



Department of Health and Human Services National Institutes of Health

Fiscal Year 2007 Budget Request

Witness appearing before the House Subcommittee on Labor-HHS-Education Appropriations

April 6, 2006

and the Senate Subcommittee on Labor-HHS-Education Appropriations

May 19, 2006

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

Director, National Human Genome Research Institute

Mr. Richard J. Turman, Deputy Assistant Secretary, Budget

Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2007 President's budget request for the National Human Genome Research Institute (NHGRI). The FY 2007 budget includes \$482,942,000, a decrease of \$3,107,000 from the FY 2006 enacted level of \$486,049,000 comparable for transfers proposed in the President's request.

On October 26, 2005, an international consortium of dedicated scientists from six countries, led by the NHGRI, published a new map of the human genome called "HapMap" that may prove even more powerful than the human genome sequence because of its medical applications.

The Human Genome Project (HGP) spelled out the letters of the 99.9 percent of the DNA code that we all share. The haplotype map, or HapMap for short, provides detailed knowledge of the 0.1 percent that represents variation in the genome. The HapMap reveals the way in which this genetic variation is organized into chromosomal neighborhoods and provides a powerful tool to uncover those spelling differences in the human instruction book that predispose some people to diabetes, Alzheimer's disease, heart disease, or cancer. As with the HGP, all of the data has been placed in the public domain.

Since early deliberations about the HGP 20 years ago, scientists and physicians have dreamed of the day when we would be able to apply the tools of genomics to the diagnosis, treatment, and prevention of those common diseases that fill up our hospitals and clinics, causing untold suffering, misery, and premature death. The completion of the HapMap brings us a major step closer to the realization of that dream.

The HapMap project could not have succeeded without the support of multiple NIH institutes, the U.S. Congress, and the dedication of more than 2,000 scientists across the world who delivered on every promise of the project. In fact, in its brief three-year life, this project produced a map three times more detailed than originally thought possible. The NHGRI and other NIH institutes can now move quickly to build on this success to discover the genetic and environmental factors that cause disease, and to utilize this information to develop better means of individualized prevention and treatment.

Ongoing NHGRI Initiatives

Use of Comparative Genomics to Understand the Human Genome

The NHGRI continues to support the sequencing of the genomes of non-human species such as the chimpanzee, dog, and mouse because of what they tell us about the human genome. The first comprehensive comparison of the genetic blueprints of humans and chimpanzees, published in *Nature* to wide acclaim in September 2005, shows our closest living non-human relatives share identity with 96 percent of the human DNA sequence. The sequence of the dog genome was published in December 2005, revealing many interesting details about the remarkable diversity of man's best friend, and greatly empowering the ability to track down the genes involved in many chronic illnesses (like cancer) where dogs are excellent models for human disease.

Sequencing technology advances, on the way to the \$1,000 genome

DNA sequencing enables a detailed description of the order of the chemical building blocks, or bases, in a given stretch of DNA, and is a powerful engine for biomedical research. Though DNA sequencing costs have dropped by three orders of magnitude since the start of the HGP, sequencing an individual's complete genome for medical purposes is still prohibitively expensive. Two bold new advances in sequencing technology recently developed by NHGRI-funded researchers promise to greatly reduce this cost. Ultimately, the NHGRI's vision is to cut the cost of whole-genome sequencing to \$1,000 or less. If achieved, this would enable the sequencing of individual genomes as part of routine medical care, providing health care professionals with a more accurate means to predict disease, personalize treatment, and preempt the occurrence of illness.

Knockout Mouse Project

The technology to "knockout" or inactivate genes in mouse embryonic stem cells has led to many insights into human biology and disease. However, information about knockout mice have only been published and made available to the research community for about 10 percent of the estimated 20,000 mouse genes. Recognizing the wealth of information that mouse knockouts can provide, the NHGRI coordinated an international meeting in 2003 to discuss the feasibility of a comprehensive project. These discussions have now resulted in a trans-NIH, coordinated, five-year cooperative research plan that will produce knockout mice for every mouse gene and make these mice available as a community resource.

Chemical Genomics-Roadmap-Molecular Libraries and PubChem

The NHGRI has taken a lead role in developing a trans-NIH chemical genomics initiative. This is part of the NIH Roadmap, and now offers public-sector researchers access to high throughput screening of libraries of small organic compounds that can be used as chemical probes to study the functions of genes, cells, and biochemical pathways. This powerful technology provides novel approaches to explore the functions of major components of the cells in health and disease. All the data generated for this project is stored in the new PubChem database at the National Library of Medicine.

Bench-to-Bedside in Intramural Research-The Example of Progeria

As just one example of the focus of the NHGRI intramural program on translational research, rapid advances have recently been achieved in the study of progeria, a rare genetic disease of childhood characterized by dramatic acceleration of aging. In 2003, NHGRI researchers discovered that progeria is caused by a single letter misspelling in a gene known as lamin A. The lamin A protein undergoes a particular modification known as farnesylation. That same modification activates the protein product of the famous ras oncogene; ten years of hard work has made available a class of cancer drugs that blocks this step. Remarkably, cell culture and mouse model experiments suggest these drugs may also have benefits for children with progeria. Serious consideration of a clinical trial is now underway, just three years after gene discovery.

The Surgeon General's Family History Initiative

Family medical history is a source of genetic information that can help more accurately determine an individual's risk for specific diseases. However, to date, this resource has been underutilized in health. To address this, Surgeon General Richard Carmona established the U.S. Surgeon General's Family History Initiative, a collaborative effort between a number of Department of Health and Human Services agencies, with leadership from NHGRI. The second annual National Family History Day was celebrated on Thanksgiving Day 2005, when a new and improved version of the software tool called "My Family Health Portrait" was released to help individuals compile their own family history information. This initiative should have an impact on patient-healthcare provider interaction, facilitating the development of more accurate family history information for patient medical records, and leading to more personalized and effective disease prevention and treatment strategies.

New NHGRI Initiatives

The Genes and Environment Initiative (GEI) and the Genetic Association Information Network (GAIN).

Just this February, the Department of Health and Human Services announced the creation of two related groundbreaking initiatives in which NHGRI will play a leading role, to speed up research on the causes of common diseases such as asthma, arthritis, the common cancers, diabetes, and Alzheimer's disease.

The Genes and Environment Initiative (GEI) is a trans-NIH research effort to combine comprehensive genetic analysis and environmental technology development to understand the causes of common diseases. NIH will invest \$68 million in GEI in FY 2007. Using the newly derived HapMap, GEI will search for the specific DNA variations that are associated with an increased risk of common illnesses. For the more than a dozen disorders chosen for investigation under GEI, NIH will study roughly 1,000 cases and 1,000 controls will be studied. Finding the variants that predispose a person to common disease is one of the highest priorities of current biomedical research, as this will enable developing personalized medicine and identifying new drug targets.

To ensure that GEI takes advantage of the wide breadth of expertise that is available on DNA variations for common disorders, NIH has begun partnering under the Genetic Association Information Network with the Foundation for the NIH, Pfizer, and Affymetrix to begin research on seven diseases during this fiscal year.

But genes alone do not tell the whole story. Recent increases in chronic diseases like diabetes, childhood asthma, obesity or autism cannot be due to major shifts in the human gene pool as those changes take much more time to occur. They must be due to changes in the environment, including diet and physical activity, which may produce disease in genetically predisposed persons. Therefore, GEI will also invest in innovative new technologies/sensors to measure environmental toxins, dietary intake and physical activity, and using new tools of genomics, proteomics, and understanding metabolism rates to determine an individual's biological response to those influences.

The Cancer Genome Atlas (TCGA)

In December, the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI) jointly launched a very important new effort to accelerate our understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing. Thanks to the tools and technologies developed by the Human Genome Project and recent advances in using genetic information to improve cancer diagnosis and treatment, it is now possible to envision a comprehensive effort to map the changes in the human genetic blueprint associated with all known forms of cancer. The overall effort, called The Cancer Genome Atlas, will begin in 2006 with a three year, pilot project totaling \$100 million to determine the feasibility of a full-scale effort to explore the universe of genomic changes involved in all types of human cancer. This atlas of genomic changes will provide: 1) new insights into the biological basis of cancer which in turn will lead to new tests to detect cancer in its early, most treatable stages; 2) new ways to predict which cancers will respond to which treatments; 3) new therapies to target cancer at its most vulnerable points; and 4) ultimately, new strategies to prevent cancer altogether.

Other Areas of Interest

Education of Health Care Professionals

To enable the translation of basic genetic discoveries into health care practice, the NHGRI has developed numerous educational programs to prepare health care professionals for this revolution. Specifically, the NHGRI continues to play a lead role in the National Coalition for Health Professional Education in Genetics (NCHPEG), which is leading a national effort to achieve genetic literacy amongst health professionals. NHGRI also worked closely with the American Academy of Family Physicians, who featured genomic medicine as their educational focus for 2005.

Minority Outreach Activities

The NHGRI has been at the forefront of ensuring that minority scientists and students are equipped to meet the new challenges of genome research for the 21st century. The institute has sponsored new initiatives to reach out to diverse populations including research, education, and outreach collaborations on the role of genetic factors in health disparities. In conjunction with the National Council of La Raza, NHGRI has developed a community-based model education program for provision of genetics information to underserved Latino communities. NHGRI is also working with Alaska Native communities and the University of Washington to expand community-based education programs in Alaska Native communities.

Genetic Nondiscrimination

The NHGRI remains very concerned about the impact of potential genetic discrimination on research and clinical practice. Through many surveys and research projects funded by the Ethical, Legal, and Social Implication (ELSI) program of the Institute, it is clear many Americans remain concerned about the possible misuse of their genetic information by insurers or employers. In February 2005, the Senate unanimously passed the Genetic Information Nondiscrimination Act of 2005 (S. 306), which would address these concerns; the companion bill H.R. 1227 is now pending in the House. The Bush Administration has issued a Statement of Administrative Policy in support of the legislation. This issue remains a high priority for the Institute.

Thank you, Mr. Chairman. I would be pleased to answer any questions that the Committee might have.

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

Director, National Human Genome Research Institute

Education:

University of Virginia, 1970 - B.S. (with Highest Honors);

Yale University, 1974 - Ph.D.;

University of North Carolina School of Medicine, 1977 - M.D. (with Honors)

Professional History:

1977-1981, Intern, Resident, Chief Resident in Medicine, North Carolina Memorial Hospital, Chapel Hill, North Carolina.

1981-1984, Fellow in Human Genetics and Pediatrics, Yale University School of Medicine, New Haven, Connecticut.

1984-1993, Assistant, Associate and then Full Professor of Internal Medicine and Human Genetics, University of Michigan, Ann Arbor, Michigan.

1987-1993 Assistant, Associate and then Full Investigator, Howard Hughes Medical Institute.

1993 to present, Director, National Human Genome Research Institute, NIH, Bethesda, Maryland.

Biographical Information:

Dr. Collins is a physician-geneticist noted for his landmark discoveries of disease genes and his leadership of the Human Genome Project. With Dr. Collins at the helm, the Human Genome Project consistently met projected milestones ahead of schedule and under budget. This international project culminated in April 2003 with the completion of a finished sequence of the human genetic blueprint. From its outset in 1990, the public sequencing effort swiftly deposited all of its data into free, public databases for use by scientists around the world. Building on the foundation laid by the Human Genome Project, Dr. Collins is now leading the NHGRI effort to ensure that this new trove of sequence data is translated into powerful tools and thoughtful strategies to advance biological knowledge and improve human health.

Dr. Collins' own research initiatives have included the discovery of a number of important genes, including those responsible for cystic fibrosis, neurofibromatosis, Huntington's disease and most recently, the gene that causes Hutchinson-Gilford progeria syndrome, a dramatic form of premature aging. In addition to his scientific achievements, Dr. Collins is known for his continuing emphasis on the importance of ethical and legal issues in genetics. He has been a strong advocate for protecting the privacy of genetic information and has served as a national leader in efforts to prohibit gene-based insurance and employment discrimination.

Professional Organizations:

American Society of Human Genetics; American Society for Clinical Investigation; Association of American Physicians; Institute of Medicine; National Academy of Sciences; American Academy of Arts and Sciences.

Richard J. Turman

Department of Health and Human Services Office of Budget

Mr. Turman is the Deputy Assistant Secretary for Budget, HHS. He joined federal service as a Presidential Management Intern in 1987 at the Office of Management and Budget, where he worked as a Budget Examiner and later as a Branch Chief. He has worked as a Legislative Assistant in the Senate, as the Director of Federal Relations for an association of research universities, and as the Associate Director for Budget of the National Institutes of Health. He received a Bachelor's Degree from the University of California, Santa Cruz, and a Masters in Public Policy from the University of California, Berkeley.

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