. Pentel, MD *Minneapolis, Minn, Omaha, Neb, Madison, Wis, and Rockville, Md*



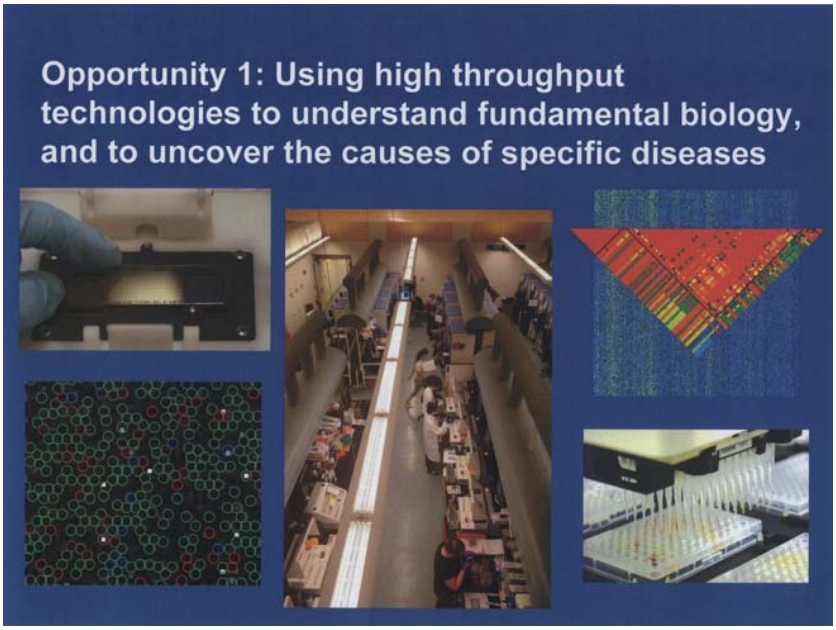
POLICYFORUM
1 JANUARY 2010 VOL 327 SCIENCE www.sciencemag.org

RESEARCH AGENDA

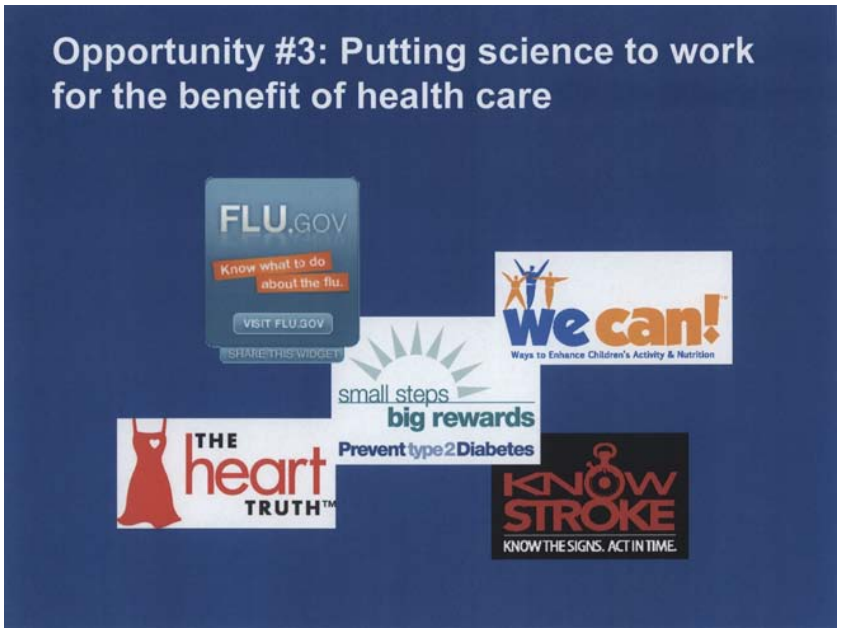
Opportunities for Research and NIH

The promise of fundamental advances in diagnosis, prevention, and treatment of disease has never been greater.

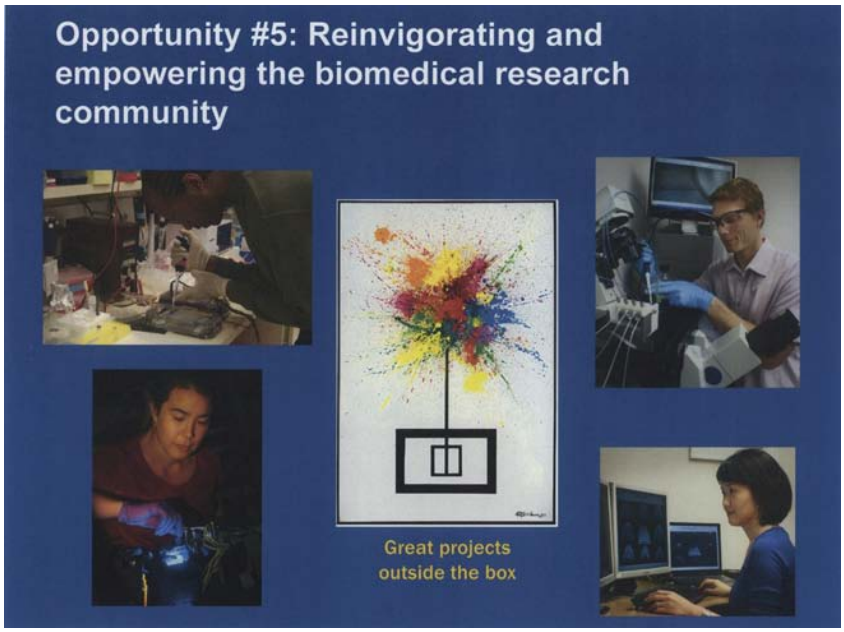
Francis S. Collins


Opportunity 1: Using high throughput technologies to understand fundamental biology, and to uncover the causes of specific diseases


Opportunity #2: Translating basic science discoveries into new and better treatments
Basic Research
Drugs
Drugs
Basic Research


Opportunity #3: Putting science to work for the benefit of health care
FLU.GOV
Know what to do about the flu.
VISIT FLU.GOV
SHARE THIS WIDGET
we can!
Ways to Enhance Children's Activity & Nutrition
small steps
big rewards
Prevent type 2 Diabetes
THE heart TRUTH™
KNOW STROKE
KNOW THE SIGNS. ACT IN TIME.


Opportunity #4: Encouraging a greater focus on global health
DISEASE CONTROL PRIORITIES PROJECT
HOME | PUBLICATIONS | CUSTOM BOOKS AND SLIDES | NEWS AND EVENTS | TOOLS AND RESOURCES
Tropical Diseases Lacking Adequate Control Measures: Dengue, Leishmaniasis, and African Trypanosomiasis
Depression
Leading cause of disability worldwide...
World Health Organization
nature
MALARIA PARASITES



NICVAX SMOKING VACCINE

Senator HARKIN. Well, Dr. Collins, thank you very much.

I asked my staff to get me some more information on that smoking vaccine. It's just something I had not heard about. That could be phenomenal.

[The information follows:]

SMOKING VACCINE

Tobacco remains the leading cause of preventable death in the United States, linked to more than 400,000 deaths each year. That is why the National Institutes of Health is accelerating research to eradicate tobacco addiction, including working with a private partner, Nabi Biopharmaceuticals, via a $10 million grant from the National Institute on Drug Abuse, to achieve that goal.

American Recovery and Reinvestment Act (ARRA) funding released in September will help pay for the first phase III trial of NicVAX, a smoking cessation vaccine designed to help people quit and remain abstinent. It was given fast track designation by the Food and Drug Administration and has already successfully completed a proof-of-concept trial; successful completion of the phase III study will bring the vaccine closer to final approval.

As a result of ARRA funding, Nabi entered an agreement with GlaxoSmithKline to receive an additional $40 million to exclusively in-license NicVAX on a worldwide basis and develop follow-on, next-generation nicotine vaccines, with the possibility of additional $500 million depending on the outcome of the trial. This work is an excellent example of leveraging Government resources to further develop and market a medication for tobacco addiction.

Similar to vaccines for infectious diseases, NicVAX works by stimulating the immune system to produce antibodies; in this case, however, to the drug nicotine. Nicotine (a small molecule) normally travels quickly through the lungs into the bloodstream and then to the brain. However, when nicotine molecules are bound to antibodies, they become too large to enter the brain, thus subverting the behavioral effects of the drug. Results to date show that smokers who achieved high antibody levels had higher rates of quitting and longer stretches of abstinence than those given placebo (18 percent vs. 6 percent complete abstinence after 52 weeks). The vaccine was also well tolerated, with few side effects.

NicVAX's unique immunological mechanism of action elicits anti-nicotine antibodies lasting for several months—a potential benefit over current therapies. Early results showed that it reduced craving and withdrawal symptoms, which often prompt relapse. This should improve smokers chances to end the addiction/relapse cycle that plagues the great majority of those trying to quit.

A successful phase II proof-of-concept trial was completed in late 2007, in which NicVAX showed significant improvement in smoking cessation rates and continuous long-term smoking abstinence compared to placebo, in those who achieved high antibody levels. For the phase III trial, modifications were made to the original protocol to improve the likelihood of success. An additional vaccination was added and the timing of the quit attempt was modified to coincide with the optimal level of antibody response. Twenty-two investigative sites have been selected, and include highly experienced academic-based smoking cessation centers and experienced nonacademic sites. The study will enroll 1,000 subjects who want to quit smoking. They will be randomized to 1 of 2 treatment groups: (1) placebo control or (2) active vaccine treatment.

Participants will be followed for 1 year from the start of immunization. The study's main goal is to determine the percentage of those who are abstinent during the final 16 weeks of the study (weeks 37–52). Other endpoints include safety, withdrawal symptoms, craving, cigarette consumption, evaluation of the smoking experience, short-term cessation rates after each injection, and assessment of abstinence.

Recruitment for the phase III trial is on target and the study is going well. Final data are expected within 2 years of study start, which was in November 2009.

Dr. COLLINS. Yes, indeed.

Senator HARKIN. I mean, from prevention we know what smoking leads to, and all the diseases it leads to, and the cost to society. And most people I meet that have been on smoking want to stop, but they just have a tough time.

Dr. COLLINS. They do, indeed.

Senator HARKIN. So, this could be remarkable. Do you know when—how—that trial is ongoing right now?

Dr. COLLINS. It's ongoing, reasonably recently started. I can find out for you the expected end date of the trial, but they're certainly pushing this forward with all due speed.

[The information follows:]

To find the recent clinical trials go to: http://www.cancer.gov/clinicaltrials/lung-cancer-updates.

Senator HARKIN. Now, let me ask you this, Doctor——

Well, let's start a 6-minute round? Is that what we have, here? Who's operating my clock? There we go. Okay, fine.

Dr. Collins, I noticed, on the funding, here, for next year, how some Institutes go up by 3.2 percent, some by 2.5 percent, some by 2.8 percent, some by—and they're all over the place. I assume they are some of these differences accounted for by focusing on those thematic areas that you just mentioned, those five theme areas? Is that what is driving that now?

Dr. COLLINS. That's exactly right.

Senator HARKIN. What——

Dr. COLLINS. Those five themes seem to be areas of exceptional opportunity. When we looked at the investments of the various Institutes in those areas a couple of years ago—which is not a perfect, but a somewhat good predictor of what might be possible in fiscal year 2011—it was clear that those opportunities are not entirely evenly distributed. And so, recognizing that that $1 billion, although it's only going to keep up with inflation, still ought to be invested in innovative ways, we attempted to do some arranging of the budget to reflect that, and that's what you see in those differences between Institutes. They're modest, but they are impor-

tant, I think, to point out, that we're not just doing everything in lockstep.

Senator HARKIN. Well, one has to always be careful when you're dealing in percentages.

Dr. COLLINS. Yes.

Senator HARKIN. As I've often pointed out, zero-to-one is an infinite increase. So, sometimes those that get very little funding, to get them up a little bit, looks like it's a huge percentage increase. So, I always want to be careful and look at the percentage increases there.

Dr. COLLINS. Point taken.

Senator HARKIN. Well, for instance, the Library of Medicine has 4 percent. Well, but it's so small, line of increase amounts for that. So, I always like to look at that very carefully.

Dr. COLLINS. You're quite right, Senator.

FISCAL YEAR 2010 AND POST-ARRA

Senator HARKIN. The other one I wanted to get into, here, with you is on the funding cliff. So, we put the money in the ARRA. At the time, it was decided that we'd put that in, it was a 2-year slug of money for at least the following reasons: one, because we didn't want researchers being laid off; we wanted to keep people employed. A lot of researchers were in the middle of projects and studies that we did not want to interrupt. But, we knew that we were probably going to face this, 2 years from now. So, I guess my question is, What kind of challenges are you facing? How do you provide for this soft landing? Are we facing any interruptions at all—in terms of some science that's being done right now because of this cliff?

Dr. COLLINS. So, Senator, this is the question that keeps me up at night. On the screen there, you'll see what the total funding for NIH has been over the last 10 years, and those red bars there are the dollars that came from the ARRA, which we are deeply grateful for, and which provided a real shot in the arm for some exciting, innovative research that, otherwise, would have had to wait a long time to get started; things like the Cancer Genome Atlas, for instance, which really was able to move forward at an unprecedented pace because of the availability of those funds.

But, as you can see, the difference between fiscal year 2010, total, when you include the $5.2 billion of ARRA dollars, compared to the President's budget for fiscal year 2011 is certainly a drop, and that's the cliff that everybody talks about, right there, about $4 billion.

Senator HARKIN. Right.

Dr. COLLINS. We have done what we can, in anticipation that this might be a really challenging year, to try to be sure that the ARRA dollars were invested, as much as possible, in short-term needs. So, for example, $1 billion of this has gone to construction in the extramural community. Additional dollars have gone to equipment needs, things that were one-time requirements. And some dollars have gone to projects that we thought we could get done in 2 years, although that's a very short cycle time for a scientific project.

But, we also felt that this was an opportunity to stimulate some real innovations and to get people to put forward some out-of-the-box ideas; and they did, in huge numbers. The Challenge Grants, for example, we thought we might get 4,000 applications; we got 20,000. There was a great pent-up need here for support for new ideas. And many of those are, in fact, funded and will have, now, the question in their minds, "What do we do after the 2 years is expended?"

One thing we are doing is to encourage those who believe that they can't quite finish their project and they haven't quite spent all the money in 2 years, to ask for a no-cost extension, and we will consider those quite seriously. And if it seems reasonable, and they're making reasonable progress, we will grant that, so at least to stretch out this cliff a little bit.

But, there's no question that the consequences of this situation are going to be significant. We currently estimate success rates for NIH grantees—which have been in the 25 to 35 percent level for most of the last 30 years, and are now at 21 percent, are going to drop further in fiscal year 2011, at this budget level, probably to about 15 percent. That's one chance out of seven that a given grant would get supported. And there's no question that is going to be stressful for all of us.

Senator HARKIN. That's not good.

Well, we've been wrestling with this, ourselves. I am of the opinion that we need to do more at NIH. The question is, Where do we get the funding and—with all of the other things that the Appropriations Committee has to do, and with budget constraints? But, we'll see what we can do.

I want to get one question—well, I'm down to zero. I'll ask the question after Senator Cochran gets through with his.

Senator Cochran.

DISCOVERIES ON THE HORIZON

Senator COCHRAN. Mr. Chairman, thank you very much.

Dr. Collins, thank you again for being here and helping us review the budget request and pointing out your views of how we should identify the priorities and the most important ways we can use the funds available to this subcommittee.

We know that you're a research scientist, and you've been rewarded with a lot of recognition, medals, and honors, because of the outstanding research you have done, and it reminds me of Dr. Arthur Guyton's success as a researcher at the University of Mississippi Medical Center. The University continues to perform research there. And although he's no longer with us, he had a fascinating and very influential impact on heart disease and its understanding and therapies to help people live longer and have better lives.

Is there anything going on in the research field right now that rivals the work you, personally, did and were praised so highly for, and Dr. Arthur Guyton, as well? Do we have any, really, blockbuster researchers out there that you've identified in helping us provide funding for?

Dr. COLLINS. Well, yes, I'm happy to tell you, there is an amazing cadre of creative, innovative, productive scientists now involved

in biomedical research. I certainly agree that Dr. Guyton was a legendary character. I studied his book when I was in medical school; that's how I learned a lot about physiology and about the heart.

And when you look around today—well, you could count Nobel Prizes, I suppose. NIH has been the source of support for no less than 131 Nobel Prizes over the last few decades. And, in fact, this past fall, when the Nobel Prizes were given out, both for medicine and for chemistry, of the six awardees, five of them were our grantees. Remarkable people, people like Liz Blackburn and Carol Greider, who were awarded the prize for discovering telomeres and the enzyme that maintains those ends of the chromosomes, so they don't get ratty, like your shoelaces, if you didn't have some way to protect those ends. Remarkable stories, all of those.

Many of them coming from a direction you couldn't have predicted, but one of the wonders of the way NIH has been able to support research is that we base our decisions, many of them, on what comes across to us by investigators with ideas that go through the most rigorous peer-review system in the world, and then are given the funds to chase after those ideas.

A new program that we're investing in, called the Pioneer Awards, is particularly trying to identify those very creative individuals who we could unleash to follow their ideas, and not have them quite so constrained by the systems that sometimes are in place, that—we need to track research, but there are times where you want to let somebody just go for it. And we're determined to use those kinds of mechanisms and things like New Innovators to make that happen.

In that—particular areas that NIH is supporting, I will mention cancer, because I think we are, actually, at a remarkable moment, in terms of being able to understand, at that most detailed DNA level, what goes wrong in a cancer cell; not just some of the things, but all of the things that go wrong in a cancer cell. Why does a good cell go bad? And what could we use as—with that information, to develop therapies that are targeted—like Kate Robbins, the case I told you about—specifically toward their tumor? That was a pipedream 5 or 6 years ago. Now it is absolutely transforming people's ideas of how to go forward. And the researchers working on that—many of them 20-somethings, many of them with computational backgrounds, because a lot of the challenge now is to figure out how to analyze the mountains of data that can be produced. They are remarkable to hang out with.

So, I'm actually quite inspired by our cohort of researchers. My concern is, we need to be sure we're giving them the confidence that that support is going to be there, so that they stick it out and are willing to take risks and not just do the obvious next steps.

JACKSON HEART STUDY

Senator COCHRAN. One of the undertakings in our State is the Jackson Heart Study, which has been a comprehensive review of the individual medical histories of people who have heart problems, and seeing if we can identify factors that can be changed or corrected to help us do a better job of providing opportunities for healthy lives, rather than a destiny that is more likely to involve heart problems. What is the status of that study? And are you re-

questing funding, in this budget request, to continue or go forward from that study to something else?

Dr. COLLINS. We are very enthusiastic about that study, Senator, and delighted by your strong support of this from the beginning. So, this is carried out in Mississippi, in Jackson, with the University of Mississippi and Tougaloo College participating. NIH has a big role in this, supported by the National Heart, Lung, and Blood Institute (NHLBI). And already, a lot of very important observations have come forward studying, particularly, cardiovascular disease in African Americans, about which we didn't know enough, and now we're starting to learn.

So, for instance, we're learning that hypertension and obesity and diabetes, the three of those together, the so-called "metabolic syndrome," occurs at phenomenally high rates in this group. We're also learning that even individuals of normal body weight have a higher incidence of hypertension and diabetes in this group, and that's a puzzle, and a question is trying to be answered now: Is that diet? Is that environment? Is that genetics? We have to figure out what are those causes, because obviously these are diseases that have a great deal of consequence, in terms of heart disease and strokes.

We are learning that this kind of gathering together is also a great way to get community involvement. And the ways in which the Jackson Heart Study has embraced the community, and been embraced by the community, is a wonderful model for doing research on health disparities.

The funding for 2011 for the Heart Study is very much a part of this budget, and the NHLBI intends to continue that at least through 2013. At that point, they will be evaluating what progress has been obtained. But, everything I have heard from the leadership is, they're—they expect to continue this for a long time.

Senator COCHRAN. Well, thank you very much.

Thank you, Mr. Chairman.

INSTITUTE OF MEDICINE (IOM) REPORT ON CLINICAL TRIALS

Senator HARKIN. Thank you, Senator Cochran.

I've got two or three things I'd like to follow up on, here.

Dr. Collins, last year President Obama vowed to find, quote, "a cure for cancer in our time." But, I remember when President Nixon declared a war on cancer. They've been fighting that thing ever since. So, while I appreciate the President's vow, I just wonder if we're going in the right direction.

Now, you've come up with some things here that give us a lot of hope, but, just recently, the IOM issued a report that was very critical of the National Cancer Institute's (NCI) Clinical Trial Network (CTN). According to the IOM, the CTN is underfunded, and is approaching, "a state of crisis." Most disturbing of all, about 40 percent of its cancer trials are never completed, which might suggest that we're wasting valuable time and money.

So, again, I want to give you the opportunity to respond to that. The IOM report found that the CTN is too bureaucratic, its research is poorly coordinated. Due to cumbersome review procedures, the average time between developing an idea for a trial and getting it started is about 2 years. Another problem they pointed

out was the distressingly low participation rate of adults in clinical trials. So, I wanted to kind of go over that with you and how are you responding to this IOM study.

Dr. COLLINS. Senator, I think all of us are quite concerned about this situation. Certainly, I've studied that IOM report carefully and talked to the leadership at the NCI about this. The cooperative groups, 10 of them, that have been conducting clinical trials on cancer for as long as 50 years, have certainly produced wonderful data over the course of time. But, there's no question that the current system is not functioning as well as it should. And that's what this report pointed out.

I should mention that it was Dr. Niederhuber and the leadership of the NCI that asked for the IOM to look at this, so they were fully aware of the need for some changes, and asking IOM to help out with this, and are now, I think, embracing that report and already moving forward to try to make such changes.

Clearly, there are a number of serious issues here. One is the very long time, as you've mentioned, between the time when a protocol is conceived and when the first patient is enrolled. And that had stretched out to 2½ years. Well, here we have a field that's moving so quickly, by the time you get to the point of enrolling a patient, sometimes the protocol didn't seem like one that you would really want to support at that point. So, that timetable has to be shortened. NCI has moved forward, now, to make changes that will limit that to 1 year, and no more.

And obviously, part of this is our own system of trying to run multicenter trials, which has gotten really quite convoluted and complicated, in the sense that, particularly, for human-subjects approval, every center has its own IRB, and the IRB has to review the consent form. And if you're trying to run a trial that involves dozens of centers, and every IRB wants to tweak things a little bit, you can see how time passes and you don't end up with things getting underway very quickly.

Senator HARKIN. Why can't——

Dr. COLLINS. Furthermore, there may be——

Senator HARKIN. Why don't we consolidate that?

Dr. COLLINS. Well, exactly. We need central IRBs, and there is a major move underway to implement that. It has been, I think, delayed by the fact that many legal minds have been involved, saying that institutions shouldn't really deem anyone other than their own IRB as capable of reviewing——

Senator HARKIN. Do we have to do anything legislatively, Dr. Collins?

Dr. COLLINS. I think this actually can be handled without legislation. I will tell you, there's a great groundswell now, not just from cancer, but from many other areas of clinical research, to do something to streamline our human-subjects effort, that we are not really, in every instance, using this in a way to protect participants in research, but we've gotten all tangled up in the bureaucracy. And sometimes we are mixing up the things that are really high risk with things that are very low risk. And we need a revamping there. And I think this is something that's going to get attention quite soon.

Other areas—there's a problem, in some instances, where protocols may be run in too many centers, and each center is only enrolling a very small number of patients. And so, it's not an efficient way to do things.

There may not be a sufficient evaluation of whether a protocol is actually the best use of the money for that disease at that point. There needs to be more of a scientific rigor in the process.

All of those are accepted, now, I think, by the NCI.

There will be new leadership of the NCI; an announcement of that sort is imminent. And I am sure the new NCI Director will take this on as a very high priority, to try to understand how best to re-engineer this CTN, because this is critical for our future. We're going to have a much higher throughput of new molecular entities coming forward from this molecular understanding of cancer, and we have to have an engine in place to test them and see what works and what doesn't. So, this could not be more important, and I appreciate your raising the issue.

ALZHEIMER'S DISEASE

Senator HARKIN. Well, thank you. I have a couple more. I had a question that has to do with Alzheimer's, but maybe a little bit broader than that.

A panel, convened by NIH, issued a finding, last month, that left a lot of people confused, I think, about Alzheimer's. According to this panel, there is no evidence that any of the strategies that people have been told to use to prevent Alzheimer's actually makes any difference. That includes getting exercise, taking supplements, keeping your mind active, doing crossword puzzles, and so forth. According to this panel, there's no evidence that any of these measures prevent you from getting this disease.

So, one question on that would be how we interpret a finding like that. The other question about Alzheimer's has to do with a broader level of funding, and how we think about funding for different diseases.

But, let's focus on this one, first, about the finding. What do we tell people? How do we interpret this finding?

Dr. COLLINS. Well, I think there have been a lot of messages out there that people were confused by—what works, what doesn't work. The whole point of the NIH panel was to actually look at the evidence and try to see, What do we objectively know about measures that could be used to delay or prevent this disease? Because this is a disease that affects, obviously, very large numbers of people, and we're all concerned about it. I just turned 60; I'm thinking about this more than I used to.

And, basically, all of the things that were put forward as potentially being beneficial in reducing the risk haven't held up very well to rigorous scientific evaluation. It looks as if doing crossword puzzles or doing Sudoku, it makes you better at doing crossword puzzles and doing Sudoku.

It isn't clear that there's evidence it has a more global effect, in terms of protecting your mental capacities as you're getting older.

The one exception that they thought perhaps there was some evidence for is diet, and particularly Omega-3 fatty acids, which are something that you find in fish. And there is some data supporting

that as a possible preventive measure, and that one deserves more study. But, it was one bright light.

And then, of course, there are well-documented environmental influences that we know about. Smoking, for instance, is clearly a risk factor for Alzheimer's, as well as a long list of other things. And certainly, obesity seems to have a connection, as well.

But, in terms of the specific mental exercises, which I think was one of the disappointments for a lot of people who hoped that that would be a way that you could take control of the situation and help yourself, there didn't seem to be evidence to support that.

Senator HARKIN. Thank you.

Senator Cochran.

INSTITUTIONAL DEVELOPMENT

Senator COCHRAN. Mr. Chairman, thank you.

We were talking, in my first round of questions, about the University of Mississippi and the legacy of Dr. Arthur Guyton. One thing that this subcommittee decided to do a few years ago was to earmark—oh, heaven forbid—some money, in this particular bill, and target the funding for grants and research to institutions in States that were getting less money and less attention to their work and applications than many other States had—which had long records of success and notoriety in certain areas.

Now, the University of Mississippi Medical Center, it was benefited greatly from one person's influence—Dr. Arthur Guyton. We talked about that. But, there are other institutions—within small States, in particular—who just come out on the short end of the stick when they apply for grants and try to get Federal support for work they're doing. Some of the ideas may be good, but the money is just never—never finds its way to those institutions.

So, we set aside, in fiscal year 2009, $224 million in a program designated for Institutional Development Awards. The purpose of that is to spread the money out in areas that would not, probably, be seriously considered for grants, finding and looking for the activities and the research that's being done, and having national impact and importance.

I guess my question is—Mississippi received $5 million—a little over—of the amount appropriated. That's only 2.4 percent of the total, so it's not like we out-maneuvered everybody; we didn't. But—and I guess that's the reason for my question. Some States do better than others in this, and I was just wondering, Is there any way for—a more careful review can be made to be sure that the intent of the set-aside is carried forward and that some States are not treated too much better than everybody else, so—the consequences of being left out?

Mississippi shares 2.4 percent, for example. That doesn't sound like much to me. What are your thoughts about how we could better define what this money is for to make sure it carries out the intent of the Congress?

Dr. COLLINS. Well, thank you, Senator.

So, yeah, the Institutional Development Awards (IDEA), have been strongly supported by NIH. They're administered by the National Center for Research Resources. And, yes, the budget for fiscal year 2010 was—went up $229 million. These are competitive,

they are available to the States who are identified as IDEA States, one of which is Mississippi, but there are a number of others that are traditionally underfunded by NIH, oftentimes because they have a lower proportion of institutions that are heavy in research efforts. But, we felt that we needed to be sure—we were finding opportunities in those States, and that those States had opportunities for NIH funding.

There are a couple of specific programs: The Centers of Biomedical Research Excellence, COBRE, or "Cobra," is one. There's an IDEA Network of Biomedical Research Excellence, INBRE. And, in fact, most of the States in the IDEA Network have been applying for those, and many of them with considerable success. But, it is a competitive program, where the peer-review system kicks in. And so, because of our interest in making sure that, with the funds available, we support what seems to the experts, who are not biased toward any particular State, but are trying to identify the best use of the money—we have to see where those outcomes fall.

Another program, though, that is, I think, relevant, here, is actually the ability, through the ARRA, to support construction efforts that have been asked for in the IDEA States. And Mississippi recently received such a construction grant; Arkansas did. In fact, a number of the IDEA States, for this $1 billion of construction money, that were part of the ARRA, have been quite successful. And we're delighted to see that, because that may be a way, then, to build that capacity, so that, in the coming years, they'll be in an even better position to be highly competitive for these funds.

Senator COCHRAN. Thank you very much.

Senator HARKIN. Senator Specter.

STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Thank you, Mr. Chairman.

Dr. Collins, I join my colleagues in welcoming you here. Thank you for taking on this important job.

My view, as expressed repeatedly, is that the National Institutes of Health are the crown jewels of the Federal Government—perhaps the only jewels. And in an era where we are searching for ways to prolong lives, save lives, and save money, it seems to me that we ought to be funding NIH a lot more aggressively than we are.

Senator Harkin and I led the way, with Senator Cochran's concurrence, and others, to raise NIH funding from $12 to $30 billion, $10 billion more than the stimulus. And the stimulus, I have heard, has created a whole wave across America of a—may the record show the witness is nodding in the affirmative——

Dr. COLLINS. Yes, he is.

CAN

Senator SPECTER [continuing]. Great surge of enthusiasm and rekindled a lot of interest in young people, who had been very much concerned because the funding had tapered off. There had been a loss of real dollars—in excess of $5 million—when we had to—accommodated for cost of living adjustments and also some across-the-board cuts.

And last year's funding was disgraceful, at $772 million. And this year's funding is also disgraceful, in my opinion, at $1 billion, with the comment made, "Well, you got $10 billion before," but it wasn't meant to lessen the annual funding. So, I'm going to repeat a message to you, which I have made frequently; that is that the scientific is going to have to become a lot more politically active blowing your horn. The statistics are very impressive as to what the increased funding did for NIH on mortality rates, on strokes, and much progress on many strains of cancer, and heart disease, and right down the line. And I think what you have to do, for the Congress and for the administration, is show how many dollars it saves.

Senator Harkin has been a real leader here on what he has done on wellness, the new concept, the Harkin Wellness Doctrine, a little exercise and annual exams and catching off ailments before they become chronic and debilitating and expensive. A lot of money to be saved by research; tremendous amounts of money to be raised by research.

And your medical communities have gotten a lot of money. University of Pittsburgh has gotten $4 billion in the last decade. And it's so across the country. You got a lot of prominent people on those boards, politically influential people. And appropriations run on politics, on the pressure. You've got a great case, but it hasn't been expressed very well. And I don't fault Dr. Zerhouni or the prior—he was a great director——

Dr. COLLINS. I agree.

Senator SPECTER [continuing]. And staffed by great people.

Now, I understand that you convened a meeting of your 27 Institutes to talk about CAN, which is new. And it has been put forward to bridge the gap, so-called valley of death, as I've heard it expressed in the scientific community, between the bench and bedside, between research and practical application. It has an authorization of $500 million, not a whole lot of money for that kind of a project, but what is—first of all, can you confirm the meeting that the 27 Institutes got together on CAN and what was the thrust of the conversation?

Dr. COLLINS. Well, thank you, Senator. And let me, first, say how appreciative your leadership has been over these years in supporting the cause of biomedical research, and particularly the critical role you've played for NIH support, including the ARRA funding, which, as you've alluded to, provided a remarkable shot in the arm for the research community and is being spent, I think, in truly exciting ways.

With regard to the CAN, this part of the healthcare reform legislation, as you know, puts forward a proposal of having the NIH take on, in new and flexible ways, the acceleration of the process of going from a basic science discovery to a clinical advance; a drug therapy, most likely, but this would also apply to other kinds of clinical advances. We did discuss this last Thursday, all of the Institutes' directors together for a full-day retreat.

Senator SPECTER. I heard there was a lot of enthusiasm for it.

Dr. COLLINS. There was a lot of enthusiasm. People were delighted about the potential, here, because the science has reached the point of making this a real possibility. Not that NIH would be-

come a drug development company, but the partnerships that we could now establish between NIH and the private sector through this kind of legislation are really exciting and unprecedented and are being very well received, both by the academics and people in companies.

Senator SPECTER. What is your professional judgment as to the kind of priority attention that the CAN ought to receive?

Dr. COLLINS. From my perspective, this is one of the five themes that I published in Science magazine as being most worthy of high-priority attention. The CAN fits very nicely into that, but provides some additional flexibility. So, this is a very high priority for us, and obviously we are mindful of the fact that, at the moment, this is authorized, but not appropriated. And we are also mindful of the fact that this may be a difficult year, in fiscal year 2011, with the ending of the ARRA dollars. But, certainly, from my perspective, as the NIH Director, and speaking for all those other Institute directors, this is something people are very anxious to get started on, and they have great hopes for, recognizing this is high-risk research, that many drug development programs fail, that if we're going to undertake this, we have to be prepared for that. But, I think we could learn a lot by doing this in a new way.

Senator SPECTER. Many programs fail and many programs succeed.

Dr. COLLINS. Indeed.

Senator SPECTER. And the successes have been monumental in what you have done for prolonging and saving lives. What could you do with the $500 million, Dr. Collins? Tell this subcommittee how much you could accomplish with it.

Dr. COLLINS. So, to undertake a project where you go from a basic science discovery to a Food and Drug Administration (FDA) approval of a drug is several years and expensive effort. With $500 million, we could probably proceed with about 20 projects, simultaneously, that went all the way from soup to nuts in that pipeline, and probably another 20 where we identify compounds, that are already in freezers of companies, that have been abandoned for various reasons, because they didn't work out for one application, but they might work out for a different one, so-called "repurposing," which would allow you to skip over many expensive steps. That would be quite a bold effort, indeed, to take on roughly, then, 40 projects on 40 different targets.

Senator SPECTER. One final comment, with the red light on. I would like you to go back to your office and review what could be accomplished with the $500 million, in as specific terms as you could, what you project you could do with that. And I know it is very hard to talk about saving lives, but you have some experience in what has gone on in other lines, statistically; and to the extent you could quantify it on saving lives, prolonging lives, or saving money, I think it would be very helpful, when the Chairman and the rest of us sit down to allocate the funds, here.

This is a very difficult subcommittee, having the Labor and Health and Human Services, and Education Departments. The competition for the money is absolutely fierce. So, the more specific you can be, the stronger the case can carry.

Thank you, Dr. Collins.

Thank you, Mr. Chairman.

Senator HARKIN. I just want to, first of all, say that this whole CAN that we put into the healthcare reform bill was a singular effort by Senator Specter.

[The information follows:]

CURES ACCELERATION NETWORK (CAN)

As you know Senator Specter, the Cures Acceleration Network (CAN), authorized in the Patient Protection and Affordable Care Act of 2010, would provide the National Institutes of Health (NIH) with new authorities to advance the development of "high need cures" by smoothing the pathway for developing new drugs, biologics, and devices, particularly through the so-called "valley of death" phase of the therapeutic pipeline. CAN would provide NIH with new authorities and flexible funding mechanisms, including the ability to leverage the Government's investment through matching funds. In addition to supporting the development of novel compounds and the repurposing abandoned products, it would provide NIH with an opportunity to carry out systematic process engineering that would result in a more efficient and effective therapeutic development pipeline. The program would operate in close coordination with the Food and Drug Administration and private sector stakeholders. CAN's authorities would allow us to use three novel funding mechanisms—Cures Acceleration Grant Awards, which could allow up to $15 million per award and additional funds in subsequent years; Cures Acceleration Partnership Awards, which could allow us to leverage additional funds so that a total of $20 million could be put toward every $15 million award; and, Cures Acceleration Flexible Research Awards, which could allow discretionary use of other funding mechanisms for up to 20 percent of the appropriation.

Methicillin-resistant Staphylococcus aureus (MRSA) provides an example of how CAN could contribute to improving health, saving lives, and lowering healthcare costs. MRSA is a major and growing clinical and public health challenge, and there is a need to develop antibiotics that are effective in treating this potentially life-threatening infection. MRSA occurs in hospitals and other settings where people are in close contact with one another, including nursing homes, dormitories, military barracks, athletic centers, and prisons. All sectors of the population are vulnerable, and certain groups are at higher risk, including children, the elderly, and people with concurrent health conditions. In 2005, MRSA caused approximately 94,000 invasive infections and 19,000 deaths. Total hospital costs for patients with MRSA infections were more than twice as high as those for patients with methicillin-treatable Staph infections ($34,657 compared to $15,923).

Industry interest in developing new antibiotics for drug-resistant infectious diseases like MRSA has declined considerably in recent years. Since 1999, 10 of the 15 largest companies have fully abandoned, or cut down significantly, discovery efforts in this field.[1] CAN could help address the deficits in the antibiotic drug development pipeline for treatments for MRSA and other drug resistant pathogens by leveraging established research resources, bringing together the pharmaceutical industry, regulatory and the financial communities, and applying necessary incentives to identify compounds for later phase development of new antibiotics. CAN's approach could make important contributions to this area.

The de novo development and characterization of each new drug ready for clinical testing would require approximately $20 million. The repurposing of a drug, which has already undergone considerable chemical and biologic characterization, would require approximately $5 million. An appropriation of $500 million would therefore allow us to support approximately 20 novel drug development projects and another 20 projects using compounds that have been abandoned for lack of capital, market demand, or regulatory and developmental hurdles. We anticipate that the program would eventually make major contributions to improving health, saving lives, and lowering healthcare costs associated with many serious human disorders and conditions that currently lack effective therapies and pose major burdens for individuals, their families, and society.

Senator SPECTER. Thank you, Mr. Chairman.

Senator HARKIN. He really dogged that one. And since I wear the other hat, as chairman of that other committee, too—this is one

[1] Kresse, H et al. The antibacterial drugs market. Nature Reviews Drug Discovery, January 2007.

that Senator Specter championed and got in there and was on us all the time to make sure that it was not dropped. And so, it was held in there, and I thank him for that.

I agree that this is something that really needs to be done, and we've talked about it personally many times in the past. And, Senator Specter, I think, has really been the great leader on this one.

Again, of course, Arlen also put his finger on it—we have a lot of competition for a lot of money here, and we have constrained budgets. So, I'm going to play a little bit of the devil's advocate here.

What would funding the CAN up to that $500 million, or however close—what would that allow NIH to do, that it can't do now?

Dr. COLLINS. No, it's appropriate to——

THERAPEUTICS FOR RARE AND NEGLECTED DISEASES PROGRAM

Senator HARKIN. Why can't you do it now?

Dr. COLLINS. It's appropriate to ask those questions. So we are, in fact, pushing this translational agenda in innovative ways. There's a program that this Congress has funded, the Therapeutics for Rare and Neglected Diseases, the TRND program, which aims to try to fill in some of the missing pieces in the "valley of death" that's necessary to cross if you're going to go from a promising compound to an FDA application for a clinical trial. And we're pursuing that quite vigorously.

And, Senator, I do understand the pressures on the budget system are severe. And I should have said earlier that, in that condition, the fact that the President's budget was able to come up with a $1 billion increase for NIH is something that—we should all, sort of, credit the administration with their vision for science. And I, personally, am delighted to see that this is an administration that has put science at such a high priority, even with frozen discretionary budgets.

What we could do that the CAN legislation provides is not just about money, though, it's also about flexibilities. So, what that legislation allows is that some proportion of that money can be used in a Defense Advanced Research Projects Agency (DARPA) like model, where you have flexible research authority to go beyond traditional grants, contracts, and cooperative agreements, to manage projects in very forward-looking ways. And that, for this kind of science, where you need to make decisions quickly, where you need to bring in other partners in a quick turnaround when you see you need to fill a void in what the science is showing you needs to be done, can be quite valuable. And we do not, at the present time, have that kind of flexibility for this sort of project. And we could benefit from that.

FLEXIBLE RESEARCH AUTHORITY

Senator HARKIN. But, Dr. Collins, you have the flexibility, now that it's authorized. I know, you have that—what you're saying is, you don't have the money.

Dr. COLLINS. Well actually, the way the bill was written, it says that the flexibilities of this bill may not be utilized unless the appropriation is put forward. Some appropriation is required before this is activated. So, unless, in the appropriations process that you

all are thoughtfully leading, there is a green light offered to this project by providing some kind of funding, I am not permitted to take advantage of the authorized flexibilities. That's the way the legislation was put together.

Senator HARKIN. Even if we just appropriate a dollar?

Dr. COLLINS. A dollar would, I suppose, do it, although it. It might be a little hard to do a DARPA program with $1. I don't know.

Senator HARKIN. I mean, I'm just talking about the trigger mechanism that allows this—you just told me something I didn't know. I didn't know that. So, this is very interesting.

Dr. COLLINS. And, of course, Senator, the other question is, in trying to figure out all of the priorities that I now struggle with, How does this fit? And obviously, you might say, "Well, why don't you just do this with the budget you've got?" Well, that would mean I would have to do less of something else. And already, with our 15 percent success rates looming, you can imagine how much of a stress and strain that is.

Senator HARKIN. Dr. Collins, I feel your pain.

Dr. COLLINS. I'm sure you do.

Senator HARKIN. That same thing is hitting us here—not just here, but in health, education—we're going to have some real problems in education, meeting our needs in higher education. So, we've just got a lot of things that are pulling at us, and we just are not going to have the funds to do it. So, we've got to make some pretty tough decisions, too. And some of our friends are not going to be very happy with some of the decisions that we make, but we're all going to have to sharpen our pencils and just try to prioritize things. And what I'm hearing about the CAN is—it's a very high priority.

Dr. COLLINS. That's correct.

Senator HARKIN. The translational research. And so, I'm going to take a look at what you just told me about—that there's a trigger mechanism in the legislation.

I think, Senator Specter, that's something we're going to have to take a look at here.

And I accept your word on that. We'll just have to see how much we need to put in there that would trigger that.

Now, I know Senator Specter would like the full $500 million. Yes.

Senator HARKIN. Actually, so would I.

Senator SPECTER. We could——

Senator HARKIN. I don't have any problem with the $500 million, but I——

Senator SPECTER. We could do more than that. That was the appropriation for fiscal year 2010.

Senator HARKIN. Oh——

Senator SPECTER. And now it's a set sum, so we could do $1 billion.

Senator HARKIN. It was $500 million for 2010, such sums after that.

Senator SPECTER. So, we're now at a set sum, so it could be $1 billion or $2 billion.

Senator HARKIN. You tell me where to get the money, and——

Senator SPECTER. I will.

Senator HARKIN. Okay. And we'll just put it out there, who we're going to take it away from to get that money. Like I said, we just have a lot of different demands on our money.

I had one follow up——

Senator SPECTER. Mr. Chairman, you and I have found as much as $3.77 billion, in the past. And it was just exactly what you mentioned, it was the sharp pencil.

Senator HARKIN. Well, in the past——

Senator SPECTER. And there are other accounts which do not rate with curing cancer or Parkinson's or Alzheimer's. And you and I did it before, and we can do it again.

Senator HARKIN. Yeah, we did it before, when we had some budget flexibility. I don't see much of that there right now. I just don't. Unless you've got some way of getting it.

Anyway, I ran up my time. I'm yielding to Senator Specter for another round. Do we have another round?

Senator SPECTER. No, that's it, Mr. Chairman. That really is.

Well, I have one other item that I would like to take up, and that is the funding on minority health.

NATIONAL CENTER ON MINORITY HEALTH AND HEALTH DISPARITIES (NCMHD)

Senator SPECTER. I note that it is in the budget for $219 million. The health reform bill elevated the NCMHD at NIH to an Institute. And the administration requested a budget of $219 million, which, by comparison, seems low. What do you recommend on that, Dr. Collins?

Dr. COLLINS. Well, actually, the NCMHD, is a major coordinator of minority health and health disparity research at NIH, but certainly all of the Institutes are invested in this area. If you look at the graph, here on the screen, the total investments estimated for 2011, with this budget, would be more like $2.7 billion, so more than 10 times what the funding is, specifically for that Institute.

Because we actually think that minority health and health disparities ought to be a priority for all of the Institutes. Whether it's the NCI or the NHLBI, or the Diabetes Institute, these are all areas where health disparities are a critical matter.

Senator SPECTER. Well, then why was a new Institute established for minority health, if it's accommodated at other places?

Dr. COLLINS. I think there was a desire to have it more visible, to have a coordinating function, which that——

Senator SPECTER. $219 million doesn't give you a whole lot of visibility.

Dr. COLLINS. It has provided an opportunity to give endowments, for instance, to some of the traditionally minority-serving institutions. That's a major part of what that Center, and now Institute, has done, when that flexibility didn't exist before. And certainly this Institute, every 4 years, puts forward a strategic plan, which they coordinate, on health disparities. And that didn't really have a home before, in terms of doing that kind of strategic plan coordination; and now it does.

Senator SPECTER. Thank you.

Thank you, Mr. Chairman.

BURDEN OF DISEASE

Senator HARKIN. Thanks, Senator Specter.

Let me follow up on the Alzheimer's thing that I started off with on. The first part just had to do with that finding of that panel. But, here's the whole issue of how NIH decides how much to spend on individual diseases. It's something that keeps coming up; year after year, I hear about it.

First of all, Congress does not earmark funding levels by disease. And I hope we never do. As long as I'm chairman, we never will.

I'm often asked, by patients and advocates, for example, how to explain the NIH funding level for a disease like Alzheimer's.

As we know, Alzheimer's is an enormous burden on our society, not just in human terms, but in terms of our overall economy. There's an estimate out there that, from 2010 to 2050, the Medicare and Medicaid costs of Alzheimer's will total—ready for this one?—about $20 trillion. That's just for the care of Alzheimer's. Now, I don't know if that's high or low; I'm just tossing this estimate out there. Even if it was half that, it would be staggering.

And yet, if you look at the NIH budget, funding for Alzheimer's makes up a much smaller share than one might expect; about 1.5 percent.

Another example: pancreatic cancer is the fourth leading cause of cancer-related death, but less than 2 percent of the NCI's budget is devoted to this disease.

So, my question, basically, is this, Dr. Collins. What role does the burden of a disease—the burden on society—play in where NIH allocates its money?

Dr. COLLINS. Senator, it's a great question, and it's a question that all of the people who have sat in this chair in prior years have also wrestled with. From the very beginning of NIH and its system of trying to define how to set priorities, there have always been debates about what are the right weighting factors to apply to particular diseases. And I would say that it's a complicated enough calculus that it'll take a minute to explain.

So, first of all, some of what NIH does needs not to be focused on a specific disease; otherwise, we will not have the foundational discoveries that result in Nobel Prizes and transformative understandings about neuroscience and immunology and cell biology and all of those things that are the really important foundation upon which everything rests. So, we would not want to have our entire budget specifically focused on disease research, or we would probably be mortgaging our future.

When it comes to those things that are clearly in need of attention, how do we decide? So, this—certainly, the burden of disease has to be a big factor, and the cost of that disease has to be a big factor. And you've quoted numbers for Alzheimer's that are staggering in that regard. And diabetes could also be cited in that way—and cancer and heart disease.

But, if we based our decisions solely on those issues, then rare diseases would tend to get ignored, or funded in only the very smallest amounts. If a rare disease happens to strike your own family, it's hard to say it doesn't matter. For that person, the bur-

den of disease is very high. So, we clearly have a responsibility there, as well.

And oftentimes, studying rare diseases gives us insights into common diseases. We study progeria, that affects maybe 30 kids in this country, and we learned something about aging that we never knew before, which affects all of us. Those kinds of connections keep popping up over and over again. We wouldn't have statins if we hadn't started out by studying a rare cause of very high cholesterol levels. All of those, I think, are reasons not to focus solely on burden of disease.

And then, there's scientific opportunity, which has got to be a big part of this. To say, "We have a disease problem, and we're going to throw money at it," if nobody has an idea about what to do, is unlikely to be productive.

And to take another area, which maybe is not quite as much of a burden, or quite as much of an expense, but where you can see the scientific field is just poised for a breakthrough, you don't want to miss that opportunity.

So, the job of those 27 Institute Directors, and my job, is to try to survey the landscape, sort of, weekly, and figure out how to do that steering of the ship to try to be sure we are investing most wisely. Do we always get it completely right? I wouldn't say we could claim that, but I think we do pretty well. And we are supported, of course, by this remarkable peer-review system. There's two levels which both looks at the scientific rigor of a grant proposal and then, at the second level, tries to figure out where are the highest program priorities, factoring in things like burden of disease. And when you look at the landscape of what we do across diseases, it doesn't match up precisely with what you might have guessed, just based on epidemiology, but I think it's fair to say there's a pretty strong connection.

Alzheimer's—you know, we are working hard on that. There are 30 new drugs that are in various stages of being developed for this approach, using things that we've learned about the amyloid deposits in the brain, and the enzymes that are involved in breaking that down, and how to encourage them to do a better job.

Vaccination—we talked about vaccination against nicotine; maybe a vaccination against amyloid, for Alzheimer's, which, unfortunately, in the early trials, a few years ago, ran into some unfortunate side effects. But, people are developing new ideas about how to get around that.

I couldn't agree more that, if there's an area that desperately needs a breakthrough, it's Alzheimer's disease. A lot of people trying.

PANCREATIC CANCER

Senator HARKIN. Again, that gets me to another question about causes and the rapid growth of certain diseases. It just seems like Alzheimer's is exploding.

Pancreatic cancer—the huge increase in pancreatic cancer in just the last few years. And different medical personnel I've talked to about this says that there's something going on out there; something is causing this huge increase in pancreatic cancer, but no one can quite figure out what it is.

And so, that's why I say, you need to look at this—I mean, it—I'd like to have some sort of satisfaction, or some feeling, positive feeling, that NIH is pivoting a little bit on this and saying, "What is causing this? Why?" and guiding some more research into pancreatic cancer and what's happening there.

We always knew that it was one of those secret kinds of cancers; in other words, you didn't know about it until it was too late——

Dr. COLLINS. Yeah.

Senator HARKIN [continuing]. Because there was no markers for it or anything. But, it's not only that now, but it's just the huge increase. I forget the figure, but it's just up tremendously, the number of people being diagnosed with pancreatic cancer.

Do you think NCI is pivoting and looking at this and putting more emphasis on it?

Dr. COLLINS. I think pancreatic cancer is a cause of major concern at NCI, and is for me, personally, when you see the number of individuals being diagnosed with this disease, which, as you say, often comes to light after it's already too late, because it doesn't reveal itself until it's already, oftentimes, spread. It is, all too often, a disease that we don't do much for, at the present time, except chemotherapy, which may gain a few months. And, of course, some notable figures—Patrick Swayze, diagnosed with this disease, and the way in which that created a new personal face, has brought even more attention to this, as well it should.

So, pancreatic cancer is one of the cancers being pursued by the Cancer Genome Atlas. This comprehensive effort to try to identify what exactly goes wrong in a pancreatic cell to cause it to grow out of control this way, and not just look under the lampposts, where we've been looking all along for clues, but actually using the tools of genomics to get all the answers that—all of the ways that a cell in the pancreas can start to go bad. And that will, I am confident, Senator, give us a comprehensive ability, both to do a better job of early diagnosis, but, most importantly, to identify new therapeutic magic bullets that will go to the heart of that cancer, like Gleevec does for leukemia; except we need a Gleevec for pancreatic cancer, don't we? And the problem right now is, we don't know what the target is that we're shooting at. The Cancer Genome Atlas will reveal the complete list of targets.

Of course, that doesn't happen overnight. That's a process. And again, the CAN, we talked about a minute ago, may assist, once the target's identified, in speeding up the process of getting something ready for a clinical trial. All of those steps have to be integrated together.

Again, I think having new leadership, imminently, for the NCI, is going to be quite timely in this regard. I am impatient, just as you are—frustrated, as you are—about this terrible disease of pancreatic cancer, and how many people we lose to it, and how impotent we seem to be, so often, in being able to stop the course of the disease.

Senator HARKIN. Yes.

Dr. COLLINS. And I would not want to have a day go by where we were passing up on the opportunity of new ideas to do something about this.

Senator HARKIN. Yes, because like B-cell lymphoma and things like that, and what NCI has done has been miraculous.

Dr. COLLINS. Yes.

Senator HARKIN. The cure rate there is just phenomenal.

Dr. COLLINS. Yes.

Senator HARKIN. It's very, very good.

Dr. COLLINS. Well, that's a good point, because there you have targets, and——

Senator HARKIN. Yes.

Dr. COLLINS [continuing]. There, the drugs have developed against those targets. And, boy, they work.

FDA AND THE NIH

Senator HARKIN. Yes, they sure do. Okay, we'll follow up on that.

You recently joined Secretary Sebelius and FDA Commissioner Hamburg in announcing a new partnership between NIH and FDA that, again, is intended to speed up the process of turning basic scientific discoveries into treatments. Well, what is this effort? How does this correlate with CAN? What are the goals? Is this different than what we've been talking about?

Dr. COLLINS. It's a part of the whole system that needs to be coordinated, integrated, optimized. I think it's clear that relationships between NIH and FDA have to be really well orchestrated in order for all of those complicated steps, in going from an idea to having a successful clinical trial, to go forward without missteps that cost time and cost money.

The FDA has enormous challenges in front of them, in terms of the way in which the development of therapeutics is evolving. The idea that you might, for instance, for cancer, need to get to a place where most patients are not being given one compound, but maybe two or three, that's targeted specifically to their tumor. Because you're going to know, in their tumor, exactly what's gone wrong. So, you look at your list of drugs, and you pick the combination that you know is zeroed in on their problem. Well, how does FDA evaluate a clinical trial of thousands of patients, where they aren't all taking the same thing? So, they need scientific research efforts to prepare them for that.

The regulatory science that Peggy Hamburg has been talking about is exactly what's needed. We, at NIH, agree. Fact, we have funded, with FDA, for the first time, a research program on regulatory science. We just announced that. We got 59 letters of intent. There are really interesting things being put forward, that the scientific community thinks they could offer to help FDA with the things that are coming down the pike, as far as regulatory challenges.

And many academic investigators, if they're getting more involved in the development of therapeutics—and the CAN will make that happen—they're not familiar with exactly how to do this, and there's a risk that they might sort of get very close to an FDA application, and then find out they've left out something really important, and have to backtrack, and waste time and money. So, we have to tighten up those relationships.

So, Peggy Hamburg and I have been meeting—and since last summer—to talk about how to do that. This new leadership coun-

cil, which she and I will cochair, will involve senior leadership of both agencies, and will involve many people at middle level, so that we could prepare for the opportunities that are coming, and not end up in some sort of bureaucratic mixup, which would be really heartbreaking to see.

I think the atmosphere is just right for this.

PATIENT ADVOCATES

Senator HARKIN. Tell me about the role of what I would call "patient advocacy groups." When you're going out to conduct human trials and, as you say, there's always risks when you conduct human trials—I think it's important to inform patients, from the beginning, help them understand what you're going through, in terms of the regulatory end of it. So, I'm just wondering when you're setting up this regime of involving these patient advocacy groups so that they can be supportive because they want to get the human trials out there. I think it might be wise to have them involved so that they understand what you're doing and that they can be a proponent of it, that they can be out in the public, advocating for this and sort of acting as a shield for you out there, perhaps, because a lot of people don't understand what you might be doing, and these groups could help you. So, I hope you'll look at involving them in this process.

Dr. COLLINS. Senator, I completely agree with you. I think there are many heroes, and "sheroes," out there in the advocacy organizations——

Senator HARKIN. Yes.

Dr. COLLINS [continuing]. Who have remarkable insight into what we could do to improve the success of our whole enterprise. And we listen to them, with great attentiveness. And certainly, with regard to this relationship, we have already had some of those informal consultations. And on June 2, we're holding a public, sort of, town meeting about this new NIH–FDA Leadership Council, and asking advocates and other members of the public to come forward and tell us what they think are the highest-priority matters for this council to address.

Senator HARKIN. So, it's an online town meeting?

Dr. COLLINS. I think we're web casting it, and it's also, certainly, encouraging people to come live and come to the microphone.

Senator HARKIN. Ah. Is that going to be out at the campus?

Dr. COLLINS. It is.

STEM CELLS

Senator HARKIN. Very good. That's on June 2. Well, I appreciate that. I think that would be important.

Is there anything—oh, yeah, of course. How could I leave you without asking about stem cells?

I wouldn't let this go.

You recently announced that—as you did, also, in your opening statement—that some additional human embryonic stem cell lines have been approved for NIH funding, and including the line that's been studied more than any other. Again, what's the significance of this? How many lines are we up to now? And give me some crystal-ball-gazing. Where are we headed?

Dr. COLLINS. Thanks for the question, because this is a very exciting area of biomedical research.

There are now 64 human——

Senator HARKIN. Sixty-four?

Dr. COLLINS [continuing]. Embryonic stem cell lines that have been approved by this NIH process that was stimulated by Obama's Executive order and that are up on the NIH registry and may now be used by researchers using Federal funds. And that is a number that is going to continue to grow. We have more than 100 additional lines that are in the process of being reviewed.

The goal, of course, of the review is to be sure that the consent process that was utilized for the embryo donors was above reproach. We want to be sure that these lines were obtained in a way that is entirely open to ethical scrutiny. And that is why the NIH has been conducting the reviews of those documents before certifying such a line.

We were very happy to be able to get the materials, just about a month ago, on a few of the lines that had been particularly heavily used since 2001, when, as you recall, President Bush's decision was that lines could not be used that were derived after that. But, there were 21 lines that were allowed, at that point.

Senator HARKIN. Right.

Dr. COLLINS. And there were a couple of them that were used particularly heavily. One, called H1, we were able to approve right away, because we had the documentation. The one that was causing a lot of anxiety in the community is a line called H9, and it just took a while for the deriver of that line—derivers, because it involved both Israel and the United States—to locate all the documents and to get them to us. Once we had them, we did a rigorous review, in a very short turnaround. We're happy to see that everything was totally in order and approved that line. And I think that settled down some of the concerns that people had about whether that line was still going to be available to them, or not. We had allowed researchers to continue to work with it, with an existing grant; but, if somebody came back for a competing renewal, we wanted them to start working with approved lines. They can now use H9 as long as they want; it's fine. And there will be hundreds more coming through.

On top of that, of course, there's great excitement about this additional way of making a pluripotent stem cell by taking a skin cell and, with just four genes, carefully chosen—and this is the remarkable work of Shinya Yamanaka, who I'm sure someday ought to win the Nobel Prize—you can take that skin cell and turn that into a pluripotent cell that basically can make any cell type that you would want it to, if you stimulate it with the right cocktail of cytokines and so on. Just phenomenal, Senator, that there's this much plasticity in the system, and that a cell that's been sitting in your skin all those years that—since you were originally born—is capable of having that ability. But, I guess it sort of makes sense, from a genome perspective; after all, that skin cell has the whole genome.

Senator HARKIN. Yes, right.

Dr. COLLINS. It just needs to be woken up again and encouraged to think that it's young and has all those potentials to do everything you could imagine.

That is an area that is just bursting with potential. We are actually starting, on the NIH campus, a special center for the so-called induced pluripotent stem cells (iPS)——

Senator HARKIN. Oh.

Dr. COLLINS [continuing]. And the specific goal there is to push the agenda toward actual clinical applications.

Senator HARKIN. Great.

Dr. COLLINS. The beauty of these, if it turns out to be as successful as we all hope, is that these are your cells; and so, if you were to need them for Parkinson's disease, because you develop that, or for a liver problem, you should be able to receive that kind of autotransplant, without the rejection problems that would otherwise apply if the cells came from somebody else. So, that is a big positive about this.

The questions are safety, particularly, because a pluripotent cell sometimes grows when it isn't supposed to. And one of the ways we actually characterize pluripotent stem cells, like iPS cells or embryonic stem cells, is by whether they can make tumors if you put them into——

Senator HARKIN. Oh.

Dr. COLLINS [continuing]. A particular mouse model. And obviously, we have to be very sure, before we try this in human applications, that we're not creating more trouble.

There is, as you may know, a single FDA-approved trial for clinical use of human embryonic stem cells. It's for spinal cord injury. It's by a company called Geron. They have not yet enrolled their first patient, but expect to later this year. Obviously, everyone is watching that, although I think, realistically, one should not assume that the very first trial of any brand new therapy is going to tell the whole tale about its promise.

But, of all the areas that are going forward right now in biomedical research, that I think have been breathtaking in their potential, this is right near the top of the list. And I think NIH, as you can maybe tell from my remarks, is pretty excited about pushing this forward with as much energy and as many resources as we're able to.

Senator HARKIN. I'd just ask my staff to get me all the information on this spinal cord. I had read about it, know a little bit, but I don't have—but, if you can get me some information on that, I'd appreciate it.

Dr. COLLINS. Happy to do that.

[Information follows:]

STEM CELLS FOR SPINAL CORD INJURIES

Geron Corporation is a biotechnology company based in California. Its lead human embryonic stem cell (hESC)-based therapeutic candidate, GRNOPC1, contains human embryonic stem cell hESC-derived neural support cells developed for the treatment of acute spinal cord injury. In pre-clinical studies, GRNOPC1 has been demonstrated to repair myelin, a protective nerve coating, and to stimulate nerve growth leading to the restoration of function in animal models of acute spinal cord injury. The initial proof-of-principle animal studies were conducted by Dr. Hans Keirstead, an investigator at the University of California, Irvine with funding from the National Institute of Neurological Disorders and Stroke.

In January 2009, Geron's Investigational New Drug application for GRNOPC1, which application the company had submitted to the U.S. Food and Drug Administration (FDA), went into effect. In May 2009, FDA placed a hold on the start of the phase 1 clinical trial and requested that Geron conduct additional pre-clinical studies to provide further assurance of GRNOPC1's safety. Geron has recently reported that additional data have been submitted to FDA, and its Web site now indicates that phase 1 clinical trials are expected to proceed in the third quarter of 2010.

If Geron's clinical trial is allowed to proceed and GRNOPC1, as the subject of a biologics license application, is shown to be safe and effective, the therapy may provide a treatment option for thousands of patients who suffer severe spinal cord injuries each year.

http://www.gemcris.od.nih.gov

Senator HARKIN. And the last issue—the last issue of Scientific American, which I always call the "layman's magazine of an NIH report"—something I can understand; it's my must-reading every month, the Scientific American—but, the last cover—get a copy of—it was all on the iPS, on the adult stem cells, as they say. And it was a fascinating article about turning the clock back. And Dr.—I forget his name.

Dr. COLLINS. Yamanaka.

SICKLE CELL DISEASE

Senator HARKIN.—Yamanaka, yes—is featured in that, and the way it was written is—just makes you think that this could be the—the way to go. I don't know. That's why I've always been in favor of all stem cell research, whether—whatever it is, whatever pathway it leads us down, within the ethical guidelines that we've established.

Dr. COLLINS. Well, think about sickle cell disease as a possible application for iPS. This has already been done in a mouse model, which is one of the reasons I think I'm——

Senator HARKIN. Yes.

Dr. COLLINS [continuing]. Particularly excited about its potential for humans. If you could take somebody with sickle cell disease, this terrible disorder, where a hemoglobin mutation causes the red cells to clog up in the vessels and cause all manner of organ damage and much pain. Take a skin cell, make it into an iPS cell, grow up a bunch of those, and then, using well-established experimental protocols, convert those iPS cells into bone marrow stem cells, and infuse them back in, after you've fixed the sickle mutation, which you can do while the—you're still working with a iPS cell in a culture dish. So, you can kind of do the whole cycle.

That has been done by Rudy Jaenisch, at MIT, in a mouse model, and cured sickle cell disease in the mouse. Now, everybody will say, "We've cured a lot of diseases in mice," and we have. But, by this protocol, it's pretty radical and pretty exciting, and certainly—one of the diseases that I hope will be high on the list for first human applications will be sickle cell. It's a 100 years since that disease was first described. This year, 100 years.

AUTOLOGOUS STEM CELLS

Senator HARKIN. Amazing. Yes.

Let me ask you about autologous stem cells. I've been meeting somewhat with FDA on this, in terms of a change in their approval process that took place in the—in about 2005, if I'm not mistaken. And—but, that's another—that's the regulatory end. I'm just more

interested in the scientific end, because I've had people in my office who have had autologous stem cell treatment. And—interesting group of people. One was a pilot who had been in an airplane crash and was, basically, paralyzed from his waist down. And through a process of autologous stem cells—I mean, he's not walking like you and I, but with canes and crutches. I mean, he's actually walking. But, you know, not fully recovered.

Another person that had some heart problems brought in his different PET scans and different things like that, and, through autologous stem cells, has never had to have heart surgery.

And there were a few others that I met. But, this is all through autologous stem—and some of that's being done in our country right now. Some of that's being done.

Can you enlighten me as to what this involves? And what is NIH doing in autologous stem cells?

Dr. COLLINS. So, this is an interesting area, and a rather controversial one——

Senator HARKIN. Yes, I know.

Dr. COLLINS [continuing]. In terms of, what capability these autologous stem cells have to home in on the site where they're needed and how they actually turn into the kind of cells that are needed there in order to compensate for what's happened, whether it's a spinal cord injury, whether it's a heart attack and you're trying to provide an opportunity to repair itself?

Frankly, the NIH-supported studies on this have not been as encouraging as many people had hoped. Take the approach to heart attack. Ten years ago, there was a lot of suggestion—enthusiasm, here—that bone marrow stem cells might, if given directly into the heart muscle after a heart attack, allow repair of that area that had suffered damage. And there were experiments done in animals that looked encouraging; and human trials that were done, in many centers, that had somewhat mixed results.

And I think, now, looking back on that, the evidence that that has actually been beneficial is not nearly as convincing as one would like.

That has not stopped, of course, the research from going forward. And it shouldn't. And I can't tell you, but I could for the record, exactly what the total is—now is, of NIH-supported autologous stem cell trials.

I will say that I've heard some heartbreaking stories of people who have gone outside of the United States to undergo these kinds of trials, in the hands of people who really are not scientifically very rigorous, and bad things have happened, in terms of the consequences—infections, stem cells that got in the wrong place, people basically spending large sums of money for the kinds of therapies that really had no scientific basis, in hopes that it would help them.

So, anybody contemplating that ought to be sort of eyes wide open, as far as what the evidence is.

And we will continue to push this approach. We spend more money on adult stem cells than we do on embryonic stem cells, because of the potential opportunities there. And obviously, there are great successes, particularly bone marrow transplant, that we can all point to, that has saved many, many lives. But, the broader ap-

plications for curing problems that involve solid organs, I think, are much more challenging.

There's a protocol just getting started, not with autologous cells, but with fetal cells, to try to treat Lou Gehrig's disease, ALS, which is obviously a disease of great frustration and great tragedy when it strikes.

So, these kinds of approaches deserve every bit of attention, as long as they're done rigorously and as long as we find out, at the end of the study, "Did it work, or did it not?" so that we can guide people who are interested in that outcome.

Senator HARKIN. I'd like to know more about autologous stem cells. Get me some information. I'd just like to know, you know, what's being done at NIH in research on autologous stem cells.

Dr. COLLINS. We're happy to provide a summary of that——

Senator HARKIN. Oh, good.

Dr. COLLINS [continuing]. For you, Senator.

[The information follows:]

AUTOLOGOUS STEM CELLS

Autologous stem cell transplantation (ASCT) is the use of an individual's own stem cells for the treatment of disease. The best known application of this technique is commonly referred to as "bone marrow transplantation," where an individual's hematopoietic (blood) stem cells are harvested and then reintroduced to reconstitute the blood and immune system. This form of ASCT has been in use for many years, and has demonstrated clinical effectiveness for the treatment of several diseases.

However, the concept of ASCT can be expanded to include stem cells harvested from one organ system to treat another organ system. Proof of principle animal studies revealed that stem cells harvested from organs such as bone marrow, skin, gut or endometrium, may be able to treat diseases in or ameliorate damage to solid organs such as the heart, brain, or spinal cord. These findings have raised hopes that these treatments could be transferred to the clinic and have led to the development of a growing cellular therapy industry within the United States and abroad. The application of ASCT across organ systems in humans is still in early experimental phases, and, unfortunately, the controlled studies conducted thus far have demonstrated mixed results, with some even having severe negative consequences.

The National Institutes of Health (NIH) continues to support research into the development of safe and effective treatments for diseases and disorders using ASCT. I am providing you with a summary of NIH-supported clinical trials using autologous stem cells. This summary is a broad overview of the many research projects being conducted.

National Cancer Institute (NCI)

ASCT is an important treatment option for several hematologic cancers as well as other types of cancer and other diseases. In this case, a patient's own bone marrow is used as a source of stem cells to reconstitute his/her blood cell producing capability following high-dose curativeintent chemotherapy. However, ASCT is not curative for all patients and NCI continues to support research to refine and improve outcomes using ASCT in both intramural and extramural research settings. Strategies under investigation include adding novel agents and agent combinations following transplant and adding immunotherapeutic drugs in conjunction with transplant. These strategies are a therapeutic tool in treatment of the following disease states (among others): multiple myeloma and other plasma cell disorders such as amyloidosis and Waldenstrom's macroglobulinemia; Hodgkin's disease and non-Hodgkin's lymphoma; acute myelogenous leukemia and acute lymphoblastic leukemia; neuroblastoma; inflammatory breast cancer; systemic lupus erythematosus; and leukocyte adhesion deficiency.

National Heart, Lung, and Blood Institute (NHLBI)

ASCT holds great potential for treating cardiovascular, lung, and blood diseases and the development of clinically feasible applications is an important part of NHLBI's strategic plan.

In the cardiovascular area, ASCT is being investigated in phase I/II trials for the treatment of damaged or malfunctioning heart muscle, and in an upcoming phase

I trial for treatment of peripheral artery disease. Bone marrow mononuclear cells and mesenchymal cells are being tested for treatment of acute myocardial infarction (heart attack) and heart failure by injecting stem cells directly into the heart. In another study, cardiac-derived progenitor cells, obtained via cardiac biopsy, are being tested for treatment of individuals with ischemic left ventricular dysfunction. Finally, parent-banked umbilical cord blood-derived stem cells will be tested for treatment of limb muscle damage by injection into the affected muscle.

In the hematology area, ASCT has been performed for more than five decades. In 2001, NHLBI initiated a network specifically to conduct multi-center trials to improve outcomes in blood and marrow transplantation, including eight clinical trials involving ASCT. Examples include a comparison of cell sources (autologous vs. allogeneic), a comparison of conditioning regimens used prior to ASCT, and the possible benefit of combining intensive chemotherapy with an autologous stem cell transplant. Investigator-initiated studies have also been implemented including a long-running program project grant on stem cell transplantation.

National Institute of Allergy and Infectious Diseases (NIAID)

NIAID researchers are investigating potential opportunities for improving immune function in patients with certain rare genetic disorders, including X-linked Chronic Granulomatous Disease, X-linked severe combined immune deficiency, and WHIMS (warts, hypogammaglobulinemia, infection, and myelokathexis syndrome) through gene therapy and other treatments targeting human hematopoietic stem cells. NIAID also is supporting two trials to assess autologous hematopoietic stem cell transplantation "to reset" the human immune system in patients who suffer from the autoimmune diseases multiple sclerosis and systemic sclerosis.

National Human Genome Research Institute (NHGRI)

NHGRI is supporting a gene therapy trial for a rare form of inherited immunodeficiency called adenosine deaminase (ADA) deficient severe combined immunodeficiency (SCID). Eligible children with ADA–SCID are admitted to the Clinical Center where their autologous bone marrow stem cells are collected and subjected to retroviral-mediated gene transfer to correct the genetic defect before being reinfused. Results from treated ADA–SCID patients indicate that this approach can regenerate immune responses in these severely immune-compromised subjects.

National Center for Research Resources (NCRR)

NCRR supports ASCT through its General Clinical Research Centers. Researchers are investigating the use of ASCT in patients with relapsed Hodgkin's or non-Hodgkin's lymphoma. Other scientists are transfusing autologous umbilical cord blood to regenerate pancreatic islet insulin-producing beta cells and improve blood glucose control is being tested. Finally, other researchers are comparing disease-free survival between two different clinical protocols for ASCT.

National Institute of Dental and Craniofacial Research (NIDCR)

Bone marrow contains a population of stromal stem cells capable of regenerating bone and supporting the formation of marrow. NIDCR-supported scientists are planning a study that would involve harvesting bone marrow from the hip of patients with cranial (skull) defects that have failed standard treatments (metal plates, plastic overlays). The stromal cells in the marrow will be expanded and then attached to ceramic particles and placed into the cranial defects. Patients will be monitored to determine if new bone is formed.

National Institute on Neurological Disorders and Stroke (NINDS)

NINDS is supporting a clinical protocol that receives biospecimens from patients with multiple sclerosis who have received autologous hematopoietic stem cells. The NINDS intramural researchers perform immunological analysis on the specimens to elucidate mechanisms of treatment action.

Senator HARKIN. That'd be good. I'd appreciate that.

Well, that's good. I enjoyed this session very much.

As you know, Dr. Collins, I have always, in the past, tried to have sessions with each of the Directors of the Institutes. However, because of some added responsibilities I have this year, now, I—my time is being crunched a lot, and I can't do that right now. I am hopeful, though—and I say this for the record—that sometime during this year, when I find some space opened up a little bit, that I might ask Mr. Fatemi and Ms. Taylor to also see if we can

pull this together again, where I can set up a few days and have three or four down at a time, and sit down, because it's very enlightening. It's better than reading Scientific American, so, I just want you to know that I'm contemplating that. I hope I can do that, at some point yet during this calendar year.

Dr. COLLINS. All of us at NIH would love that opportunity, Senator, and we do appreciate the many heavy loads that you're carrying this year, and your strong support of medical research.

ADDITIONAL COMMITTEE QUESTIONS

Senator HARKIN. Thank you.

And congratulations, again, on taking over the reins, and we're looking forward to working with you on this terrible budget crunch that we have.

Thanks, Dr. Collins.

Dr. COLLINS. Thank you, Senator.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED BY SENATOR TOM HARKIN

MEDLINE PLUS

Question. Dr. Collins, I am pleased at the importance you have placed on communicating to the American public about the valuable work done at NIH. As you may know, it was this subcommittee that first called on the National Institutes of Health (NIH) several years ago to start a magazine that would go directly to consumers to help people take charge of their health and provide reliable up-to-date information directly from the experts at NIH. What can be done to make sure that this NIH MedlinePlus magazine and its bilingual counterpart, NIH MedlinePlus Salud, gets out to every doctor's office and federally funded health center? Do you have the resources to do this?

Answer. The NIH MedlinePlus magazine is the gold standard of reliable, up-to-date health information in plain language and in a reader-friendly format. I share your enthusiasm for it and its bilingual edition, the NIH MedlinePlus Salud, which is in both Spanish and English. As you know, the magazine contains no advertising and is produced through a partnership between NIH, particularly National Library of Medicine (NLM), and the Friends of the National Library of Medicine. The magazine is distributed through community health centers, hospital emergency rooms, physicians' offices, libraries, and other locations where the public receives health services and health information. Specific issues or sections of issues are also used for targeted health education and disease prevention campaigns. At its current budget level, NLM is able to support printing and distribution of an average of 260,000 copies of each issue of the English version. To date, private sector support has allowed printing and distribution of about 100,000 copies of the Spanish version. Both versions are now available online at: http://www.nlm.nih.gov/medlineplus/magazine/.

To increase distribution of the magazines, we are working to extend our partnership to include other Government agencies and private organizations that have an interest in supporting the distribution of health information from NIH to their respective constituencies and audiences. For example, the Peripheral Arterial Disease Coalition and the American Diabetes Association supported the distribution of additional copies of two 2009 issues. The National Alliance for Hispanic Health supported the production and distribution of the first two issues of NIH MedlinePlus Salud. The NIH and the NLM will continue to encourage partnerships with other public and private organizations in an effort to ensure that this publication reaches the widest possible audience, every doctor's office, and every federally funded health center in America.

AMERICAN RECOVERY AND REINVESTMENT ACT (ARRA)

Question. NIH received $10.4 billion in ARRA—roughly $5 billion a year in fiscal years 2009 and 2010. That money is about to run out. How do you achieve the soft-

est possible landing in fiscal year 2011? What are some of the challenges you will face?

Answer. The $10.4 billion in ARRA for NIH has resulted in more than 15,000 grants and contracts to date, with more expected by September 30, 2010. These funds have served as a catalyst for inspiring innovative biomedical research in many areas of science relevant to health and disease.

With regard to ensuring the softest possible landing beyond fiscal year 2011, NIH has taken steps to limit reliance on ARRA funding. From the outset, we decided to use these funds primarily for one-time expenditures, special equipment, construction, innovative grants, and special projects, which could either be advanced or completed within 2 years. NIH also anticipated that some of the ARRA grantees who were awarded 2-year grants in fiscal year 2009 would seek continued funding in fiscal year 2011. These applications will be among those considered in the regular NIH competitive grant review process.

The nature and pace of science is often unique to each research question. We expect a staggered increase in applications over the next few years resulting from the completion of the ARRA awards. Success rates of applicants may potentially be affected by gradual increases in application submission rates. NIH will continue to support applications that are rated by peer-reviewers to be meritorious and which address the programmatic priorities of the NIH Institutes and Centers.

GRANT RESTRICTIONS

Question. Dr. Collins, in a January 2010 interview in The Chronicle of Higher Education, you suggested that universities are "becoming too reliant on NIH money, allowing faculty members to obtain all their income from Federal research grants." You said that when faculty members run multiple research projects at the same time, "that turns that investigator into a grant-writing machine perhaps more than a doing-of-science machine." You added that any new restrictions on NIH grants "would have to be phased in over a fairly long period of time because many universities and faculty members would find that quite disruptive." What sorts of changes to the NIH grant system are you envisioning for the future? Would you favor limits on the number of grants scientists could receive simultaneously from NIH? If faculty members should not expect to obtain all their income from Federal research grants, what other sources could supply the funds?

Answer. Over the past several years, the NIH has supported an increasing number of extramural research projects; ARRA provided additional support to expand and accelerate these efforts. In the upcoming and future years, we expect to see a higher number of applications for extramural awards, which could increase competition for the limited resources available. Given this, it simply may not be sustainable to have a large number of investigators deriving all or most of their salary from NIH grants. But before making any changes to our grants policy, we need to carefully explore alternatives and seek input from the relevant stakeholder groups and from the subcommittee. Any recommended changes would then have to be phased in over a period of time, as universities and researchers would find rapid change disruptive to the health of the American biomedical research community.

QUESTIONS SUBMITTED BY SENATOR DANIEL K. INOUYE

LOWELL P. WEICKER CONFERENCE ROOM

Question. I understand that you are considering dedicating a conference room in the National Institutes of Health (NIH) Neuroscience Research Center to Lowell P. Weicker. I greatly appreciate your commitment to preserving the honorable recognition of Governor Weicker and respectfully request an update on the status of the dedication of the conference room?

Answer. NIH intends to dedicate a conference room to honor Senator Weicker's legacy of contributions to the advancement of human health through research. We anticipate the dedication to take place soon after the Porter Neuroscience Research Center phase II project is completed. The Porter Center, which is being built on the western portion of NIH's Bethesda campus with funding from the American Recovery and Reinvestment Act (ARRA), is scheduled to be completed in 2013. We will keep the Senate apprised of the specific plans for the dedication as the building's completion date approaches.

NURSING RESEARCH

Question. Senator Burdick and I were instrumental in the establishment of the National Institute for Nursing Research (NINR) and for 25 years NINR has been

dedicated to improving the health and healthcare of Americans through the funding of nursing research and research training Since it was established, NINR has focused on promoting and improving the health of individuals, families, communities, and populations. How does the NIH plan to further expand this critical arm of research?

Answer. NINR supports clinical and basic research that develops knowledge to: build the scientific foundation for clinical practice; prevent disease and disability; manage and eliminate the symptoms caused by illness; enhance end-of-life and palliative care; and train the next generation of nurse scientists. In order to expand these vital areas of research at NIH, the President's fiscal year 2011 budget requests $150,198,000 for NINR, a 3.2 percent increase more than fiscal year 2010.

In fiscal year 2011, NINR will build upon the important scientific research advances the Institute has supported more than its 25-year history. For example, NINR research in health promotion and disease prevention will explore strategies to understand and promote behavioral changes in individuals; evaluate health risks within communities; and explore biological factors that underlie susceptibility and mediate disease risk. To improve quality of life for those with chronic illness, NINR will continue to support symptom management research to illuminate the biological and behavioral aspects of symptoms such as pain, insomnia, and fatigue, and to enhance the ability of patients to manage their own conditions. NINR's end-of-life and palliative care program supports science to improve the understanding of the needs of dying persons, their families, and caregivers by examining such topics as the alleviation of symptoms; psychological care; advance directives; spirituality; and family decisionmaking. NINR training programs will ensure ongoing advancements in science and improvements in health through the support and development of an innovative, multidisciplinary, and diverse scientific workforce. In addition, across all of its research programs, NINR will continue its commitment to promoting health equity and eliminating health disparities in at-risk and underserved populations through the development of culturally appropriate, evidence-based interventions.

Finally, NINR will continue to support basic and clinical research to develop the scientific basis for clinical practice. These efforts will promote the translation of research into practice; assess cost-effectiveness of clinical interventions; improve the delivery, quality, and safety of clinical care; and establish the foundation of evidence-based practice. Evidence-based practice is essential to ensuring that all Americans receive the highest-quality, most-efficient healthcare. It is NINR's emphasis on clinical research that places NINR in a position to make major contributions to the NIH Director's goals for translating basic research to clinical practice, supporting science to enable better healthcare, and reinvigorating the biomedical workforce.

ALLIED HEALTH SCHOOLS IN REMOTE COMMUNITIES

Question. At my request, the University of Hawaii at Hilo established the College of Pharmacy. The College of Pharmacy's inaugural class of 90 students began in August 2007, will graduate in 2011, and will hopefully stay in Hawaii to meet the growing demand for pharmacists. Historically, Hawaii's youth interested in becoming Pharmacists would travel to the mainland for school, and not return. It is my vision that the people of Hawaii will have educational opportunities in the health professions that will in turn increase access to care to residents in rural and underserved communities. Has there been any consideration of focusing research efforts on the benefit of establishing schools of allied health in remote communities to meet the growing needs for healthcare and improve access to care in rural America?

Answer. Allied health education is an important part of the U.S. rural healthcare infrastructure. Allied health professionals form a vital part of the healthcare infrastructure necessary to support ambulatory, pharmacy and institutional primary and preventive care, yet the complement of allied health training and subsequent rural practice choices are limited. Several studies have highlighted the gross deficiencies in the health status of those living in rural areas, as well as the disparities in the distribution of health resources. Allied health education is offered in approximately 2,000 widely dispersed rural locations. Of significance, from a health policy perspective is the realization that primary healthcare profession shortage designation areas significantly lack allied health training education and resources. These concerns have served as a catalyst for the National Center on Minority Health and Health Disparities (NCMHD) and other Federal partners such as Health Resources and Services Administration to develop new directions for rural health research and workforce studies.

Research indicates that targeted expansion of allied health training resources in rural underserved areas might improve the healthcare infrastructure, enhance ac-

cess to care, and provide career opportunities for residents of rural areas. NCMHD will continue to support a rural health research agenda as part of its activities. This includes collaborative efforts to address the distribution of allied health professions training and workforce distribution, providing research infrastructure and capacity for rural-based institutions to support allied health education training and meet NIH's goal of developing scientific resources for disease prevention. Future research will be able to identify the optimal mix of allied health professionals necessary to support healthier rural communities.

CHRONIC KIDNEY DISEASE

Question. Hawaii experiences a higher than average rate of Chronic Kidney Disease (CKD) with 1 person in 7, compared to a national average of 1 person in 9, afflicted with this disease. Among the Asian/Pacific Islander (API) population groups, Filipinos have one of the highest rates of incidence per capita. National Kidney Foundation of Hawaii in 2007 it is estimated that of the 156,000 residents with CKD, approximately 32 percent are Filipino. Has there been any consideration to focusing research efforts on preventing chronic kidney disease among the API population groups?

Answer. The National Kidney Disease Education Program (NKDEP) is an initiative of the National Institutes of Health that is designed to reduce the morbidity and mortality caused by chronic kidney disease (CKD) and its complications. NKDEP works to reduce the burden of CKD and focuses its efforts on those communities most affected by the disease including African Americans, American Indians, and APIs.

In 2008, the NKDEP initiated the Community Health Center (CHC)–CKD Pilot to identify effective strategies or improving detection and treatment of chronic kidney disease in community health centers—critical primary care settings for many people at increased risk for CKD. The pilot involves a small group of centers in the Northeast that work together to design, implement, and monitor performance improvements related to CKD. NKDEP is currently developing plans to broaden the pilot project nationally and will use data from the pilot phase pilot and lessons learned to inform this expansion. CHCs in Hawaii would be appropriate participants in this effort. Representatives from NKDEP have been in contact with Hawaii State Representatives and the Hawaii National Kidney Foundation since March 2008 and have provided technical assistance on how NIH resources could potentially be utilized to reduce the burden of chronic kidney disease among Hawaiians.

HEPATITIS B

Question. Hepatitis B and liver cancer, as caused by the hepatitis B virus (HBV), are the single greatest health disparities affecting the API populations in the United States. While up to 14 percent of the API population is infected with HBV, only 0.4 percent of the Caucasian-American population is infected. Asian Americans, native Hawaiians, and APIs comprise more than half of the 2 million estimated HBV carriers in the United States and consequently have the highest rate of liver cancer among all ethnic groups. Has there been any consideration of focusing research efforts on preventing HBV in APIs and other groups disproportionately affected by HBV?

Answer. The NIH supports research and education activities focusing on groups that are disproportionately affected by HBV. For example, the multi-center Hepatitis B Research Network, established in 2008, aims to advance understanding of disease processes and natural history, as well as to develop effective approaches to treating and controlling HBV. The network includes 21 clinical sites across the United States, including Hawaii, and a central data coordinating center. The network's centers are in the final stages of planning several clinical trials in both adults and children. Recognizing the health disparities affecting the API populations, the network plans to conduct trials testing antiviral therapy in these particularly at-risk groups. In another at-risk population, the NIH is conducting studies on the use of antiviral therapy during pregnancy to prevent the spread of HBV from a chronically infected mother to her newborn. The network will enroll pregnant women with HBV into clinical studies to assess risk factors associated with reduction in maternal-infant transmission.

Research to develop new classes of drugs that are safe and effective in treating HBV infections is essential to effectively addressing HBV disparities. It is also critical to study how HBV develops resistance to new classes of drugs. For example, in studies conducted in nonhuman primates, NIH scientists and their colleagues determined that the replication rate for HBV is higher than previously thought. A higher replication rate increases the frequency of HBV genetic mutations, including

those mutations that cause the virus to become resistant to drugs. This finding may help enhance the ability to predict when HBV virus will develop drug resistance which, in turn, will inform the use of existing antiviral therapies, including the use of a single antiviral drug versus combination therapies. NIH-funded researchers also discovered that selective combinations of existing drugs (nucleotides and nucleosides) may work better together not only to inhibit the emergence of mutated strains, but also to do a better job of reducing circulating virus.

A workshop, arranged by NIH together with the U.S.-Japan Cooperative Medical Sciences Program and the Asia Pacific Association for the Study of Liver, was held in Hong Kong in February 2009. Its purpose was to understand the issues related to antiviral drug resistance encountered in the treatment of HBV infected patients in the countries of the Asia-Pacific region. Issues discussed included determining the extent and burden of resistance in Southeast Asia, which has the highest prevalence and incidence of HBV infection worldwide. Other issues discussed were the need for databases to catalogue and track virus mutations associated with resistance; to track patient management; and to study correlations between treatment and clinical outcome.

Other NIH-supported basic and clinical research holds promise for populations disproportionately affected by HBV. For example, currently licensed antiviral drugs for HBV target a single step in the viral replication cycle. As resistance with this class of drugs seems inevitable, NIH-supported investigators, through partnership initiatives and investigator-initiated proposals, are redirecting their research to novel targets in the replication cycle and are pursuing the development of different classes of drugs. Other studies are ongoing to explore host responses to HBV infection, how the virus spreads in the liver, the influence of viral inoculum on outcome, and the cascade of host responses leading to chronicity or resolution.

There are ongoing efforts to promote coordination and planning of all HBV research within NIH and across the Department of Health and Human Services. Strategic plans, such as the trans-NIH Action Plan for Liver Disease Research (http://liverplan.niddk.nih.gov) and the plan produced by the National Commission on Digestive Diseases (http://NCDD.niddk.nih.gov), were developed with trans-NIH and trans-DHHS input, and highlight important research goals relevant to controlling HBV. In 2008, NIH convened a Consensus Development Conference on the Management of Hepatitis B. The conclusions of this conference can be found at the following Web site: (http://consensus.nih.gov/2008/hepbstatement.htm). The NIH is also providing expert input on the HHS Viral Hepatitis Interagency Working Group to coordinate the responses to the challenges described in the recent Institute of Medicine report on HBV and liver cancer.

In addition to research activities, the National Digestive Diseases Information Clearinghouse provides educational materials for the public on HBV to improve knowledge and awareness (available at: http://digestive.niddk.nih.gov/diseases/pubs/hepatitis/index.htm). Materials on HBV are available in several languages, which include Chinese, Korean, Vietnamese, and Tagalog. There is a new series of fact sheets focusing on hepatitis B-related issues affecting API.

DIABETES

Question. One of the gravest threats to the healthcare system is the chronic disease of diabetes with its impact on both the economy and on the quality of life for nearly 24 million Americans. In Hawaii, Native Hawaiians have more than twice the rate of diabetes as Whites and are more than 5.7 times as likely as Whites living in Hawaii to die from diabetes. Education and prevention are essential to controlling this serious, costly, and deadly disease. What innovative research efforts have been considered to improve diabetes outcomes and prevent diabetes?

Answer. NIH research has helped to significantly increase the life expectancy of people with diabetes and led to the development of a proven method to help prevent or delay the most common form of the disease, type 2 diabetes. For example, the landmark Diabetes Prevention Program (DPP) clinical trial demonstrated that a lifestyle intervention aimed at modest weight loss achieved a 58 percent reduction in diabetes rates among people at risk in a 3-year trial. The intervention was effective in both men and women and in all ethnic groups tested and was especially effective in older participants. Results published since the original findings have shown that the intervention remains effective for at least 10 years. In addition to reducing rates of diabetes, the intervention also led to improved blood pressure and lipid levels with less use of medications. The study included a site in Hawaii.

To develop lower cost methods to deliver the DPP intervention to the 57 million Americans with pre-diabetes who could benefit, the NIH has vigorously pursued DPP translational research. One innovative NIH sponsored study tested a group

lifestyle intervention, modeled after the DPP's, that is delivered at YMCAs. This approach yields a sharp reduction of cost per patient, and appears to be achieving excellent interim results. Importantly, YMCAs are located throughout the United States, including in many communities at high risk of type 2 diabetes. For example, the State of Hawaii is home to 17 YMCA branches. A fully national implementation of these methods would have the potential to affect diabetes treatment for Native Hawaiians in significant ways. Because of the excellent results achieved in this program to date, the Centers for Disease Control and Prevention (CDC) is planning to expand it to 10 more YMCA locations around the country. Similarly, the United Health Group, a private insurer, has announced plans to pay for its subscribers in six cities who are at risk of diabetes to receive at no charge a YMCA-based diabetes prevention intervention modeled on the program. These are outstanding examples of the adoption of evidence-based prevention methods to alleviate a serious national healthcare problem.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is also sponsoring a major multi-center trial to study the effects of lifestyle change and weight loss on the course of type 2 diabetes. Exciting preliminary results at 4 years have shown improved diabetes control and reductions in cardiovascular disease risk factors despite less use of medication. As with the DPP, the study includes a substantial representation of minority groups disproportionately affected by type 2 diabetes. To build on the findings from major NIH-supported trials that have transformed diabetes care by establishing therapies that reduce diabetes complications and premature mortality, ongoing studies are examining translation of these approaches into communities at risk. One such research effort is employing community health workers in American Samoa, where diabetes rates are 3-fold higher than in the U.S. mainland, to test methods for delivering care there, as informed by results from previous NIH studies.

It is particularly important to understand how diabetes is affecting children in America. The SEARCH for Diabetes in Youth study, a joint program of the CDC and the NIH, is collecting data on the incidence and prevalence of type 1 and type 2 diabetes in young people of diverse ethnicity, and thus is providing information to better understand the diabetes disparity among young APIs as well as other groups. One SEARCH center, located at the Kuakini Medical Center in Honolulu, will help provide the most accurate statistics to date on childhood diabetes in Hawaii. The National Diabetes Education Program (www.ndep.nih.gov), another joint effort of NIH and CDC, distributes educational materials conveying the vital health messages that have come from the major NIH-sponsored diabetes studies. Many of these materials have been translated into a wide array of languages, including the Pacific Island languages of Chamorro, Tagalog, Tongan, Chuukese, and Samoan, as well as Japanese, Indonesian, and other languages of the Pacific Rim. These programs are helping to extend the benefit of NIH diabetes research to people of diverse ethnicity in the United States and throughout the world.

COLLABORATIVE CANCER RESEARCH

Question. What is the status of the administrations' efforts to continue collaborative cancer research and program efforts focused on reducing cancer health disparities in native Hawaiians?

Answer. The administration's efforts to continue collaborative cancer research and program efforts focused on reducing cancer health disparities in Native Hawaiians are exemplified in a number of community-based participatory research programs supported by the Center to Reduce Cancer Health Disparities of the National Cancer Institute (NCl/CRCHD). These include:

Community Networks Program (CNP)

This program was recently renewed and the new CNP centers initiative (RFA–CA–09–032) extends the previous efforts of NCI to support community-based participatory research (CBPR) in racial and ethnic minorities and other underserved populations. The goals of the CNP Centers are (1) to develop and perform evidence-based intervention research to increase use of beneficial biomedical and behavioral procedures for cancer prevention, detection and treatment, which may include related co-morbid conditions; and (2) to train and promote the development of a critical mass of competitive new researchers using CBPR to reduce health disparities. This program and its predecessors have promoted and continue to promote CBPR-based cancer health disparities research. As part of the current NCl/CRCHD CNP, NCI supports two projects aimed at reducing cancer health disparities in native Hawaiian populations.

The 'Imi Hale Native Hawaiian Cancer Network is aimed at reducing cancer incidence and mortality among native Hawaiians by maintaining and expanding an in-

frastructure that: (1) promotes cancer awareness within native Hawaiian communities; (2) provides education and training to develop native Hawaiian researchers; and (3) facilitates research that aims to reduce cancer health disparities experienced by native Hawaiians. 'Imi Hale is housed at Papa Ola Lkahi, a nonprofit native Hawaiian community-based agency in Honolulu, is dedicated to improving native Hawaiian health and well being. They collaborate with key partners at the community, State, and national levels. Examples of clinical partners are the five Native

Hawaiian Health Care Systems (NHHCS, providing access and prevention services to Native Hawaiians on the State's seven inhabited islands), the Queen's Medical Center, and Breast and Cervical Cancer Control Program. Examples of program partners include CIS, ACS, and Hawaii Primary Care Association. Examples of educational and research partners include the University of Hawaii, Oregon Health and Sciences University, and the NHHCS IRB.

Weaving an Islander Network for Cancer Awareness, Research, and Training (WINCART) is a community-academic consortium employing CBPR to reduce preventable cancer incidence and mortality among five API communities in southern California. The specific aims of WINCART are to: (1) identify individual, community, and health service barriers to cancer control among APIs; (2) improve access to and utilization of existing cancer prevention and control services; (3) facilitate the development, implementation, and evaluation of community-based participatory research studies; (4) create opportunities to increase the number of well-trained API researchers through training, mentorship, and participatory research projects; (5) sustain community-based education, training, and research activities by increasing partnerships with governmental and community agencies, funders, and policy makers; and (6) disseminate research findings to aid in the reduction of cancer health disparities for APIs. Project methods include implementation and evaluation of community awareness activities in each API population; conducting cancer prevention and control research; and recruitment/training/mentorship of API researchers.

Basic Research in Cancer Health Disparities (R21/U01)

Two new NCI-supported funding opportunities, PAR09–160 and PAR09–161, have been developed to encourage basic research studies to determine whether there are biological causes and mechanisms of cancer health disparities and support the development of a nationwide cohort of scientists with a high level of basic research expertise in cancer health disparities research. PAR09–160 will focus on the development of resources and tools, such as racial/ethnic specific biospecimens, cell lines and methods that are necessary to conduct basic research in cancer health disparities. PAR09–161 will provide an avenue for entry into cancer disparities research through collaboration and association with researchers with specific expertise in emerging technologies in cancer research.

Minority Institution/Cancer Center Partnership (MI/CCP)

The MI/CCP program supports a partnership program that promotes research in cancer health disparities. The University of Guam (UOG), and the Cancer Research Center of Hawaii (CRCH), an NCI-designated cancer center at the University of Hawaii at Manoa, have been engaged in a unique and successful partnership over the past 6 years to establish a Cancer Research Center of Guam on the campus of UOG, to increase number of faculty and students engaged in cancer research at UOG, and to increase the number of faculty from CRCH addressing issues of particular relevance for cancer health disparities in the Hawaii/Pacific region.

CANCER PREVENTION

Question. How will the NIH continue to support an infrastructure that has identified and mentored more native Hawaiian researchers in cancer prevention and control than any other institution has done in the past 20 years?

Answer. NIH is committed to enhancing workforce diversity within the research enterprise, and as part of that effort, seeks to support infrastructures that recruit and retain a strong cadre of competitive researchers from diverse backgrounds working in cancer prevention and control. Within NCI, there are a number of current activities that will continue to support an infrastructure to train and mentor native Hawaiian and other Pacific island cancer researchers. Examples of programs within NCI's CRCHD that support training infrastructure for native Hawaiians include:

MI/CCP

The NCl/CRCHD supports a partnership program between minority serving institution partners and a NCI-designated cancer center to foster training and research activities. For example, the newly awarded 5-year U54 University of Guam and the

University of Hawaii at Manoa MI/CCP partnership has a well-established infrastructure for mentoring of Hawaiian and Guamanian researchers in cancer research as part of their diversity training program.

CNP

The goal of the NCl/CNP program is to develop and increase capacity building in support of community-based participatory education, research and training to reduce cancer health disparities. The program has increased the development of a cadre of new investigators, including among native Hawaiian researchers, in the field of cancer health disparities research. To date, a total of 34 native Hawaiians have been trained, representing 7 percent of the total CNP trainees. The CNP native Hawaiian trainees have submitted 40 grant applications and a total of 12 were funded for a 30 percent success rate. Building on the success of the CNP program, the new 5-year CNP centers program has been established, and will continue to support infrastructure for diversity training.

Promote Workforce Diversity (PAR–09–162)

The Exploratory Grant Award to Promote Workforce Diversity in Basic Cancer Research (PAR–09–162) supports underrepresented minorities, such as native Hawaiians, in basic cancer research. Through this funding opportunity, NCI encourages institutions to diversify their faculty populations, and increase the participation of individuals currently underrepresented in basic cancer research, such as individuals from underrepresented racial and ethnic groups, individuals with disabilities, and individuals from socially, culturally, economically, or educationally disadvantaged backgrounds that have inhibited their ability to pursue a career in health-related research.

Continuing Umbrella of Research Experiences (CURE)

The ongoing CURE program offers unique training and career development opportunities to enhance diversity in cancer and cancer health disparities research. With a focus on broadening the cadre of underrepresented investigators engaging in cancer research, the ongoing CURE program identifies promising candidates from high school through junior investigator levels and provides them with a continuum of competitive funding opportunities. Today, there are 30 CURE supported trainees and 14 high school and undergraduate students who are native Hawaiians.

Diversity Supplements

These diversity supplements are designed to foster diversity in the research workforce. These supplements support and recruit students, postdoctoral, and eligible investigators from groups shown to be underrepresented in biomedical research. Currently, two native Hawaiian junior investigators are supported by diversity supplements.

NCI Community Center Centers Program (NCCCP)

The NCCCP is designed to create a community-based cancer center network to support basic, clinical, and population-based research initiatives, addressing the full cancer care continuum—from prevention, screening, diagnosis, treatment, and survivorship through end-of-life care. The NCCCP pilot has added the Queen's Medical Center, Honolulu, Hawaii (The Queen's Cancer Center) to its 30-hospital network.

Cancer Health Disparities Geographic Management Program (GMaP)

GMaP, a new initiative, is developing transdisciplinary regional networks dedicated to the coordination and support of cancer health disparities research training and outreach using regional management approach. Creating sustainable partnerships among institutions and agencies involved in cancer health disparities research and cancer care, this initiative seeks to advance cancer health disparities, diversity training and ultimately, contribute to disparities reduction. A companion program, the Biospecimen/biobanking Management Program, will support research and training infrastructure specific to biospecimen collections among underrepresented populations across the country.

CANCER RESEARCH

Question. How will NCI support entities like 'Imi Hale, who engage Hawaiian communities in identifying and addressing cancer health disparities and invest in building community capacity to mobilize local resources and train local staff? The mission of the NCI CRCHD is to reduce the unequal burden of cancer in our society and train the next generation of competitive researchers in cancer and cancer health disparities research.

Answer. The NCI's CRCHD coordinates multiple programs that focus on community based participatory cancer disparities research and multi-institution collaborations to reduce the unequal burden of cancer and train the next generation of competitive cancer researchers. These programs include CNP, Patient Navigation Research Program (PNRP), MI/CCP, and CURE. All of the following programs are either in Hawaii or extend to native Hawaiians and address cancer health disparities and community building among Hawaiian communities.

CNP

The NCl/CRCHD CNP builds capacity in community-based participatory research, educational outreach, and professional training through partnerships with community organizations and institutions working with multiple racial/ethnic and underserved populations, including Hawaiian populations. The goal of the program is to improve access to beneficial cancer interventions and treatment in communities experiencing significant cancer health disparities. Currently, the NCI is supporting 25 CNP projects developing programs to increase the use of cancer interventions in underserved communities. Interventions include proven approaches including smoking cessation, increasing healthy eating and physical activity, and early detection and treatment of breast, cervical, and colorectal cancers.

Each CNP has put together an advisory group that serves as the "voice of the community." These advisory groups work with local community members to gather information and then deliver back results. A steering committee of community-based leaders, researchers, clinicians and public health professionals provides additional support.

To sustain successful efforts in their communities, CNP grantees work closely with policymakers and nongovernmental funding sources. Together, CNP grantees and NCI train investigators, identify potential research opportunities, and work to ensure that best practice models are widely disseminated.

MI/CCP

MI/CCP is designed to: (1) increase Minority Serving Institutions participation in cancer research and research training and (2) increase the involvement and effectiveness of NCI-designated Cancer Centers in developing effective research, education, and outreach programs to encourage diversity among competitive researchers and reduce cancer health disparities. These partnerships foster and support intensive collaborations to develop stronger cancer programs aimed at understanding the reasons behind significant cancer health disparities among racial and ethnic minority and socioeconomically disadvantaged populations. NCI supports grants under this program that establish such a partnership program in Hawaii.

The NCl/CRCHD supports a partnership program with UOG and CRCH, an NCI-designated cancer center at the University of Hawaii at Manoa. Engaged in a unique and successful partnership over the past 6 years, this program has established a Cancer Research Center of Guam on the campus of UOG to (1) increase the number of faculty and students engaged in cancer research at UOG; (2) increase the number of minority scientists of API ancestry engaged in cancer research, and providing pertinent undergraduate, graduate, and postgraduate education and training opportunities for API students; (3) further strengthen the research focus at CRCH on cancer health disparities with particular emphasis on aspects of particular relevance for the people of Hawaii and the Pacific; and (4) enhance the awareness of cancer and cancer prevention and, ultimately, to reduce the impact of cancer on the population in the Territory of Guam, the other U.S.-associated Pacific island territories, and Hawaii.

CURE

The CURE program is a strategic approach for training a diverse generation of competitive cancer researchers. The CURE provides educational support to students and junior investigators from high school through postdoctoral studies and mentors them in the early phases of their careers in cancer research. This approach builds on the success of the research supplements to promote diversity and strategically addresses each level of the biomedical research and education pipeline to increase the pool of researchers from underserved populations. There are currently 14 high school and undergraduate students being supported by a CURE supplement in Hawaii.

Diversity Supplements

These research supplements are designed to foster diversity in the research workforce. They support and recruit students, postdoctoral, and eligible investigators from groups shown to be underrepresented in biomedical research. There are currently two junior investigators being supported by diversity supplements in Hawaii.

NCCCP

Another program within NCI addressing health disparities is the NCCCP program. The NCCCP is designed to create a community-based cancer center network to support basic, clinical and population-based research initiatives, addressing the full cancer care continuum—from prevention, screening, diagnosis, treatment, and survivorship through end-of-life care. The NCCCP has seven major focus areas to: (1) improve access to cancer screening, treatment, and research; (2) improve quality of care at community hospitals; (3) increase participation in clinical trials; (4) enhance cancer survivorship and palliative care services; (5) participate in biospecimen research initiatives to support personalized medicine; (6) expand use of electronic health records and connect to cancer research data network; and (7) enhance cancer advocacy.

Reducing and eliminating cancer disparities continues to be a major commitment for NCI, the research community, healthcare providers and policymakers. In recent years, the cancer research community has also begun to focus on understanding why members of some population groups experience higher cancer incidence and mortality rates than others.

CANCER RESEARCH

Question. Hawaiian researchers have been very effective in addressing the unequal burden of cancer among native Hawaiians; however Hawaiian researchers are not equally represented in the researcher pool. How will the administration demonstrate its long-term commitment to programs like 'Imi Hale that address disparities at all levels and identify, mentor, and provide research training, fellowships and grant opportunities to native Hawaiians interested in cancer research?

Answer. The NIH continues to promote its diversity programs to underrepresented individuals at the college, graduate school, postdoctoral, and faculty stages of a scientist's career. Native Hawaiians are a key target group within these programs. Examining NIH's efforts in its formal research training programs at the pre- and postdoctoral levels, the most recent data from 2007 are encouraging regarding native Hawaiians and APIs. They show that 4 percent of NIH trainees self-identified as native Hawaiian and APIs, which is higher than the proportion of this group in the total U.S. population.

The challenge is to retain and sustain these individuals as they transition into their independent research careers. NIH has several key programs in place that are aimed at addressing this challenge. Specifically, CNP (http://grants.nih.gov/grants/guide/rfa-files/rfa-ca-09-032.html) is designed to support community-based participatory research in underserved populations and provide a training venue for preparing a new cadre of scientists to address health disparities research. Second, new initiatives in research in cancer health disparities (http://grants.nih.gov/grants/guide/pafiles/PAR-09-160.html and http://grants.nih.gov/grants/guide/pa-files/PAR-09-161.html) are also designed to provide a venue for young scientists to prepare for careers in health disparities research. MI/CCP between the University of Hawaii and UOG, and community-based programs, including the 'Imi Hale Native Hawaiian Cancer Network supported by the NCI, are dedicated to health disparities research in the Hawaii and Pacific region.

Finally, native Hawaiians and APIs are encouraged to apply for the Diversity Supplement to Research Grants Program (http://grants.nih.gov/grants/guide/pa-files/PA0908190.html) both on the Mainland and in Hawaii. This program has supported more than 500 APIs at stages of their careers ranging from college education to faculty research scientists. NIH intends to continue its support for all of these programs.

TUBERCULOSIS

Question. Dr. Collins, thank you for your continuing leadership on biomedical research issues. I would like to turn for a moment to tuberculosis (TB), one of the oldest diseases known to mankind. As you know, TB continues to impact millions of people around the world, including in my home State of Hawaii, which has the highest rates of TB in the Nation: 128 cases in 2008 or a rate of 9.6 per 100,000 Hawaiians. Further, complicating this already serious situation is the 20 percent increase Hawaii has experienced in the more difficult and expensive to treat multidrug resistant forms of TB, in part because of the decades that have passed since new treatments have been developed. Could you give me an overview of the research initiatives NIH is currently undertaking to address the drug resistant forms of TB.

Answer. TB research at NIH is primarily conducted and supported by the National Institute of Allergy and Infectious Diseases (NIAID). Through grants and

other mechanisms and through its intramural research program, NIAID supports a globally relevant TB research agenda. NIAID TB research is focused on all aspects of TB, including drug-susceptible and drug-resistant TB, as well as TB in HIV co-infected persons. NIAID-sponsored basic TB research includes studies to better understand the biology of TB and the host-pathogen interaction, including latent TB infection in human hosts and in animal models of infection and disease. NIAID-supported translational and clinical research is focused on the identification and development of new diagnostics, drugs, and vaccines. To better understand TB in special populations, NIAID's research agenda includes studies of TB in children and immune suppressed persons as well as studies to clarify the interaction of HIV and TB to improve TB prevention and treatment. To date, NIAID's investment in basic, translational, and clinical science has led to the development of several new candidate TB drugs, diagnostics, and vaccines. In addition, the NIAID developed a research agenda in fiscal year 2008, the NIAID Research Agenda for Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis (MDR/XDR–TB), to complement and leverage ongoing efforts and focus on specific research gaps for MDR/XDRTB.

Specific NIAID research activities include the following:

Research on the pharmacological basis of drug resistance in infectious diseases.

—Studies to characterize drug-resistant TB strains, their epidemiology and their impact on disease progression, host immune response, and response to therapy.

—An initiative in fiscal year 2010 to support targeted clinical trials to evaluate and improve the optimal use of currently existing therapies for TB and support for phase I clinical studies of new TB drug candidates.

—Intramural and extramural studies of a multitude of international basic science, translational, diagnostic, and clinical research activities to better characterize drug-resistant TB and gain insight into what specific healthcare interventions need to be developed to combat and prevent drug-resistant TB.

—Collaborations with the HIV/AIDS clinical trials networks to expand studies of drug- sensitive and drug-resistant TB as a co-infection in patients with HIV/AIDS, enhance the capacity for international clinical trials on TB, and increase efforts to combat the co-epidemics of TB and HIV.

—An intramural research program project at the South Korean Masan National Tuberculosis Hospital, which cares for the largest population of MDR–TB inpatients in the world, to study the natural history of MDR–TB and the occurrence of extensively drug-resistant TB (XDR–TB) in patients who have completely failed chemotherapy.

—Coordination of drug-sensitive and drug-resistant TB research activities with other Federal agencies through the U.S. TB Task Force, as well as with other Government and nongovernmental organizations such as the WHO/Stop TB Partnership, programs funded by the Bill & Melinda Gates Foundation, and not-for-profit product development partnerships.

UNDERREPRESENTED BIOMEDICAL RESEARCHERS

Question. For the past 19 years, the Distance Learning Center has been pioneering a new training paradigm, the STEMPREP Project, to create the next generation of researchers from native Hawaiian and other underrepresented minority students. The project provides an earlier start in the training pipeline (7th grade) to a national pool of minority child prodigies who desire a career in STEM and medicine. As we continue our efforts to reduce and ultimately eliminate the racial and ethnic health disparities that plague our healthcare system, we must support a generation of physician scientists and researchers who have the skills to develop sound public health solutions and advance public health through scientific discovery. How will the administration demonstrate its commitment to programs like the Physician Scientist Training Program that has called for an increase in the supply of biomedical researchers from underrepresented racial and ethnic minority populations?

Answer. The NIH has a history of creating and supporting policies and programs with the goal of promoting and providing a diverse workforce in the biomedical, behavioral, clinical, and social sciences. NIH programs are designed to recruit, train, retain, and develop the careers of underrepresented individuals, and every NIH research training, fellowship, career development, and research education project award Funding Opportunity Announcement explicitly States this policy. A number of programs target talented science undergraduates by providing funds for their college tuition and a stipend for living expenses to promote their pursuit of a career in biomedicine. At the doctoral level of education, the NIH awards fellowships, traineeships, and research grant supplements to individuals in support of their studies toward the research doctorate degree. At the postdoctoral level, NIH offers

fellowships, career development, and research grant supplements to promote the transition of young scientists to independent investigators.

In terms of a commitment to providing a diverse workforce in the future, the NIH continues to evaluate and explore new and creative programs to promote a diverse workforce. Most recently, the NIH has committed ARRA funds to support the NIH Director's Pathfinder Award to Promote Diversity in the Scientific Workforce (DP4) which was announced on March 5, 2010. This new research grant program encourages exceptionally creative individual scientists to develop highly innovative approaches for promoting diversity within the biomedical research workforce. The proposed research must reflect ideas substantially different from those already being pursued or apply existing research designs in new and innovative ways to unambiguously identify factors that will improve the retention of students, postdocs and faculty from diverse backgrounds in the workforce (http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-10-013.html).

New studies and grant programs are also underway to identify barriers to underrepresented individuals being incorporated into the biomedical workforce and to more effectively address those barriers. The National Institute of General Medical Sciences has launched two new research grant programs to explore the development of new interventions to improve diversity (http://grants.nih.gov/grants/guide/rfa-files/RFA-GM-10-008.html and http://grants.nih.gov/grants/guide/rfa-files/RFA-GM-09-011.html).

In addition, the Office of the Director is undertaking studies to more explicitly identify attrition points along the pathway between high school and achieving independence as a biomedical scientist. Relating this information to variables such as race, ethnicity and gender should enable NIH to target interventions more selectively and improve our ability to recruit and retain a diverse population of researchers.

QUESTIONS SUBMITTED BY SENATOR ARLEN SPECTER

CURES ACCELERATION NETWORK

Question. Moving the new authorized Cures Acceleration Network (CAN) forward is of critical importance. What would the timeline be for getting the program started if funding is provided?

Answer. If funding is provided, the first step would be to appoint CAN's advisory board and identify priority areas. After this, the National Institutes of Health (NIH) would prepare grant and contract solicitation announcements within approximately 2 months of the first board meeting. Applicants would be given 60 days to prepare applications in response to the solicitation(s). The application reviews would occur within several weeks following receipt, and awards made rapidly thereafter. Under this timetable, we would expect to disburse awards within the first year.

CLINICAL CENTER

Question. What is the current number of patients being treated at the Mark O. Hatfield Clinical Research Center in Bethesda? As the largest clinical research hospital in the world, what capacity is it? If it is not at full capacity when do you anticipate that it will be?

Answer. As of May 26, 2010, the Mark O. Hatfield Clinical Research Center has seen 17,450 patients in the inpatient and outpatient settings; approximately 38,000 inpatient days and 61,000 outpatient visits this fiscal year. The current inpatient capacity at the Mark O. Hatfield Clinical Research Center is 234 beds. A new 6-bed high containment unit that will allow us to study patients with infectious diseases is scheduled to open shortly and will increase the Center's total capacity to 240 beds.

In fiscal year 2010, the Mark O. Hatfield Clinical Research Center has been operating at an average daily census of 166 inpatients per day which represents an occupancy level of approximately 70 percent. Based on plans that the Institutes are making fiscal year 2011, we anticipate an increase in inpatient activity of approximately 2 percent more than fiscal year 2010. In addition, NIH leaders are exploring the feasibility of opening the Mark O. Hatfield Clinical Research Center to the outside research community, and discussions are underway with the NIH Scientific Management Review Board. Such a change could lead to increased utilization.

PANCREATIC CANCER

Question. Pancreatic cancer research accounts for only about 2 percent of NIH's budget, even though it is the forth leading cancer killer and has one of the lowest survival rates. What can be done to increase funding?

Answer. Since the publication of Pancreatic Cancer: An Agenda for Action in 2001, the National Cancer Institute (NCI) has expanded its portfolio of pancreatic cancer research from $21.8 million in fiscal year 2001 to $89.7 million in fiscal year 2009, an increase of more than 300 percent. During this period, the total NCI budget increased by about 30 percent; thus, the growth in the pancreatic cancer portfolio has been approximately tenfold larger than the growth in the total NCI budget. As documented in Pancreatic Cancer: Six Years of Progress in 2007, the NCI pancreatic cancer research portfolio has grown within each of the six major research priority areas identified in 2001.

In addition to an increase in funding, there have also been increases in the number of projects funded (up more than 275 percent since fiscal year 2000), unique RO1 Grant Principal Investigators funded (up more than 200 percent since fiscal year 2000), and training/career development awards (up more than 65 percent since fiscal year 2005). Part of the growth came about through planned actions and funding opportunities specific to pancreatic cancer, and part grew out of an increasingly larger pool of pancreatic cancer researchers successfully competing for general funding opportunities and unsolicited research grants.

In addition, pancreatic cancer projects were also funded through the American Recovery and Reinvestment Act of 2009 (ARRA). In fiscal year 2009, 79 pancreatic cancer-related projects received ARRA funding totaling $10.7 million. These projects include some focused on training/career development that are relevant to growing the critical mass of pancreatic cancer investigators, a group of traditional RO1 research grants, a Challenge Grant, and a Grand Opportunity or "GO" grant. The NCI Community Cancer Centers Program, a group already working on pancreatic cancer, has been further developed with ARRA funds. The ACTNOW initiative, which supports high-priority, early-phase clinical trials of new cancer treatments on an accelerated timeline includes a clinical trial addressing pancreatic cancer. Finally, The Cancer Genome Atlas project (TCGA) is using ARRA funds to rapidly increase the number of cancers covered by the project, including pancreatic cancer. ARRA has provided a unique opportunity to accelerate progress in pancreatic cancer research.

NCI has focused considerable expertise on assessing the state of the science in pancreatic cancer and developing a targeted network of pancreatic cancer experts for consultation with NCI program staff In 2006, NCI created a Gastrointestinal Cancer Steering Committee (GISC) with seven specific disease-site task forces, including one focused on pancreatic cancer. GISC members include all Cooperative Group gastrointestinal disease committee chairs, representatives from the Specialized Programs of Research Excellence (SPOREs), Cancer Center and R01/P01 investigators, along with community oncologists, biostatisticians, patient advocates and NCI staff. Through GISC, NCI convened a Pancreas State of-the-Clinical Science meeting in 2007 to discuss the integration of basic and clinical knowledge into the design of clinical trials for pancreatic cancer and to define the direction for clinical trials investigation for pancreatic cancer over the next 3 to 5 years. A Consensus Report from the meeting, published in the Journal of Clinical Oncology in November 2009, emphasized the importance of enhanced molecular targets and targeted drugs for pancreatic cancer, better preclinical models, and improved phase II studies. The GISC is an active part of NCI's programmatic development for pancreatic and other gastrointestinal cancers. The GISC' s pancreatic cancer task force provides important leadership, meeting on a monthly basis to coordinate strategy between the cooperative groups, identifying new leads to explore, and monitoring ongoing trials. Within the pancreatic cancer task force, a working group has been created to focus on development of trials for locally advanced disease. In addition, as part of the operational efficiency working group guidelines for the development of clinical trials, the pancreatic cancer task force is now operating under an accelerated timeline for the development of phase II and III clinical trials.

Finally, in response to earlier congressional language, NCI will be holding an internal meeting this summer to discuss research and training initiatives relevant to pancreatic cancer.

Question. In 2001, NCI developed a set of 39 recommendations for increasing pancreatic cancer research, including attracting more scientists to this field of study. Nine years later, only five of its own recommendations have been implemented. Over the same time period the NCI's budget has grown by more than $1 billion, so it's not a question of funds being available. Given the fact that pancreatic cancer

deaths are increasing, what concrete steps will you take to make this field of study a higher priority?

Answer. Since the publication of Pancreatic Cancer: An Agenda for Action in 2001, the NCI has expanded its portfolio of pancreatic cancer research from $21.8 million in fiscal year 2001 to $89.7 million in fiscal year 2009, an increase of more than 300 percent. During this period, the total NCI budget increased by about 30 percent; thus, the growth in the pancreatic cancer portfolio has been approximately tenfold larger than the growth in the total NCI budget. As documented in Pancreatic Cancer: Six Years of Progress in 2007, the NCI pancreatic cancer research portfolio has grown within each of the six major research priority areas identified in 2001.

A genome-wide association study to uncover the causes of pancreatic cancer, known as PanScan, has identified five important genetic regions that greatly influence the risk of developing pancreatic cancer. NCI is now focused in detail on each of these genetic risk regions. NCI is active in the Pancreatic Cancer Genetic Epidemiology Consortium, founded to examine susceptibility genes in familial pancreatic cancer.

Other initiatives include the Pancreatic Cancer Cohort Consortium, and pancreatic and GI SPOREs. In November 2009, NCI launched one of the largest phase III trials ever undertaken in pancreatic cancer (RTOG 0848), intended to enroll 900 patients to evaluate both Erlotinib and chemoradiation as adjuvant treatment.

Pancreatic cancer studies have been funded within the Cancer Nanotechnology Platform Partnerships, the Early Detection Research Network, and the Tumor Glycome Laboratories of the NIH Alliance of Glycobiologists for Detection of Cancer and Cancer Risk. NCI is collaborating with the Pancreatic Cancer Action Network (PanCAN) and the Lustgarten Foundation for Pancreatic Cancer research on the Pancreatic Cancer Research Map. This project facilitates collaborations among pancreatic cancer researchers to speed the development of national strategies, and leverage resources for pancreatic cancer research. The map provides a unified collection of pancreatic cancer research projects, funding opportunities, and investigators.

QUESTIONS SUBMITTED BY SENATOR THAD COCHRAN

SPINAL MUSCULAR ATROPHY (SMA)

Question. What role can the National Institutes of Health (NIH) play in laying the groundwork for SMA and to develop new therapies and work with the Food and Drug Administration (FDA) to support new therapies? Please update the subcommittee on what are the next steps that NIH is planning to take to prepare for, support and sustain the efforts that will be necessary up to and through clinical trials for SMA?

Answer. Due to NIH's continued investment in SMA research, including studies on disease mechanisms and preclinical/translational therapy development, the first treatments for SMA are now advancing through the therapeutic development pipeline. The NIH has taken a number of steps to continue to support development of potential treatments up to and through clinical trials.

NIH supports a variety of projects for translating basic research findings into therapies that can be tested in a clinical setting. The SMA Project, funded by the NIH and guided by experts from industry, academia, NIH, and the FDA, is an innovative, contract-based, "virtual-pharma" program to develop drugs and test them in the laboratory. The project holds two patents on two sets of compounds that show significant promise and, assuming successful preclinical testing, a phase I clinical trial to assess safety should begin in 2011. The project is also continuing to pursue other leads.

To complement the SMA project, the NIH also funds investigator-initiated therapy development projects. This year, National Institute of Neurological Disorders and Stroke (NINDS) began funding a major milestone-driven collaboration between an academic lab and a biotech company to develop a lead compound into a drug that is ready for clinical testing in SMA patients. An investigator-initiated grant funded by the National Institute of Child Health and Human Development is designed to assess the natural history of the disease and perform pilot studies to evaluate potential interventions in a broad cohort of SMA patients. Additionally, NIH has used American Recovery and Reinvestment Act (ARRA) funds to make investments in rapidly developing opportunities, including a Grand Opportunity grant on delivery of therapeutic genes for motor neuron diseases. Stem cell research relevant to SMA has also been funded, including studies of induced pluripotent stem cells derived from SMA patients.

NIH has also made a commitment to support high-quality clinical trials for SMA and other pediatric disorders. In February, the NINDS Council approved NINDS–NET, a multi-site clinical research network to expedite early phase clinical trials of therapies from academic research, foundations, or biotech companies. Because all network participants are required to have expertise in clinical trials for pediatric neurological disorders as well as adult diseases, this clinical research network provides the framework for high-quality trials for SMA and other rare disorders.

The NIH, working with SMA volunteer organizations, has organized a workshop for later this year that will focus on therapies that are approaching readiness for clinical testing, what hurdles remain, and what is needed for effective SMA clinical trials. A second workshop, organized by both the NIH and FDA, will address specifically the use of anti-sense oligonucleotides in treating neuromuscular disorders including SMA, and will provide FDA input into clinical and preclinical studies. Both of these workshops will not only facilitate communication among SMA researchers, NIH, and the FDA, but will also help the research community plan for moving therapies into clinical trials.

CROHN'S DISEASE

Question. Dr. Collins, I want to thank you and the leadership of the National Institute of Diabetes and Digestive and Kidney Diseases for advancing research on Crohn's disease and ulcerative colitis. As you know, these are extremely painful and debilitating disorders that are increasing in prevalence. Can you tell us what needs to be done to translate the remarkable genetic discoveries of recent years into better treatments for patients?

Answer. The NIH support for research on the genetics of Crohn's disease and ulcerative colitis—the two major forms of inflammatory bowel diseases (IBD)—is providing the foundation for the development of unique and effective therapies for patients who suffer from these diseases. Following the discovery of the first IBD-associated gene, the NIH established a major program in 2002—the IBD Genetics Consortium—to accelerate the discovery of genetic variants that are associated with the disease. To date, this very successful program has uncovered nearly 50 genetic variants that are associated with both major forms of IBD. Progress in this area was bolstered by recent investments from ARRA, which provided additional support for the consortium to enhance its ability to expand and develop resources. In addition, ARRA supported innovative projects to identify genetic variations that are less common amongst people with Crohn's disease and extend the success of genome wide association studies to identify genetic variations that predispose individuals from different ethnic groups to developing IBD. As researchers continue to discover additional genetic variants associated with IBD, it will be important for these advances to be translated into better treatments for patients. Through ARRA and regular appropriations, the NIH is supporting research to define the biological processes that are perturbed by genetic variants associated with IBD. In some cases, genetic variants that have limited direct associations with IBD may have significant biological consequences, and it will be important to consider these factors when developing models of disease risk. By further understanding the genetic variants associated with disease and their molecular consequences, researchers will be able to develop and validate biomarkers as indicators of disease risk, disease prognosis, and patient responses to therapies. In addition, as the biological pathways underlying IBD are better defined, researchers will identify targets for developing new therapeutics to help treat these painful and debilitating disorders.

MINORITY HEALTH

Question. How will the new data collection requirements on race and ethnicity, primary language, geographic location, and disability status affect research at NIH? How will this information be used? Are you collaborating with the existing Department of Health and Human Services, Office of Minority Health (OMH) in order to coordinate and establish an effective Government effort to address minority health issues?

Answer. The new data collection requirements will advance NIH's research-based efforts for improving the health of the Nation. The limited specificity, uniformity and quality of data collection and reporting procedures has been a significant restraint in identifying and monitoring efforts to reduce health disparities. According to a recent report by the Institute of Medicine (IOM) "Race, Ethnicity, and Language Data: Standardization for Health Care Quality Improvement, "from the Subcommittee on Standardized Collection of Race/Ethnicity Data for Healthcare Quality Improvement," consistent methods for collecting and reporting healthcare data on

racial and ethnic minorities are essential to informing evidence-based disparity reduction initiatives.

In addition, as the demographics of the United States continue to shift, it is essential to understand the diversity of the Nation based on race, ethnicity, primary language, and disability status. Collecting information on the geographic distributions of racial and ethnic populations will aid researchers in understanding how geographic location and environmental factors for example, contribute to the existence and persistence of health disparities. During the past 10 years there has been a growing appreciation of the role these factors play in health disparities. Collecting this data will assist researchers in understanding how these factors, working independently and dependently, contribute to the excess burden of disease, morbidity, and mortality experienced by racial and ethnic minorities relative to majority populations.

This enhanced data collection will be useful in clinical research, especially in Comparative Effectiveness Research, where there will be the need to collect information on these racial and ethnic subgroups to produce statistically reliable evidence-based results. Statistical oversampling of certain subpopulations in clinical comparative effectiveness research will be done as needed. In addition to improving data collection across Federal categories of race and ethnicity, information is needed on racial and ethnic subgroups. This new data collection will be critical to monitoring the health status and needs of immigrant and language minority populations. This calculates to approximately 100 different ethnic groups with populations more than 100,000 living in the United States.

Health disparities are persistent and eliminating them requires an in-depth understanding of how multiple factors—social and biological—act independently and dependently. Collecting information on race, ethnicity, primary language, disability status, and geographic location will allow researchers to better understand these factors and their interactions. Scientists will use it to design interventions tailored to meet the needs of racial and ethnic populations as a function of primary language or geographic location, or other factors.

The NIH, through the National Center on Minority Health and Health Disparities (NCMHD), has had a long-standing tradition of collaboration and coordination of minority health and health disparities activities with the HHS OMH. Over the years the NCMHD and OMH have worked collaboratively to address a number of minority health issues both domestically and internationally, as well as support several minority health initiatives with funding from some of the Institutes and Centers. Most recently, the NIH has participated in:

—The development of the HHS National Partnership Action Plan led by OMH;
—NIH is represented on the HHS Health Disparities Council which deals with minority health and health disparities issues across the HHS and for some time has been led by the OMH;
—NCMHD and OMH are collaborating on an ARRA initiative to develop Centers of Excellence for Comparative Effectiveness Research through the NCMHD Centers of Excellence; and
—NCMHD and OMH serve as two of three Federal Government co-leads for the Federal Collaboration on Health Disparities Research (FCHDR) which is aimed at enhancing wide Federal Government coordination around minority health and health disparities.

INSTITUTIONAL DEVELOPMENT AWARD (IDEA)

Question. Does the list of eligible States ever change to reflect their greater or lesser success over time in attracting competitive NIH research funding?

Answer. When Congress authorized the Institutional Development Award (IDeA) program in 1993, its intent was to promote geographic distribution of NIH funding across the United States. in order to increase the research capacity in eligible States. The eligibility to participate in the IDeA program has been evaluated on a yearly basis and the list of eligible States has not changed over the years with the exception of Alabama, which was once an IDeA eligible State that became ineligible based on its success in obtaining NIH funding. The current list of IDeA eligible States can be found on the National Center for Research Resources' (NCRR) Web site at http://www.ncrr.nih.gov/research__infrastructure/institutional__development__award/.

The current IDeA eligibility criteria are based on two components: (1) a success rate for competing research projects and centers of less than 20 percent for obtaining NIH grant awards during 2001–2005; or (2) less than $120 million average NIH funding during 2001–2005 (regardless of success rate), excluding IDeA awards and R&D contracts.

NCRR is currently evaluating whether the IDeA eligibility criteria are still appropriate to accomplish the legislative intent. As it does so, the eligibility criteria and the IDeA-eligible States will remain the same.

QUESTIONS SUBMITTED BY SENATOR RICHARD C. SHELBY

BIODEFENSE

Question. In National Institute of Allergy and Infectious Diseases (NIAID)'s Strategic Plan for Biodefense Research 2007 Update, NIAID outlined three "broad spectrum" strategies as a way to maximize biodefense capabilities. One of these strategies was the exploration of broad spectrum platforms, which NIAID describes as standardized methods that can be used to significantly reduce the time and cost required to bring medical countermeasures to market. Please explain how much funding has been spent in this area and what milestones have been reached.

Answer. NIAID's product development strategy has broadened from a "one bug-one drug" approach toward a more flexible, broad-spectrum approach. This process involves developing medical countermeasures that are effective against a variety of pathogens and toxins, developing technologies that can be widely applied to improve classes of products, and establishing platforms that can reduce the time and cost of creating new products. The broad-spectrum strategy recognizes both the expanding range of biological threats and the limited resources available to address each individual threat. NIAID provided $653 million in fiscal year 2009 to a number of initiatives that have the potential to lead to the development of broad spectrum platforms. Examples of milestones in the development of broad-spectrum strategies that have been facilitated by NIAID funding include:

—The preclinical development of Advax™, a vaccine adjuvant platform technology. Advax™ has been approved for human use in Australia for at least five different candidate vaccines and currently is being tested in seasonal and pandemic influenza vaccines and hepatitis B vaccines that are ready to enter phase III clinical trials.

—The development of LJ001, a broad-spectrum antiviral that has shown activity against multiple viruses, including influenza, Ebola, Marburg, hepatitis C, and West Nile.

—Syntiron's broad-spectrum vaccine technology that is currently used for candidate vaccines for Staphylococcus, Salmonella, plague, and anthrax.

BIODEFENSE

Question. Specifically, equine source plasma has been successfully used in the development of passive antibody therapy for postexposure treatment of agents such as botulinum toxin. I understand this same technique can be used for treatment of a number of the Category A biological threat agents such as Bacillus anthracis, hemorrhagic fevers (i.e., Ebola and Marburg), and Yersinia pestis. Is NIAID familiar with this platform of therapeutics and its successes? Has NIAID applied funding either from within its directly appropriated funds or from BARDA transferred funds to the development of passive antibody therapeutics? If so how much and on what projects?

Answer. NIAID is significantly involved in the development and use of passive antibody therapy for postexposure treatment of agents such as botulinum toxin and has provided more than $92 million in funding over the past 3 years for the development of passive antibody therapy for Category A agents. Among other efforts, NIAID supported the development of the botulinum toxoid antibody from horses for a product that is now included in the Strategic National Stockpile; coordinated with the Biomedical Advanced Research and Development Authority (BARDA) for development of animal models in support of licensure of botulinum anti-toxins; and supported initial work to develop ricin polyclonal antibodies from equine antisera.

CONCLUSION OF HEARINGS

Senator HARKIN. The subcommittee will stand recessed.

[Whereupon, at 11:05 a.m., Wednesday, May 5, the hearings were concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]