DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2009 Budget Request

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

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Richard J. Turman, Deputy Assistant Secretary, Budget

Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2009 President's budget request for the National Human Genome Research Institute (NHGRI). The FY 2009 budget includes $487,878,000; an increase of $1,099,000 from the FY2008 enacted level of $486,779,000.

NIH's investment in the Human Genome Project (HGP) and the International HapMap Project have moved us closer to a future that uses genomic information to diagnose, treat, and prevent disease.

DISEASE-GENE ASSOCIATIONS

The HapMap has introduced a new paradigm to genomic research, primarily in the form of genome-wide association studies (GWAS), enabling cost-efficient assessment of much of the common genomic variation within an individual. The GWAS approach is novel in that it surveys the genome comprehensively and without preconception as to the relationships between genetics and disease, whereas earlier research efforts were largely focused on candidate genes thought to be associated with specific diseases. The innovative GWAS approach allows for the identification of genes involved in common diseases, contributing to a better understanding of the development and progression of common diseases, and pointing to follow-up research that may lead to improved diagnostic, therapeutic, and preventive approaches.

With unprecedented speed, researchers have applied used GWAS to identify a stunning number – over 70 in 2007 alone – of genetic factors associated with the most common causes of morbidity and mortality in the United States, such as diabetes, cardiovascular disease, obesity, cancer, and multiple sclerosis. Identification of gene variants associated with disease raises the possibility of using genetic testing, in combination with family history information, to identify susceptible, pre-symptomatic subjects for screening and preventive therapies. The pace of disease-gene discovery is likely to accelerate even further over the next two or three years due to the completion in 2007 of the second-generation map of human genetic variation (Phase II HapMap).

This updated and powerful tool allows researchers to identify variations associated with disease even more quickly and accurately.

APPLYING NEW KNOWLEDGE ABOUT THE GENOME TO HEALTH

The NHGRI has increasingly directed the power of its large-scale sequencing program, which fueled the completion of the Human Genome Project, toward the long-range objective of making human DNA sequencing a tool for both research and medical practice. New directions include obtaining genomic sequence data from many individuals with various physical traits and disease states -- data that will prove critical for addressing a wide range of questions important for advancing biomedicine. To move these advances more rapidly into clinical care, in 2007 the NHGRI established the Genomic Health Care Branch within its Office of Policy, Communication, and Education. The new branch's mission is to help facilitate the translation of genomic research into advances in clinical medicine, especially in the primary care setting.

THE CANCER GENOME ATLAS

The Cancer Genome Atlas (TCGA) is a joint NCI-NHGRI effort to accelerate understanding of the molecular basis of cancer through application of genome analysis technologies. TCGA began in 2005 with a three-year, $100 million pilot project to determine the feasibility of a full-scale effort to explore the universe of genomic changes involved in all human cancers.

THE HUMAN MICROBIOME

There are more bacteria in the human gut than cells in the entire human body. Furthermore, microbes in the gut, skin, oropharynx, and vagina have a profound effect on many human physiological processes, such as digestion and drug metabolism, and play a vital role in disease susceptibility and even obesity. The Human Microbiome Project, conducted under the auspices of the NIH Roadmap Project and co-led by the NIAID, NIDCR, and NIDDK, represents an exciting new research area for the NHGRI.

TECHNOLOGY ADVANCES, ON THE WAY TO THE $1,000 GENOME

In August 2007, the NHGRI awarded grants to advance the development of innovative sequencing technologies intended to reduce even further the cost of DNA sequencing and expand the use of genomics in biomedical research and health care. With NHGRI support, excellent progress has been made toward both the near-term goal to lower the cost of sequencing a mammalian-sized genome to $100,000, and the longer-term goal of $1,000 or less.

CHEMICAL GENOMICS AND MOLECULAR LIBRARIES

The chemical genomics initiative offers public sector researchers access to high-throughput screens to test small organic molecules for potential uses as research tools. This initiative will even help expedite the development of innovative drugs for rare diseases, by demonstrating how early stage compounds interact with novel molecular targets. This program provides direct translation of genomic medicine by identifying small molecule drug-like compounds that can be used as starting points for new treatments, or as new applications of that agent.

KNOCKOUT MOUSE PROJECT

The technology to "knock out," or inactivate, genes in mouse embryonic stem has led to many insights into human biological processes and human disease. However, information about knockout mice has only been published and made available to the research community for about 20 percent of the estimated 20,000 mouse genes. Recognizing the wealth of information that mouse knockouts can provide, the NHGRI launched a trans-NIH, coordinated, five-year cooperative research plan that, in cooperation with European and Canadian programs, will produce knockout mice for every mouse gene and make these mice available as a resource to the entire community.

1,000 GENOMES

The 1000 Genomes Project is an international research project that will sequence the genomes of at least a thousand people from around the world to create the

most detailed and medically useful picture to date of human genetic variation. The 1000 Genomes Project seeks to produce a publicly available catalog of variants that are present at 1 percent or greater frequency in the human population across most of the genome.

ClinSeq

The purpose of ClinSeq, an intramural NHGRI research initiative, is to pilot large-scale medical sequencing (LSMS) in a clinical research setting and to investigate some of the technical and medical issues that accompany the implementation of LSMS in clinical settings. Currently, ClinSeq is recruiting 1,000 participants across the spectrum of risk for coronary heart disease (CHD). Relationships between patients' genetic makeups and observed phenotypes will be explored to better understand how variations in genes relate to cardiac health status.

MULTIPLEX

The NHGRI and the NCI have teamed up with Group Health Cooperative in Seattle and Henry Ford Health System in Detroit to launch the Multiplex Initiative, a prospective study that is enrolling young, healthy adults to learn how they react to the offer of genetic testing for a panel of 15 genes linked to eight common conditions. The study will follow individuals who decide to have the testing to see how they interpret and use the results in making future health care decisions. This study should provide insights that will be important to advancing the realization of personalized medicine.

ENCODE (Scale Up and ModENCODE)

We are continuing to expand the ENCyclopedia Of DNA Elements (ENCODE) project, a research consortium that, in its pilot phase, yielded provocative new insights into the organization and function of the human genome. The NHGRI is moving forward with a full-scale initiative which should provide a more comprehensive picture of the biological roots of human health and disease. We are also engaged in a new effort, called the model organism ENCODE (modENCODE), to apply many of the ENCODE methods and technologies to the genomes of model organisms such as

worms and fruit flies, to inform our efforts to understand how the human genome functions.

MINORITY OUTREACH ACTIVITIES AND HEALTH DISPARITIES

The NHGRI remains at the forefront of ensuring that minority scientists and students are equipped to meet the challenges of genome research in the 21st century. With support from several Institutes and Centers, the NIH has created the NIH Intramural Center for Genomics and Health Disparities (NICGHD) within the NHGRI Division of Intramural Research, with a mission of advancing research into the role of culture, lifestyle, genetics, and genomics in health disparities

GENETIC DISCRIMINATION

The NHGRI remains concerned about the impact of potential genetic discrimination on research and clinical practice as a wealth of research has demonstrated that many Americans are concerned about the possible misuse of their genetic information by health insurers or employers. The Genetic Information Nondiscrimination Act of 2007 passed the House by a vote of 420-3 in April 2007. The Senate bill is still pending. The President visited the NIH in January 2007 and reiterated his previously declared desire to see Congress pass such a bill to protect Americans from genetic discrimination in health insurance and employment, and the administration issued a Statement of Administrative Policy in support of H.R. 493 after it passed the House last spring.

MEDICINE IN THE FUTURE

Broad investment in innovative, large-scale and adaptable models of research such as GWAS may accelerate the timeline for the development of advances in clinical options and thereby contribute to a decrease in the public health burden of many common diseases. We expect that federal legislation preventing discriminatory uses of genetic information will have been enacted. With such protections in place, we anticipate that individual genome sequencing will become both commonplace and affordable, and that primary care physicians will routinely consult their patients' genome analyses for prediction of risk, diagnosis, and drug and dosage selections. If

the public and the medical community are appropriately educated about both the significance and the limitations of genomic information, it may be possible to lessen the burden of disease through better screening and prevention programs, to minimize or avoid toxicities from drugs, and to select the right drug for the right patient, at the right time.

FRANCIS S. COLLINS, M.D., PH.D.

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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 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.

Department of Health and Human Services
Office of Budget
Richard J. Turman

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