National Human Genome Research Institute

Department of Health and Human Services
National Institutes of Health

Fiscal Year 2006 Budget Request

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

March 9, 2005

and

Senate Subcommittee on Labor-HHS-Education Appropriations

April 6, 2005

Francis S. Collins, M.D., Ph.D.
Director, National Human Genome Research Institute

Mr. William Beldon, Deputy Assistant Secretary, Budget

Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2006 President's budget request for the National Human Genome Research Institute (NHGRI). The FY 2006 budget includes $490,959,000, an increase of $2,351,000 over the FY 2005 enacted level of $488,608,000 comparable for transfers proposed in the President's request.

Cable News Network (CNN) recently named the completion of the Human Genome Project (HGP) the number one health news story of the past 25 years. CNN reported, "Much of the marvel of medicine has to do with discovery. Mapping the human genome, the complete sequence of DNA, gave scientists a blueprint for building a person, making it the No. 1 medical story, according to a distinguished panel CNN gathered to rank the top 25 medical stories of the past quarter-century." As the leader of the HGP, the National Human Genome Research Institute (NHGRI) is very proud of this recognition, but as CNN also pointed out there is still a great deal more to learn.

Ongoing NHGRI Initiatives

Analysis of the Completed Human Genome Sequence

In October 2004, the International Human Genome Sequencing Consortium, led in the United States by the NHGRI and the Department of Energy, published a description of the finished human genome sequence in the journal Nature. An international team worked to convert the draft genome, published in 2001, into a highly accurate form. The new analysis reduces the estimate of the number of human protein-coding genes from 35,000 to only 20,000-25,000-a surprisingly low number for our species, considering that only a decade ago most scientists thought there would be over 100,000 genes. We now focus on the more difficult task of understanding the function of each of these genes.

Use of Comparative Genomics to Understand the Human Genome

The availability of the genome sequences of the human, the mouse, the rat and a wide variety of other organisms is driving the development of an exciting new field of biological research, comparative genomics. The NHGRI is funding research comparing the finished reference human genome sequence with that of other organisms, to identify regions of similarity and difference, thus dramatically increasing understanding of the structure and function of human genes to enable development of new strategies to combat human disease.

ENCyclopedia Of DNA Elements (ENCODE) project

With the goal of identifying the precise location and function of all sequence-based functional elements in the human genome, the NHGRI launched the ENCyclopedia Of DNA Elements (ENCODE) project in the fall of 2003. The project is an international consortium of computational and laboratory-based scientists open to all investigators who agree to abide by the project's criteria and guidelines for participation. A manuscript describing the ENCODE project appeared in the October 22, 2004 issue of Science, detailing the rationale and strategy behind the quest to produce a comprehensive catalog of all parts of the human genome crucial to biological function, including all protein-coding genes, non-protein-coding genes, regulatory elements involved in the control of gene transcription, and DNA sequences that mediate chromosomal structure and dynamics. All data generated for the ENCODE project are being deposited in free, public databases as soon as they are experimentally verified.

Progress with the HapMap

All diseases have a hereditary component, but for most common diseases like diabetes, heart disease, and mental illness, the gene variants responsible for the increased risk have been difficult to identify. To solve this problem, an approach to scan large regions of chromosomes to find the genetic variants (called SNPs, or single nucleotide polymorphisms) that increase or decrease the risk of disease is needed. NHGRI has taken a leadership role in the International HapMap Consortium and the development of the HapMap (haplotype map), a catalog of human genetic variations and how that is organized into haplotype "neighborhoods" across the gene. Researchers are already starting to use the HapMap to find genes and variants that contribute to many diseases; it will also be a powerful resource for studying the genetic factors contributing to variation in individual response to disease, drugs, and vaccines.

In February 2005, the International HapMap Consortium completed phase I of the project, ahead of schedule. Boosted by an additional $3.3 million in public-private support, the NHGRI announced plans to create an even more powerful map of human genetic variation than originally envisioned. The consortium's new goal is an improved version of the HapMap about five times denser than the original plan. This "Phase II" HapMap will test another 4.6 million SNPs from publicly available databases and add that information to the map. The HapMap will be completed in the fall of 2005.

Gene Variants May Increase Susceptibility to Type 2 Diabetes

Understanding the genetic basis of the more common, polygenic diseases has traditionally been very difficult. But the tools of genomics, especially HapMap, are beginning to reveal many details about the risk of common diseases that had previously been unapproachable. One disease for which excellent progress has been made towards understanding

its genetic cause is Type 2 diabetes. Affecting about 17 million people nationwide, it accounts for 90 to 95 percent of all diabetes cases in the U.S. This past year, two international research teams, including one at NHGRI, each found variants in a gene that appears to predispose people to type 2 diabetes, the most common form of the disease. Homing in on a wide stretch of chromosome 20, the teams identified four genetic variants (SNPs) that are strongly associated with type 2 diabetes in Finnish and Ashkenazi Jewish populations and that appear to raise the risk of type 2 diabetes by about 20 to 30 percent. Translating this discovery into a treatment that benefits people with diabetes or those at risk is still years away, but this is a major step in that direction.

New Initiatives

Roadmap - Chemical Genomics

The Molecular Libraries Roadmap initiative will offer public sector researchers access to libraries of novel small organic molecules that can be used as chemical probes to study the functions of genes, cells, and biochemical pathways. This marriage of chemistry and biology will provide new ways to explore the functions of major components of cells in health and disease. In June 2004, NHGRI announced the establishment of the NIH Chemical Genomics Center, and up to eight pilot extramural centers will be funded at academic institutions and other locations across the country in the spring of 2005. These will function as an integrated network, including a common publicly available database (PubChem, already activated in September 2004) which will display the results of all screens of chemical compounds.

Human Cancer Genome Project

The dramatic drop in costs of DNA sequencing, catalyzed by the Human Genome Project, now makes it possible to use sequencing as a major tool for medical research. Doctors and research scientists have long known that cancer is, essentially, a genetic disease. Inherited mutations or acquired genetic alterations can set a normal cell on a path of uncontrolled growth and malignancy. It is now conceivable to identify the complete universe of genes involved in every type of cancer. That is the intent of a bold new NCI/NHGRI proposal for a Human Cancer Genome Project. Such a complete inventory of cancer genes will provide powerful new ways to prevent, diagnose, and treat every major form of the disease.

The $1,000 Genome Project

The ability to determine the complete genome sequence of an individual could revolutionize medical care. In October 2004, NHGRI awarded more than $38 million in grants to spur the development of innovative technologies designed to reduce the cost of DNA sequencing dramatically. NHGRI's near-term goal is to lower the cost of sequencing a mammalian-sized genome to $100,000, which would enable researchers to sequence the genomes of hundreds or even thousands of people as part of studies to identify genes that contribute to cancer, diabetes, and other common diseases. Ultimately, NHGRI's vision is to cut the cost of whole-genome sequencing to $1,000 or less, which would enable the sequencing of individual genomes as part of medical care. The ability to sequence each person's genome cost-effectively could give rise to more individualized strategies for diagnosing, treating, and preventing disease. Such information could enable doctors to tailor therapies to each person's unique genetic profile.

The U.S. Surgeon General's Family History Initiative

The U.S. Surgeon General's Family History Initiative was launched on November 8, 2004, with the NHGRI as the lead collaborating federal agency. The purpose of this national public health campaign is to: increase the awareness of the American public and their health professionals about the importance of family history in health; provide tools to gather, understand, evaluate, and use family history to improve health; give health professionals tools to communicate

with patients about family history; and increase genomic and health literacy. A web based and print tool entitled "My Family Health Portrait" was developed in both English and Spanish to facilitate collection of family history data. To date, the initiative has been highlighted in more than 1,000 media stories and over 170,000 copies of the tool have been distributed via the World Wide Web and in paper form. This public health campaign is intended to be an annual event.

ELSI Centers for Excellence Program

On August 31, 2004, the NHGRI's Ethical Legal and Social Implications (ELSI) research program announced the funding, with contributions from the Department of Energy and the National Institute of Child Health and Human Development, of four interdisciplinary centers as part of its Centers for Excellence in ELSI Research (CEER) program, a new initiative to address some of the most pressing ethical, legal, and social questions facing individuals, families, and communities in the genome era. Each of the centers, based at Duke University, Case Western Reserve University, Stanford University, and the University of Washington, will assemble a team of experts in several disciplines, such as bioethics, law, behavioral and social sciences, clinical research, theology, public policy, and genomic research.

Other Areas of Interest

Genetic Education for Health Care Professionals

The NHGRI has developed numerous educational programs to prepare health care professionals for the integration of genomics into primary health care. A new effort by the NHGRI in this area in 2004 was its work with the American Academy of Family Physicians (AAFP) to develop the AAFP's 2005 Annual Clinical Focus program, which has Genomic Medicine as its theme.

Genetic Nondiscrimination

Possibly the greatest impediment to the advancement of genomic science and its application to human health is the fear of genetic discrimination. The NHGRI has worked for ten years to realize a federal solution to this problem. The Secretary's Advisory Committee on Genetics Health and Society has also strongly supported the need for federal legislation. On February 17, 2005 the Senate passed the Genetic Information Nondiscrimination Act of 2005 (S. 306), which would address these fears, and the Bill has now been referred to the House. The Bush Administration has also 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, 1972 - M.S.; 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 that is 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.

William R. Beldon

Department of Health and Human Services
Office of Budget

Mr. Beldon is currently serving as Deputy Assistant Secretary, Budget in the Department of Health and Human Services. He has been a Division Director in the Budget Office for sixteen years, most recently as Director of the Division of Discretionary Programs. Mr. Beldon started in federal service as an auditor in the Health, Education and Welfare Financial Management Intern program. Over the course of more than 30 years in the Budget Office, Mr. Beldon has held Program Analyst, Branch Chief and Division Director positions. Mr. Beldon received a Bachelor=s Degree in History and Political Science from Marshall University and attended the University of Pittsburgh where he studied Public Administration. He resides in Fort Washington, Maryland.

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