DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2014 Budget Request

Witness appearing before the

Senate Subcommittee on Labor – HHS – Education Appropriations

Francis S. Collins, M.D., Ph.D.

Director, National Institutes of Health

Accompanied by:

Anthony S. Fauci, M.D.
Director, National Institute of Allergy and Infectious Diseases

Gary H. Gibbons, M.D.
Director, National Heart, Lung, and Blood Institute

Richard J. Hodes, M.D.
Director, National Institute on Aging

Story C. Landis, Ph.D.
Director, National Institute for Neurological Disorders and Stroke

Harold E. Varmus, M.D.
Director, National Cancer Institute

May 15, 2013

Good afternoon, Mr. Chairman and distinguished Members of the Subcommittee. I am Francis S. Collins, M.D., Ph.D., and I am the Director of the National Institutes of Health (NIH). Accompanying me today are: Anthony S. Fauci, M.D., Director of the National Institute of Allergy and Infectious Disease; Gary H. Gibbons, M.D., Director of the National Heart, Lung, and Blood Institute; Richard J. Hodes, M.D., Director of the National Institute on Aging; Story C. Landis, Ph.D., Director of the National Institute for Neurological Disorders and Stroke; and Harold E. Varmus, M.D., Director of the National Cancer Institute.

It is an honor to appear before you today to present the Administration's fiscal year (FY) 2014 budget request for the NIH.

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance human health, lengthen life, and reduce illness and disability. I can report to you that NIH leadership, employees, and grantees continue to believe passionately in our mission.

NIH has been advancing our understanding of health and disease for more than a century, and scientific and technological breakthroughs generated by NIH-supported research are behind much of the gains this country has enjoyed in public health. For example, deaths from heart attack have fallen by more than 60 percent over the past 40 years; deaths from stroke by more than 70 percent. HIV/AIDS treatment and prevention may now enable us to envision the first AIDS-free generation since this virus emerged more than 30 years ago. More than 90 percent of children diagnosed today with the most common form of childhood leukemia will survive. NIH research has given us vaccines for cervical cancer, influenza, and meningitis. We can look forward to a future in which advanced prevention and treatment strategies such as these allow everyone to have a much better chance of living a long and healthy life.

I would like to begin today by highlighting just a few areas in which NIH-supported research is opening up extraordinary new opportunities to improve the health of the American public.

Let's consider cancer. One person dies from cancer every minute in the United States—that equates to 1,500 deaths every day, the equivalent of five crashing jumbo jets.[1] NIH research has contributed to real progress, with cancer death rates falling by one percent per year for the past 15 years—but we aim to do much more. With the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI) as leads, NIH established The Cancer Genome Atlas (TCGA) as a coordinated effort to accelerate our understanding of the molecular basis of cancer, using dramatic advances in genome sequencing technologies to carry out comprehensive genomic analysis of more than 20 types of cancer. By identifying the molecular changes in a cancer cell as compared to a healthy cell of the same individual, we are gaining a better understanding of the driving forces behind the disease. That is leading to identification of new drug targets, as well as of subsets of disease with different responses to therapy that can empower personalized interventions instead of one-size-fits-all chemotherapy. As an example, a

[1] http://cancergenome.nih.gov/PublishedContent/Files/pdfs/1.1.0_CancerGenomics_TCGA-Genomics-Brochure-508.pdf

TCGA research network of investigators recently identified promising new therapeutic targets in squamous cell carcinoma of the lung, the second most common form of lung cancer, including three families of enzymes that act as molecular switches.[2] These findings lay the foundation for the development and implementation of advanced diagnostics and treatments for squamous cell cancer. Moreover, they underscore the value and promise of our nation's investment in TCGA.

Another new and exciting area of basic research is the Human Microbiome Project. Microbes inhabit many parts of the human body and have often had a bad reputation for causing sickness. But more often than not, they actually contribute to the health of their human hosts. In a five-year endeavor supported by the NIH Common Fund, 200 scientists at 80 institutions sequenced the genomes of bacteria from multiple body sites of 250 individuals, with striking results. The research showed that certain communities of bacteria help keep people healthy, whereas others appear to make people more susceptible to disease.[3] When the bacterial population in the intestinal tract gets disrupted, chronic conditions such as obesity can result; this new understanding may provide us with novel ways to address this serious health threat. An unexpected result from another NIH-funded study was that poor diet is not the only contributor to malnutrition. In fact, a bad assortment of microbes in the gut can conspire with a nutrient deficient diet to lead to severe malnutrition.[4]

A final example I want to provide of how NIH-supported research is accelerating scientific discovery is in the area of stem cells. Induced pluripotent stem (iPS) cell technology is revolutionizing the way we study disease, and holds the promise of dramatic advances in treatment. iPS cells are patient-derived cells, typically from skin, that scientists can reprogram back to an embryonic stem cell-like state. These cells can then be induced to turn on specific sets of genes to differentiate into a variety of cell types, including blood cells, liver cells, or neurons. This means researchers can re-create a patient's disease in a dish and screen drug compounds against the cells—rather than the patient—to determine drug toxicity and efficacy. But it's also possible that these cells could be used therapeutically, especially if an individual's genetic misspellings could be corrected in their own iPS cells, and then programmed and delivered to a tissue where they are sorely needed. Recent NIH-funded studies have developed copy-editing enzymes that are making it faster, easier, and cheaper to correct genetic typos. In 2011, researchers used a specially engineered copy-editing enzyme to find and correct the mutation that causes sickle cell anemia using iPS cells derived from a patient with the disease.[5] Two very recent, groundbreaking discoveries along this same avenue are the development of the next generation methodology of 'find and replace' enzymes that are making it much simpler to copy-edit the genome.[6,7]

While these exciting findings have led to a much deeper understanding of health and human disease, much more work needs to be done in order to move these strategies and others like them out of the lab and into the clinic—and to do so as quickly as possible. To this end, the

[2] http://www.nature.com/nature/journal/v489/n7417/pdf/nature11404.pdf
[3] http://www.nature.com/nature/journal/v486/n7402/pdf/nature11209.pdf
[4] http://www.sciencemag.org/content/339/6119/548.full.pdf
[5] http://onlinelibrary.wiley.com/doi/10.1002/stem.718/pdf
[6] http://www.sciencemag.org/content/326/5959/1501.full.pdf
[7] http://www.sciencemag.org/content/339/6121/819.full.pdf

Administration's FY 2014 budget request for the NIH is $31.331 billion, $471 million above the FY 2012 level. This budget request reflects the President's and the Secretary's commitment to improving the health of the nation and to maintaining our nation's leadership in the life sciences. The request highlights investments in innovative research that will advance fundamental knowledge and speed the development of new therapies, diagnostics, and preventive measures to improve public health.

The FY 2014 budget request, a 1.5 percent increase over FY 2012, will enhance NIH's ability to support cutting-edge research and training of the scientific workforce. Within the Administration's FY 2014 budget, we will continue to increase Research Project Grants (RPGs), NIH's funding mechanism for investigator-initiated research. NIH expects to support 10,269 competing RPGs in FY 2014, an increase of 1,283 over FY 2012 levels. For FY 2014, NIH anticipates funding a total of 36,610 RPGs. The budget request allocates resources to areas of the most extraordinary promise for biomedical research, while maintaining the flexibility to pursue unplanned scientific opportunities and address unforeseen health needs.

A major initiative for NIH in FY 2014 will be in the area of Alzheimer's disease research. As many as 5.1 million Americans suffer this irreversible, progressive, and devastating brain disease that slowly destroys cognitive functions including memory and the ability to reason and think.[8] At the same time, millions of American families struggle with the physical, emotional, and financial costs of caring for a loved one with Alzheimer's. A recently published NIH-supported study found the costs of caring for people with dementia in the United States in 2010 ranged from $157 billion to $215 billion.[9] This disease is not just a burden on our health, but also a burden on our economy.

NIH, with the National Institute on Aging (NIA) taking the lead, currently supports a number of studies aimed at understanding, diagnosing, preventing, and treating Alzheimer's disease. In FY 2014, NIA would plan to award a total of 591 new and competing RPGs, an increase of 277 from FY 2012. This includes an $80 million increase for Alzheimer's research.

A seminal finding that has recently generated a lot of excitement is the discovery that the protein, tau, which appears to be in part responsible for the cognitive decline in Alzheimer's patients, spreads from neuron to neuron like an infection.[10] This means that if researchers could find a way to prevent cell-to-cell transmission, perhaps by blocking tau with an antibody, the disease process could be halted. There is also growing evidence that successful treatment of Alzheimer's disease needs to happen very early in the course of the disease, perhaps even before any symptoms have appeared at all. This kind of Alzheimer's disease prevention is at the heart of new clinical trials being conducted by scientists at the Dominant Inherited Alzheimer's Network (DIAN), a NIA-funded international research partnership. One of the investigational drugs being tested is a monoclonal antibody that binds to certain forms of amyloid beta, a main constituent of the signature plaques in Alzheimer's disease. Trying to prevent Alzheimer's symptoms from ever occurring in individuals at very high genetic risk is a new strategy—one

[8] http://www.nia.nih.gov/alzheimers/topics/alzheimers-basics
[9] http://www.nejm.org/doi/pdf/10.1056/NEJMsa1204629
[10] http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0031302

that we are eager to pursue in order to determine if early intervention can influence this terrible disease.

With advancing scientific and technological capabilities, such as genome sequencing machines and high resolution medical imagers, biomedical researchers are generating huge amounts of data at an unprecedented pace. The need to integrate and analyze massively complex datasets is referred to as the Big Data challenge – a challenge that we must overcome to gain a deeper understanding of disease and develop the next generation of therapeutic targets.

Managing Big Data is a critical part of translating scientific discoveries into clinical applications. To address this challenge, NIH is developing the Big Data to Knowledge (BD2K) program, which will be launched in FY 2014. BD2K will support four programmatic efforts: (1) facilitate the broad use and sharing of large, complex biomedical data sets through the development of policies, resources and standards; (2) develop and disseminate new analytical methods and software; (3) enhance training of data scientists, computer engineers, and bioinformaticians; and (4) establish Centers of Excellence to develop generalizable approaches that address important problems in biomedical analytics, computational biology, and medical informatics. In FY14, NIH will invest at least $40 million in the BD2K program through the Common Fund, and each Big Data Center of Excellence will be funded at $2 million to $5 million per year for three to five years. As Big Data challenges in biomedical research are shared with other areas of scientific research such as energy and space research, BD2K will also require effective collaboration and coordination with other government agencies tackling similar challenges, including the National Science Foundation and the Department of Energy, as well as privately funded efforts. With the proper investments and efforts, we will overcome the challenges associated with Big Data in order to accelerate the translation of bench to bedside applications.

Another exciting new initiative I would like to tell you about is NIH's efforts to recruit and retain a diverse pool of scientific talent and creativity. NIH is strongly committed to maintaining a diverse biomedical research workforce and has supported programs to enhance the diversity of our workforce for more than 30 years in order to achieve this goal. While progress has been made in some areas, more work needs to be done. The centerpiece of the newest initiative is the BUilding Infrastructure Leading to Diversity (BUILD) Program that is designed to provide relatively under-resourced institutions with the opportunity to provide a series of rigorous, mentored research experiences to their students, many of whom are from backgrounds underrepresented in biomedical research, with the goal of facilitating entry of a more diverse pool of students into graduate programs for biomedical research.

I want to emphasize that while all of these ambitious new scientific endeavors provide unprecedented promise for advancing human health, we cannot ignore the impact the sequester is having on groundbreaking medical research. The FY 2013 reduction of $1.6 billion, or 5.0 percent, is having a substantial impact on the scientific community. If the Budget Control Act-imposed caps on discretionary programs continue, and NIH funding is reduced proportionally over the next 10 years, funding will decline by about $19 billion. The consequences will be harmful to scientific progress and to American leadership in science. NIH-funded investigators are already feeling the effects as Institutes and Centers are forced to fund a lower percentage of

grant applications. In FY 2012, we funded 8,986 competing RPGs. In FY 2013, our projection is 8, 283. This trend is also reflected in our total research portfolio—we expect to fund 34,902 RPGs this year compared to 36,259 in FY 2012. With this new reality, more and more investigators will be unable to pursue the bold ideas that NIH has traditionally supported.

NIH plays a significant role in the U.S. economy by advancing scientific products and technologies that help maintain our nation's role as a global innovation leader.[11] At a time when global competition in the life sciences is intensifying, the American economy cannot afford to lose ground in scientific efforts that promote human health. Countries such as China and India are increasingly investing resources into biomedical science and technology. According to the Organization for Economic Cooperation and Development (OECD), in 2008, including both public and private sources, the U.S. invested 2.8 percent of its GDP in research and development (R&D)—less than Israel, Japan, Korea, Sweden, and Switzerland. Moreover, the U.S. ranks only eighth in R & D as a share of GDP among countries in the OECD.[12] China has made policy changes to invest heavily in the life sciences industry, moving them closer to becoming a world leader in science and technology by the end of the decade.[13] Over the past decade, Singapore has also pursued a prominent role as a global leader in the life sciences. For example, their pharmaceutical industry R&D funding was five times greater than that of the U.S. in 2009, on a share of GDP basis. Despite these factors, the United States is by far the largest R&D performer globally, contributing $402 billion in 2009, accounting for about 31 percent of the global total.[14]

But let me close on a more positive note. I began today by telling you about some exciting new initiatives NIH is planning for FY 2014. Now I want to tell you about our boldest new scientific endeavor—one that we are all very excited about.

Neurological and psychiatric disorders such as Alzheimer's disease, Parkinson's disease, autism, schizophrenia, and traumatic brain injury inflict a tremendous toll on society, yet their underlying pathologies remain unknown due to the great complexity of the human brain. This complexity was once thought to be beyond the reach of scientific understanding. Today, however, tremendous strides in neuroscience have brought forward remarkable new opportunities for unlocking these mysteries.

Indeed, neuroscience has made some extraordinary progress in recent years. For example, a group of NIH-supported researchers has developed a sophisticated neural interface that enables paralyzed people to move a robotic arm, using just their thoughts. Using this robotic arm system, 58-year-old Cathy Hutchinson recently was able to take a sip of coffee on her own for the first time since she'd been paralyzed more than 14 years earlier. A truly remarkable moment—but just a beginning, because we need a lot more of these moments for a whole lot more people.

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[11] http://www.unitedformedicalresearch.com/wp-content/uploads/2013/02/UMR_Impact_of_Sequestration_2013.pdf

[12] http://www.itif.org/publications/winning-race-2012-memos-science-and-technology

[13] http://www.itif.org/publications/leadership-decline-assessing-us-international-competitiveness-biomedical-research

[14] http://www.nsf.gov/statistics/seind12/c4/c4s8.htm

In FY 2014, NIH will begin its support of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, in order to develop a deeper understanding of brain function through the creation of new tools capable of examining the activity of millions of nerve cells, networks, and pathways in real time. By measuring activity at the scale of circuits and networks in living organisms, we can begin to translate data into models that will decode sensory experience, motor planning, and, potentially, even memory, emotion, and thought. NIH is embracing a collaborative approach in tackling this challenge, working with researchers from across the country, industry, foundations, and other government agencies including the Defense Advanced Research Projects Agency and the National Science Foundation. In FY 2014, NIH will invest $40 million in this initiative to leverage investment from a number of other sources, including private sector and leading philanthropies. We believe that successful completion of the BRAIN Initiative will revolutionize the field of neuroscience and set the stage for major advances in diseases such as Alzheimer's, Parkinson's, autism, schizophrenia, depression, and epilepsy.

Granted, this is a very ambitious goal. But we at NIH have heard and overcome such skepticism before. Take the example of the Human Genome Project, which I had the privilege to lead. In its earliest days, back in the late 1980s, many questioned the wisdom of that proposal to sequence the 3 billion letters in the human genetic blueprint. Nearly everyone in the research community agreed that it would be fantastic to have a full readout of the human DNA instruction book. But skeptics argued that it could not be done because the tools and technologies didn't exist. In fact, they were right—we didn't have the necessary technologies. But, the opportunity for dramatic progress in genetics inspired a remarkable series of technical innovations. These tools enabled the Human Genome Project to be successfully completed in April 2003, ahead of schedule and under budget. Like the Human Genome Project, we envision the BRAIN Initiative will create data, tools, and technologies that will speed the efforts of many different types of researchers all around the world. Though this program will need to extend over many years, and we must be careful not to overpromise immediate medical benefits, BRAIN will eventually lead to scientific advances that will catalyze development of new treatments and cures.

I have provided you today with a brief overview of NIH's past successes and continuing commitment to basic and translational science, as well as a glimpse into the critical role that NIH plays in our domestic and global economies. We have never witnessed a time of greater promise for advances in medicine than right now. With your support, the future of medicine will be very bright.

This concludes my testimony, Mr. Chairman.