National Human Genome Research Institute

Fiscal Year 2005 Budget Request

Department of Health and Human Services

William Beldon, Acting Deputy Assistant Secretary, Budget

Statement by:

Dr. Francis S. Collins
Director, National Human Genome Research Institute

On

Fiscal Year 2005 President's Budget Request
for the National Human Genome Research Institute

April 1, 2004

Mr. Chairman,

I am pleased to present the President's budget request for the National Human Genome Research Institute for fiscal year 2005, a sum of $492,670,000, which reflects an increase of $13,842,000 over the FY 2004 Final Conference appropriation.

Following the completion of the Human Genome Project last year, the National Human Genome Research Institute (NHGRI) of the National Institutes of Health announced an ambitious plan for applying genomics to human health benefits. *A Vision for the Future of Genomics Research,* the outcome of almost two years of intense discussions with over 600 scientists and members of the public, has three major areas of focus: Genomics to Biology, Genomics to Health and Genomics to Society. Several ambitious projects are already underway to help achieve this vision including the International Haplotype (HapMap) Project, the Encyclopedia of DNA Elements (ENCODE), the NIH Roadmap initiative on Molecular Libraries and a new Ethical, Legal and Social Implications (ELSI) Center initiative. As we enter the genomic era, the continued support of biomedical research in this area is more vital than ever.

ONGOING NHGRI INITIATIVES

International HapMap Project

To study genetic variation more effectively across the human genome, the NHGRI and a team of partners has launched the International HapMap Project. The goal of the project is to determine the common patterns of DNA sequence variation in the human genome and to make this information freely available in the public domain. This international consortium is developing a map of these patterns across the genome by determining the genotypes of one million or more sequence variants in DNA samples from populations with ancestry from Africa, Asia and Europe. When complete, the HapMap will enable the discovery of sequence variants that affect common disease, the development of diagnostic tools and the ability to choose targets for therapeutic intervention. Detailed information about the HapMap project was published in a landmark article in *Nature* and updated details can be found on the Web at http://hapmap.ncbi.nlm.nih.gov/.

Comparative Genomics to Understand the Human Genome

One of the most powerful approaches for unlocking the secrets of the human genome is comparative genomics. While the completed sequence of the human genome represents a milestone of historic proportions, a daunting challenge that still lies ahead is to interpret its biological meaning and function. Recently sequenced genomes of the mouse, rat and a wide variety of other organisms 13 from yeast to chimpanzees 13 prove that the genomes of other species are amongst the most powerful tools in advancing understanding of the human genome. The current NHGRI-supported, large-scale sequencing centers have built a prodigious capacity for and expertise in, sequencing entire genomes. The combined capacity of these centers is expected to yield the equivalent of about 20 additional draft vertebrate genomes in just the next three years. These additional species sequences will provide exciting new insights into the function of the human genome and will assist genome scientists in translating the basic findings of the Human Genome Project into tangible applications, including the diagnosis, prevention and treatment of disease.

ENCODE 13 ENCyclopedia Of DNA Elements

To understand the meaning of the human instruction book, the genome, the identities and precise locations of all functional elements must be determined. Thus, the NHGRI has launched the ENCyclopedia Of DNA Elements (ENCODE) project to identify these elements comprehensively. The ENCODE project seeks to characterize the tools needed for exploring genomic sequence, improve those tools when necessary and define a clear path for the determination of all of the functional elements in the entire human genome. On October 9, 2003, the NHGRI announced the first ENCODE grants in a three-year, $36 million project (www.genome.gov). ENCODE begins as a pilot effort to evaluate methods for the exhaustive identification and verification of functional sequence elements in a carefully selected 30 million base pairs, or about one percent, of human genomic DNA. This will require access to information, resources, ideas, expertise and technology beyond the capabilities of any single group. Therefore, a consortium of investigators with diverse backgrounds and expertise will work cooperatively to carry out this project to: (1) evaluate rigorously the relative merits of a varied set of computational and experimental techniques, technologies and strategies for identifying the functional elements in human genomic sequence and (2) test the capabilities of such methods to scale up efficiently to allow, ultimately, analysis of all the functional elements encoded in the entire human genome sequence.

Centers Of Excellence In Genomic Science (CEGS)

The NHGRI Centers Of Excellence In Genomic Science (CEGS) program has been in place for four years. This program is a centerpiece of the Institute's effort to stimulate new interdisciplinary approaches to genomic research and technology development. A total of about 10 CEGS grants are ultimately expected to be funded. These will generally be five-year awards of up to $3 million per year. Seven awards have been made to date; each involves multiple

investigators and disciplines and several cut across departments and institutions. A grantee meeting in October 2003 stimulated new collaborations and identified ways to share CEGS grant data and resources with the larger research community.

Clinical Research Activities in the NHGRI Intramural Program

Research efforts of NHGRI Division of Intramural Research (DIR) investigators are aimed at deciphering the genetic contributions to common disorders, to provide a better understanding of diseases such as cancer, diabetes and heart disease, as well as to a number of less common but equally debilitating afflictions. DIR investigators have been at the forefront of scientific innovation, developing a variety of research approaches that accelerate the understanding of the molecular basis of disease. These include the development of DNA microarray technologies for large-scale molecular analyses, innovative computer software to study fundamental biological problems, animal models critical to the study of human inherited disorders and the clinical testing of new therapeutic approaches for genetic disease. Three examples of gene discoveries within the past year include the gene responsible for Hutchinson-Gilford progeria syndrome, the disease causative gene for Charcot-Marie-Tooth disease type 2D and a gene variant that contributes to the risk of type 2 diabetes. These and other advances should ultimately lead to improved diagnostic, prevention and treatment strategies having a direct impact on human health.

NEW INITIATIVES

The NHGRI is very enthusiastic about the initiatives included in the NIH Roadmap and is deeply involved in implementation plans for several of the projects embodied in the 1CNew Pathways to Discovery 1D theme.

Molecular Libraries

As part of its *Vision for the Future of Genomics Research* and in partnership with many other NIH Institutes as part of NIH's new Roadmap for Medical Research, the NHGRI is taking a lead role in providing access to high throughput screens for small organic molecules to public sector researchers. These small molecules can be used as chemical probes to study cellular pathways in great depth and will broadly enable public and private biomedical research into basic biology and accelerate the validation of new therapeutic targets and thus the discovery of new drugs. For this effort to provide maximal benefits, the library of small molecules must contain a sufficient number of compounds. To build such a library, a network of six national centers will establish a common collection of 500,000 or more chemically diverse small molecules, of both known and unknown activities. Investigators who develop assays suitable for high throughput screening will apply for access to these centers. After peer review, suitable assays will be run through a screen of 500,000 or more compounds and the positives subjected to a first pass of chemical optimization to generate useful compounds. We anticipate that this new resource will catalyze a genuine paradigm shift, because it will give academic investigators a new and powerful research tool not previously at their disposal.

$1000 Genome Sequence

Current sequencing costs are too high to collect the quantity and quality of genome sequences optimal for research and clinical applications. Completely sequencing the genomes of many individuals would greatly advance understanding of the role of DNA sequence variation in human health, but using DNA sequence information for care of individuals is not possible at current costs. Thus, NHGRI has launched an aggressive program to develop technologies to lower the cost of DNA sequencing dramatically. The goal for the first five years of this program is to develop the capability to produce a high quality draft sequence for a large, complex (e.g., mammalian) genome for $100,000. The goal of the second phase, which is estimated to take ten years, is producing a genome sequence for $1000. Once achieved, a $1000 genome analysis would be of great use to correlate DNA information with health

outcomes. This includes determining genes in each individual that predispose that individual to specific diseases and assessing which drugs are likely to elicit adverse reactions in each individual, so that drugs can be used more effectively and with fewer side effects.

Centers for Excellence in ELSI Research

The NHGRI Ethical Legal and Social Implications (ELSI) research program recently released a Request for Applications inviting proposals for the development of Centers of Excellence in ELSI Research (CEER). The CEER program is designed to support the development of groups that will pursue research questions best approached through intensive and extended collaboration among investigators from multiple disciplines, using diverse methodologies. CEER investigators are encouraged to consider new ways to explore these questions, design innovative and efficient research projects, propose and disseminate health or social policy options based on Center research and, when feasible, facilitate policy development pertinent to a specific issue. Center applicants are particularly encouraged to identify cutting edge research topics and approaches that may lead to high payoff solutions to important ELSI problems.

Intramural Social and Behavioral Research Branch

The NHGRI has formed a new Social and Behavioral Genetics Research Branch within its intramural research program. The main focus of the Branch is to conduct research on the social and behavioral aspects of translating genomic discoveries into improved health. The Branch will also: 1) study innovative ways of applying genetic discoveries to promote health and well-being; 2) apply social, behavioral and communication theories to understand how to communicate genetic risk effectively; 3) develop and refine evidence-based methods of communicating genetic risk to individuals, families, communities and populations; 4) seek to understand how social factors influence genetic discoveries and research; and 5) investigate the ethical and public policy implications of genetic research and the use of genetics in clinical practice.

OTHER AREAS OF INTEREST FOR NHGRI

Genetic Discrimination

The NHGRI remains concerned about the risk of genetic discrimination and supports the President's call for federal legislation. Many Americans are worried that insurers and employers may use genetic information to deny, limit, or cancel their health insurance or to discriminate against them in the workplace. A total of 41 States have enacted legislation on discrimination in health insurance and 31 have enacted legislation on workplace genetic discrimination. However, only comprehensive federal legislation can guarantee everyone in the United States protection from genetic discrimination. Last October, the full U.S. Senate voted unanimously (95-0) in favor of the "Genetic Information Nondiscrimination Act of 2003 1D (S. 1053)," which would address this problem. It is hoped that the House will soon take similar steps.

Intellectual Property Rights in Genetics and Genomics Research

NHGRI has long worked on issues of intellectual property related to genetic and genomic data. The NHGRI ELSI program plans soon to issue a new initiative to encourage studies of the role of intellectual property rights in genetics and genomics research, as well as the impact of exclusivity on progress in these fields. The initiative will support legal, economic, political science and statistical analyses and empirical investigations of theories and practices of rights holders, stakeholders and researchers in genetics and genomics research and development, with the specific goal of helping build the research base necessary to inform the rational development of future policy options regarding intellectual property in genetics and genomics.

The NHGRI, with several other NIH Institutes, has recently provided funds for a National Academy of Sciences' study, 1CIntellectual Property in Genomic and Protein Research and Innovation. 1D This 18-month study, involving experts from law, public policy and genomics, will address such important questions as: What is the impact of intellectual property and licensing on genetic and proteomic research? What policy options should be considered in this area? How have other regions of the world addressed these issues? It is hoped that this study will provide insights on how to address the thorny issues surrounding the interface of intellectual property, biomedical research and patient care.

Direct-to-Consumer Marketing of Genetic Tests

Marketing of products or services that promise to provide consumers with genetic insights into personal health has proliferated dramatically in recent years. NHGRI's intramural Division of Bioethics has systematically studied this issue. So far, researchers have found that many direct-to-consumer (DTC) advertisements exaggerate the scientific basis of claims made and/or fail to communicate effectively the current limitations of the specific genetic knowledge discussed. In particular, the Internet has provided a powerful medium for the construction of 1Cinformational 1D resources through which DNA analysis is often linked to a claim to individualize consumer profiles for specific products available through the Website. Additionally, the first example of a multi-media DTC advertising campaign for a genetic test, the BRCA1/2 test, was piloted in two metropolitan areas in the last year. The NHGRI recently held a workshop to assess DTC marketing of genetic tests and considered the scope of the practice and possible policy options. The NHGRI will work with the Secretary's Advisory Committee on Genetics Health and Society on this issue.

Trans-NIH Obesity Initiative

The NHGRI Deputy Director represents the Institute on the trans-NIH obesity working group. We believe that this initiative is vitally important and that the genomic tools produced by the Human Genome Project can be of considerable utility in discerning the role of genes and environment in causing obesity and in predicting which obese individuals will develop which diseases.

CONCLUSION

With the completion of the human genome sequence, we have fully entered the genomic era. The NHGRI has now spearheaded many specific and innovative initiatives to understand how genetics affects human health, the ultimate motivation for the Human Genome Project. The most interesting and important applications of genomics lie not behind us, but ahead of us. Continued investment by the Congress in genetic/genomic research is vital to our efforts to enhance the health of all.

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

Director, National Human Genome Research Institute

Born April 14, 1950. Staunton, Virginia

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.

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.

Awards and Honors:
Award of the Cystic Fibrosis Foundation, 1989; Gairdner Foundation International Award, 1990; National Medical Research Award, National Health Council, 1991; American Academy of Achievement Golden Plate Award, 1994; The Baxter Award for Distinguished Research in Biomedical Sciences, Association of American Medical Colleges, 1994; Susan G. Komen Breast Cancer Foundation National Award for Scientific Distinction, 1995; Cystic Fibrosis Foundation, 1997; Mendel Medal, Villanova University, 1998; Champions of Pediatric Research Award, Children's National Medical Center, 1998; Shattuck Lecture, Massachusetts Medical Society, 1999; Arthur S. Flemming Public Service Award, 1999; Association of American Physicians, Scientist of the Year, The Biotechnology Industry Organization and The Chemical Heritage Foundation Third Annual Biotechnology Award, 2001; Warren Triennial Prize Lecture, Massachusetts General Hospital, 2002; Lifetime Achievement Award, Virginia Biotechnology Association, 2002; 2002 Gairdner Foundation International Award of Merit; 51st National Prayer Breakfast Leadership Luncheon Speaker, 2003; Walker Prize, Museum of Science, Boston, Massachusetts, 2003. William Belden Noble Lecturer, Harvard Memorial Church, 2003, 51 st , American College of Physicians-American Society of Internal Medicine Award, 2003, Secretary of the Department of Energy Gold Award, 2003, Colonel Sanders Lifetime Achievement Award, March of Dimes, 2004

Honorary Doctoral Degrees:
Emory University, Mary Baldwin College, Yale University, Mount Sinai School of Medicine, University of North Carolina, George Washington University, University of Pennsylvania, Brown University.

Department of Health and Human Services
Office of Budget

William R. Beldon
Mr. Beldon is currently serving as Acting Deputy Assistant Secretary for Budget, HHS. He has been a Division Director in the Budget Office for 16 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 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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