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NATIONAL INSTITUTES OF HEALTH

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Senate Subcommittee on Labor – HHS – Education Appropriations

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INTRODUCTION

Good morning, Mr. Chairman and distinguished Members of the Subcommittee. I am Francis S. Collins, M.D., Ph.D. and I am Director of the National Institutes of Health (NIH).

It is a great honor to appear before you today to present the Administration's program level request of $31.987 billion for NIH in FY 2012, and to discuss the contributions that NIH-funded biomedical research has made in improving human health. NIH is the largest supporter of biomedical research in the world, providing funds for more than 40,000 competitive research

grants and more than 325,000 research personnel at more than 3,000 research institutions and small businesses across our nation's 50 states. I also want to offer a vision of how NIH will catalyze innovation in basic and translational sciences, and will ensure future U.S. economic strength and global competitiveness.

On behalf of NIH and the biomedical research enterprise, I want to thank you as Members of the Senate for sparing NIH from deeper cuts in the final FY 2011 Continuing Resolution (CR). We know that, even as Congress and the Administration wrestled with cuts of more than three percent to the Labor-HHS portion of the CR, NIH received a one percent, or $321.7 million, cut from the FY 2010 level, while other programs and functions were cut more deeply.

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 the burdens of illness and disability. I can report to you that NIH continues to believe passionately in that mission and works tirelessly to achieve it.

Due in large measure to NIH research, our nation has gained about one year of longevity every six years since 1990. A child born today can look forward to an average lifespan of nearly 78 years – nearly three decades longer than a baby born in 1900. And not only are people living longer, but their quality of life is improving: in the last 25 years, the proportion of older people with chronic disabilities has dropped by almost one-third.

NIH research has enabled new techniques to prevent heart attacks, newer and more effective drugs for lowering cholesterol and controlling blood pressure, and innovative strategies for dissolving blood clots and preventing strokes. As a result, the U.S. death rate for coronary disease is 60 percent lower—and for stroke, more than 70 percent lower—than three generations ago. Better treatment of acute heart disease, better medications, and improved health-related behaviors—all underpinned by NIH research—account for as much as two-thirds of these reductions.

In recent years, largely as a result of NIH research, we have succeeded in driving down mortality rates for cancer in the United States. This progress comes despite the fact that cancer is largely a disease of aging and our population is growing older. Over the 15-year period from 1992 to 2007, cancer death rates dropped 13.5 percent for women and 21.2 percent for men. According to an American Cancer Society report released in July 2010, the continued drop in overall mortality rates over the last 20 years has saved more than three-quarters of a million lives.[1] And in cancers that strike children we have made near-miraculous progress—the five-year survival rate for children with the most common childhood cancer, acute lymphocytic leukemia, is now 90 percent.[2]

I would also like to offer a shining example of the Senate's strong and consistent support of biomedical research at NIH by note that we are celebrating a significant anniversary. This year marks the 10th anniversary of the establishment of the Dale and Betty Bumpers Vaccine Research Center (VRC) at NIH. Groundbreaking research performed at the VRC is making great progress toward developing a universal flu vaccine that confers longer-term protection against seasonal and pandemic influenza strains.

[1] http://pressroom.cancer.org/index.php?s=43&item=252
[2] http://seer.cancer.gov/csr/1975_2008/browse_csr.php?section=28&page=sect_28_table.08.html

Today, scientists have to make an educated guess about the make-up of the coming winter's influenza viruses. These educated guesses become the basis for the manufacture of each year's flu shot and mean that everyone has to be re-immunized in anticipation of next year's strain of flu. Recently, NIH scientists have identified pieces of influenza viral proteins that consistently appear among seasonal and pandemic flu strains. These findings raise the possibility that we might soon develop an influenza vaccine that provides near-universal protection against a broad range of current and future strains of influenza,[3] as well as make yearly flu shots a thing of the past. Most of this exciting work was performed at the VRC. Scientists at that same center are making important strides toward the development of the long-hoped-for vaccine against the human immunodeficiency virus (HIV), the cause of acquired immune deficiency syndrome (AIDS). While after so many frustrations, no one would want to predict success just yet, recent discoveries of VRC scientists about how to encourage production of neutralizing antibodies against HIV have provided renewed hope that this pressing problem may ultimately be solved.

NIH AND ECONOMIC GROWTH

Mr. Chairman and Members of the Subcommittee, I recognize that, given our nation's fiscal situation, and the extraordinarily tough decisions that you will have to make about our nation's finances, you need to be assured that NIH remains a worthwhile national investment. Even as you make these decisions and even as our country recovers from financial recession, I want to offer evidence that NIH and its research provide two strong and ongoing benefits to our economy.

First, NIH research spending has an impact on job creation and economic growth. A new economic impact study by United for Medical Research suggests that in FY2010, NIH research funding supported an estimated 487,900 American jobs, including researchers and spin-off employment.

Second, NIH research funding has a longer term impact in its role as the foundation for the medical innovation sector. Nearly one million U.S. citizens are employed by the industries and companies that make up this sector of the economy, earning $84 billion in wages and salary in 2008, and exporting $90 billion of goods and services in 2010. NIH support for biomedical research institutions catalyzes business activity in other ways as well. Such institutions constitute reservoirs of skilled, knowledgeable individuals and, thereby, attract companies that wish to locate their operations within such "knowledge hubs."

For example, in the 1990s, federal funding through research grants and the Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) programs transformed the academic research environment and helped to launch new industrial sectors in Silicon Valley and elsewhere that are flourishing today. Federal funding has been crucial in stimulating the formation of start-up companies and collaborations among academia and the private sector in the development of innovative technology. A prime example is the company Affymetrix.

In the late 1980s, a team of scientists led by Stephen P.A. Fodor, Ph.D., developed methods for fabricating DNA microarrays, called GeneChips, using semiconductor

[3] http://www.niaid.nih.gov/news/newsreleases/2010/Pages/UniversalFluVax.aspx

manufacturing techniques, melded with advances in combinatorial chemistry to capture vast amount of biological data on a small glass chip. In 1992, the first of several NIH grants was awarded to Affymetrix; with this and an SBIR grant from the Department of Energy, Dr. Fodor was able to demonstrate proof of principle of using large arrays of DNA probes in genetic analysis. Affymetrix and similar companies are building the machine tools of the genomic revolution. In 2009, Affymetrix had annual revenue of $327 million and employed more than 1,100 people.

Furthermore, NIH research leads to better health outcomes that not only ease human suffering, but also produce an economic return. A 2006 study by Kevin Murphy and Robert Topel of the University of Chicago shows that a permanent reduction of one percent in cancer deaths has a present value to current and future generations of Americans of nearly $500 billion. The article states that if we were able to defeat cancer completely, such cures would be worth approximately $50 trillion—more than three times today's Gross Domestic Product.[4]

We face a similar economic threat from diabetes. If current trends continue, by 2050 as many as one in three U.S. adults will be diagnosed with diabetes.[5] Total costs of diabetes, including medical care, disability, and premature death, reached an estimated $174 billion in the United States in 2007.[6] According to analysis from the UnitedHealth Center for Health Reform & Modernization, more than 50 percent of Americans could have diabetes or pre-diabetes by 2020.[7] Furthermore, the center's analysis predicts diabetes and pre-diabetes will account for an estimated 10 percent of total health care spending by the end of this decade, at an annual cost of almost $500 billion.

But I can offer some hope. NIH spearheaded a landmark clinical trial on type 2 diabetes prevention that showed that people at high-risk for diabetes can dramatically reduce their risk of developing type 2 diabetes through modest exercise and dietary changes that achieve modest weight loss. Called the Diabetes Prevention Program (DPP), the clinical trial included 3,234 adults at high risk for developing type 2 diabetes, including those with a family history of diabetes, as well as other risk factors. One-third of these individuals participated in a lifestyle program that included exercise training and dietary change implemented under the guidance of lifestyle coaches. The DPP research team found that this approach lowered risk of diabetes by 58 percent.[8] The DPP trial also demonstrated that the cost of the lifestyle intervention was $3,540 per participant over three years, which was significantly offset by the lowering of other healthcare costs as lifestyle participants became healthier.[9] The cost effectiveness of the DPP has continued to be followed and 10-year results will be published in the near future. Building on these critically important results, NIH partnered with the Centers for Disease Control and Prevention (CDC) and more than 200 private partners, including the YMCA, Walgreens, and UnitedHealthcare, to bring these evidence-based lifestyle interventions to communities in Ohio, Indiana, Minnesota, Arizona, Oklahoma, New Mexico, New York, New Jersey, Connecticut, and

[4] Murphy, K.M., & Topel, R.H. (2006), The value of health and longevity. *Journal of Political Economy, 114(5),* 871-904.
[5] http://www.cdc.gov/media/pressrel/2010/r101022.html
[6] CDC National Diabetes Fact Sheet. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf
[7] http://www.unitedhealthgroup.com/hrm/UNH_WorkingPaper5.pdf
[8] Knowler WC, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metiformin. *N. Engl J Med* 346:393-403, 2002.
[9] *Diabetes Care*.2003 Jan;26(1):36-47.

Georgia. In addition, the DPP Lifestyle Intervention is being used by the Indian Health Service in a large demonstration project on many American Indian reservations.

INVESTING IN BASIC SCIENCE

At NIH, we have always put our greatest percentage of our resources into basic research. This is because the fundamental observations made today become the building blocks of tomorrow's knowledge, therapies, and cures. NIH's history has repeatedly demonstrated that significant scientific advances occur when new basic research findings, often completely unexpected, open up new experimental possibilities and therapeutic pathways. Historically, NIH has put more than 50 percent of its budget into basic research and the research discoveries that led to the 132 Nobel prizes won by our intramural and university scientists are evidence of the wisdom of this investment.

Basic research is precisely the type of work that the private sector, which must see a rapid return on invested capital, cannot afford to support. NIH provides the fundamental observations that pharmaceutical and biotechnology companies can turn into diagnostics, therapies, and devices that eventually reach patients. As the Congressional Budget Office put it, "federal funding of basic research directly stimulates the drug industry's spending . . . by making scientific discoveries that expand the industry's opportunities for research and development."[10]

Because we simply cannot predict the next scientific revelation or anticipate the next opportunity, our basic research portfolio must be diverse. We set scientific priorities by considering a wide array of biomedical questions that we might try to answer. It is rather like facing a series of doors, some of which lead to vast treasures and others to much more modest payouts, without any sure way of knowing what lies behind any particular door. To improve our odds of striking scientific gold, we need a broad basic research portfolio that enables our nation to open as many doors as our resources allow.

Not all disease or scientific problems are equally ripe for new advances, nor do such advances come at the same rate across the portfolio, no matter how pressing today's public health challenges are. We can only be sure that without a strong commitment to basic research today, the new knowledge of tomorrow will remain hidden behind those unopened doors and future therapies and cures will remain out of our reach.

Let me offer a few of the exciting insights that NIH's support of basic research have provided. On April 3, 2011, the online issue of Nature Genetics presented the findings by a team of NIH-supported scientists who had identified five new genetic variants that are risk factors for late-onset Alzheimer's disease, which is the most common form of the disorder. These findings doubled from five to 10 the number of gene variants that we know are associated with Alzheimer's disease.[11]

What is even more compelling is that these newly-identified genes strongly implicate inflammation and high cholesterol as risk factors in the development of Alzheimer's disease.

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[10] Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October, 2006, p. 3.

[11] Naj, A.C. et al. Common Variants of MS4A4/MSA6E, CD2AP, CD33 and EPHA 1 are associated with late-onset Alzheimer's Disease. *Nature Genetics*, EPUB April 3, 2011, and Holligworth, P., et al. Common variants at ABCA7, MS4A/MS4A4E, EPHA 1, CD33 and CD2Ap are associated with Alzheimer's disease. *Nature Genetics*. Epub April 3, 2011.S

Although each of these newly-identified genes increases a given individual's risk of developing the disease by no more than 10 to 15 percent, the unanticipated insight that cholesterol and inflammation are contributing factors opens up new research avenues to understand the disease process, and increases the likelihood that we can glimpse potential preventions or therapies.

NIH's commitment to basic research has also provided us with one of the most promising therapeutic strategies we have seen to date for the deadliest form of skin cancer, melanoma. Since 2002, we have known that many melanoma tumors exhibit a mutation in the *BRAF* gene and that this mutation might provide a target for therapeutic intervention. A team that included NIH-supported investigators used high-throughput screening in combination with structural biology, to identify compounds that inhibit the activity of the mutant form of the *BRAF* gene found in most melanomas, but have little effect on the *BRAF* gene found in normal cells. This basic cancer research supported by NIH contributed to the development of the drug PLX4032, a drug designed to inhibit the activity of a mutant form of the protein called BRAF. This is a powerful example of how support for basic research can be translated into therapeutic potential. In August 2010, Plexxikon, a small drug development company, announced that PLX4032, had elicited a positive response in more than 80 percent of melanoma patients in early-phase clinical trials. PLX4032 caused the tumors in 24 of the 30 trial participants to shrink by at least 30 percent, while the tumors of two patients disappeared. Another clinical trial involving hundreds of participants across many institutions demonstrated that metastatic melanoma patients treated with PLX4032 lived six to eight months longer than those who had been given the chemotherapy drug dacarbazine, which is the current standard of care.

Whether it is with the hope of finding new ways to treat cancer, prevent Alzheimer's disease, or help people suffering from countless other rare and common conditions, we at NIH invest in basic research because of our conviction that it will benefit our nation in the long term.

ADVANCING TRANSLATIONAL SCIENCE

NIH also has a longstanding commitment to translating fundamental knowledge into cures and therapies for human disease. It should not be surprising that NIH-supported science underpins many of the most transformative drugs and therapies that have benefited millions of Americans and people around the world, including statins to lower cholesterol and drugs to treat depression. In 2010, we conducted a trans-NIH inventory of therapeutics development activities and found more than 550 such projects, of which approximately 65 percent were pre-clinical and 35 percent were clinical research.

An analysis published in the Feb. 10, 2011 issue of the *New England Journal of Medicine (NEJM)* underscores the depth and breadth of NIH's support for translational science that benefits patients.[12] The article's authors describe a new emphasis on "public sector research" that is almost exclusively supported or conducted by NIH, noting "the boundaries between the roles of the public and private sectors have shifted substantially since the dawn of the biotechnology era, and the public sector now has a much more direct role in the applied-research phase of drug discovery."

Drugs that represent a major advance in treatment or offer treatments for diseases for which no adequate therapy currently exists are granted "priority review" by FDA. According to

[12] Stevens, Ashley J. et al. The role of public-sector research in the discovery of drugs and vaccines. *New England Journal of Medicine,* 364,:6, February 10, 2011.

the *NEJM* article, between 1990 and 2007, 20 percent of the FDA approvals of novel compounds granted priority review were given to drugs discovered by NIH. Examples include AZT for HIV/AIDS and the targeted leukemia therapy Gleevec. Over the past 40 years, 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through work carried out by NIH-supported biomedical research institutions.

Despite NIH's historic and growing commitment to translational sciences, far more remains to be done. Millions of people still suffer from diseases, such as cancers and diabetes, for which we have no adequate treatments. There are nearly 7,000 rare diseases, yet we have therapies for fewer than 200 of them. This staggering public health need and attendant human suffering continues even as the pharmaceutical industry, beset by economic stress, is investing less in research and development, and the pool of venture capital needed by the biotech industry is drying up.

At the same time, a deluge of discoveries about the molecular basis of disease has been made possible by the sequencing of the human and many other genomes, as well as breathtaking advances in research technologies, such as high-throughput screening and bioinformatics. These discoveries reveal hundreds of tantalizing potential therapeutic targets. As the result of years of steadfast support of NIH research by Congress and the American people, we find ourselves in a paradoxical situation: we can uncover the molecular basis of common and rare diseases better than ever before and we can more readily identify therapeutic opportunities than at any point in history, but the pipeline through which these new therapeutic agents must pass is crimped and, in some places completely blocked.

Consequently, a new approach to therapeutic development, and a new partnership with the private sector, is needed. That is why we have proposed the establishment of NIH's new National Center for Advancing Translational Sciences beginning in FY 2012.

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

As previously noted, NIH has a long and rich history of significant contributions to therapeutic development. In particular, the National Cancer Institute (NCI) and the National Institute for Allergy and Infectious Diseases (NIAID) have made major contributions over many years to the discovery of new treatments. However, now is the time to consider the therapeutic development process itself as a scientific problem that is ripe for innovation. The mission of the National Center for Advancing Translational Sciences (NCATS) will be to advance the discipline of translational science and catalyze the development and testing of novel diagnostics and therapeutics across a wide range of human diseases and conditions. NIH has no intention of entering the drug development arena that is rightly the province of private sector companies. Indeed, given that it costs in the range of $ 1.3 billion to $1.8 billion to bring one drug to market, it is clear that it would be impossible for NIH to compete with private industry.[13] What NCATS intends to do is advance the science of therapeutic development and determine if there are ways

[13] DiMasi, JA, Hansen RW, Grabowski HG. Extraordinary claims require extraordinary evidence. *Journal of Health Economics* 2005;24(5):1034-1044. Tonkens, R. An Overview of the Drug Development Process. *The Physician Executive* May-June 2005.

we can re-engineer the drug development pipeline; creating new approaches and methods that will benefit everyone interested in speeding the delivery of new medicines.

Today, the development of new diagnostics and therapeutics is a complex, costly, and risky endeavor. Only a few of the thousands of compounds that enter the drug development pipeline will ultimately make it into the medicine chest or to the patient's bedside. NCATS will study the various steps in the drug development pipeline, consult with the private sector to identify bottlenecks amenable to re-engineering, and experiment with innovative methods to streamline the process.

To offer one example of the kind of pipeline challenge we might address, new ideas about assessing the toxic potential of drug candidates using sophisticated cell-based methods, instead of animal toxicology testing, hold out the promise of revolutionizing this step in validating a new therapeutic agent – and such research can be catalyzed by NIH in ways that might otherwise not be possible.

NCATS will attack the bottlenecks in the drug development pipeline by experimenting with innovative approaches in an open-access model so that all stakeholders, ranging from industry to patients, will be able to access and apply its innovations. NCATS's open access operating framework will also advance the field of regulatory science by promoting interactions among the Food and Drug Administration (FDA), NIH, patient advocates, and pharmaceutical and biotechnology companies. NCATS will encourage collaboration across all sectors, provide resources to enable therapeutic development, and support and enhance training in the relevant translational science disciplines.

NCATS will complement—not compete with—translational research being carried out elsewhere at NIH and in the private sector. In fact, in pursuing its mission of using the power of science to advance the entire discipline of translational science, NCATS will benefit all stakeholders, including academia, biotechnology firms, pharmaceutical companies, the FDA, and—most importantly—patients and their families.

NCATS will pull together existing NIH programs such as the Therapeutics for Rare and Neglected Diseases program, the Office of Rare Diseases Research, the Rapid Access to Interventional Development program, the Clinical and Translational Science Awards, the FDA-NIH Regulatory Science grants program, and components of the Molecular Libraries initiative. These relocated programs will have their respective budgets transferred to or implemented by the new center. In addition, we are hopeful that funding for the new Cures Acceleration Network will be provided within the NCATS appropriation in FY 2012. The intent of this innovative program and its exceptional DARPA-like flexibilities for supporting projects are a natural fit with NCATS.

Aside from the new funding requested in FY 2012 for the Cures Acceleration Network, resources for NCATS will come from the combination of already existing and appropriated programs and so be budget neutral.

NCATS will bring the scientific method to bear on today's drug development process and aim to improve and speed the therapeutic development process of tomorrow.

CONCLUSION

This statement has provided you with a brief overview of NIH's past successes and future commitment to basic and translational sciences, along with a quick look at the important role that NIH plays in our domestic economy and U.S. global economic and scientific leadership.

But I would like to close my testimony today with an example that demonstrates the benefits to be reaped from our continuing pursuit of "personalized medicine." It is the story of one individual, 6-year-old Nic Volker of Monona, Wisconsin. Starting about the age of 2, Nic developed a mysterious, life-threatening disease that ravaged his intestines, making it impossible for him to eat normally and causing unimaginable pain and suffering. At a loss to explain this terrible, inflammatory condition, researchers and clinicians at the Medical College of Wisconsin decided to sequence Nic's entire exome, that is, all the parts of the genome that code for the proteins that become life's building blocks. After exhaustive work over a period of months, the researchers identified a mutation in Nic's *XIAP* gene. Such mutations had been associated with rare blood disorders, but not with bowel symptoms. Based on this new insight, the research team had an idea that, as with the rare blood disorders, Nic's disease might be curable with a bone marrow transplant.

NIH investment over the years in the sequencing of genomes--and the technologies associated with such sequencing--has put us at the threshold of "personalized medicine." Young Nic Volker is one of a handful of individuals who has crossed that threshold, and it was made possible because of years of research and development supported and performed by NIH.

Transplantation of cord-blood stem cells from a matched donor occurred in July of last year and, although Nic is still on immunosuppressant drugs to prevent rejection of the donated cells, his symptoms have largely disappeared and today he can eat normally. Hot dogs are his favorite!

The local newspaper, the *Milwaukee Journal Sentinel*, was so struck by the saga of Nic and his family that they devoted a series of articles to the little boy's struggles and therapy, coverage that included posting photos, videos, blogs, and many other resources to the web. The five *Journal Sentinel* journalists did such a good job that they were awarded the Pulitzer Prize for Explanatory Reporting on April 18. Now, that is truly putting a face on the promise of today's biomedical research, tomorrow's personalized medicine, and NIH's role in making this promise possible.

Thank you Mr. Chairman. This concludes my formal remarks.

Biographical Sketch of Francis S. Collins, M.D., Ph.D.

Francis S. Collins, M.D., Ph.D. is the Director of the National Institutes of Health (NIH). In that role he oversees the work of the largest supporter of biomedical research in the world, spanning the spectrum from basic to clinical research.

Dr. Collins, a physician-geneticist noted for his landmark discoveries of disease genes and his leadership of the international Human Genome Project, served as director of the National Human Genome Research Institute (NHGRI) at the NIH from 1993-2008. The Human Genome Project culminated in April 2003 with the completion of a finished sequence of the human DNA instruction book.

Dr. Collins' own research laboratory has discovered a number of important genes, including those responsible for cystic fibrosis, neurofibromatosis, Huntington's disease, a familial endocrine cancer syndrome, and most recently, genes for type 2 diabetes and the gene that causes Hutchinson-Gilford progeria syndrome, a rare cause of premature aging.

Dr. Collins received a B.S. in chemistry from the University of Virginia, a Ph.D. in physical chemistry from Yale University, and an M.D. with honors from the University of North Carolina at Chapel Hill. Prior to coming to the NIH in 1993, he spent nine years on the faculty of the University of Michigan, where he was a Howard Hughes Medical Institute investigator. He is an elected member of the Institute of Medicine and the National Academy of Sciences. Dr. Collins was awarded the Presidential Medal of Freedom in November 2007 and the National Medal of Science in 2009.