

DEPARTMENT OF HEALTH AND HUMAN SERVICES

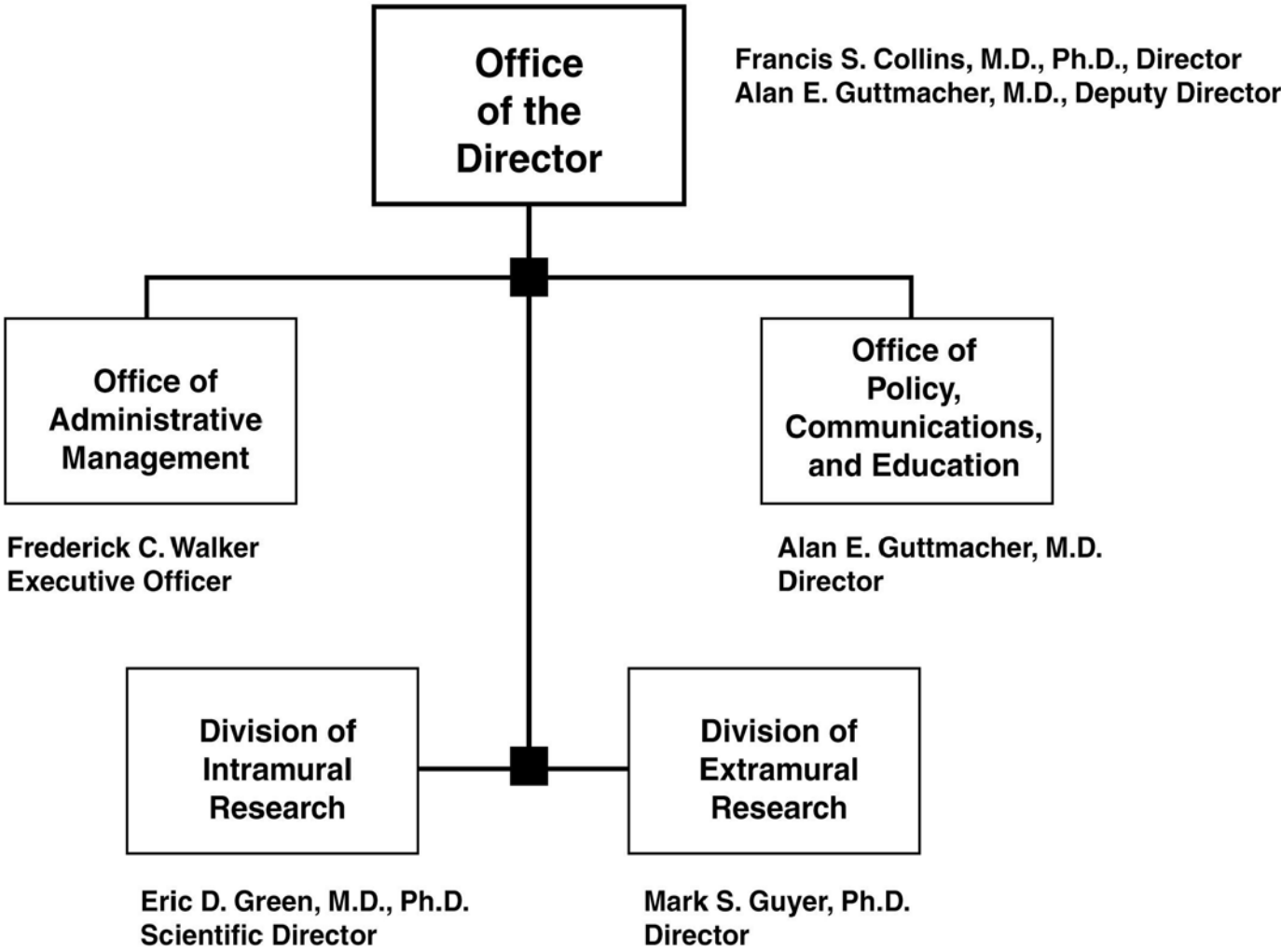
NATIONAL INSTITUTES OF HEALTH

National Human Genome Research Institute

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NATIONAL HUMAN GENOME RESEARCH INSTITUTE

Organizational Structure



NHGRI-2

NATIONAL INSTITUTES OF HEALTH

National Human Genome Research Institute

For carrying out section 301 and title IV of the Public Health Service Act with respect to human genome research, [\$482,222,000] *\$492,670,000*.

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Omnibus Consolidated Appropriations Act for Fiscal Year 2004]

**National Institutes of Health
National Human Genome Research Institute**

Amounts Available for Obligation 1/

Source of Funding	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Appropriation	\$468,037,000	\$482,222,000	\$492,670,000
Enacted Rescissions	(3,042,000)	(3,149,000)	---
Subtotal, Adjusted Appropriation	464,995,000	479,073,000	492,670,000
Comparative transfer from: Fogarty International Center for International Services Branch	25,000	0	0
Comparative transfer to NIBIB for Radiology Program	(63,000)	(62,000)	(0)
Comparative transfer to Buildings and Facilities	(157,000)	(183,000)	(0)
Comparative transfer to Office of the Director for program changes	(415,000)	(0)	(0)
Subtotal, adjusted budget authority	464,385,000	478,828,000	492,670,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	464,385,000	478,828,000	492,670,000
Unobligated balance lapsing	(34,000)	---	---
Total obligations	464,351,000	478,828,000	492,670,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:

FY 2003 - \$3,797,000; FY 2004 - \$4,198,000; FY 2005 - \$4,466,000

Excludes \$227,000 in FY 2003 and \$233,000 in FY 2004 for royalties.

Justification

National Human Genome Research Institute (NHGRI)

Authorizing Legislation: Section 301 and Title IV of the Public Health Service Act, as amended.
Reauthorizing legislation will be submitted.

Budget Authority:

FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Increase or Decrease	
<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>
289	\$464,385,000	288	\$478,828,000	289	\$492,670,000	+1	+\$13,842,000

This document provides justification for the Fiscal Year 2005 activities of the National Human Genome Research Institute (NHGRI), including HIV/AIDS activities. Justification of the National Institutes of Health (NIH)-wide FY 2005 AIDS activities can be found in the NIH section entitled “Office of AIDS Research (OAR).”

INTRODUCTION

The year 2003 was momentous for the field of genomics with the completion of the Human Genome Project (HGP) more than two years ahead of schedule and under budget, and thus the launching of a new era. This new era will transform biomedical research and is already having a profound impact on medicine.

With the essential completion of the human sequence also came a new “Vision for the Future of Genomics Research,” which sets out a clear plan for future genomic research in three main areas: Genomics to Biology, Genomics to Health, and Genomics to Society. This vision, developed with the input of over 600 advisors, not only sets out grand challenges for the field of genomics, but also delineates the role of the National Human Genome Research Institute (NHGRI) in reaching these goals. The NHGRI also coordinated with schools and museums across the country to hold a number of educational events at the time of the completion of the project so that the American people would learn more about the implications of HGP and the new vision. It is hoped that this vision will inspire the current and next generations of genetic and genomic scientists to lead the field of biomedical research to improved diagnosis, prevention, and treatment of disease.

A Vision for the Future of Genomic Research can be found at www.genome.gov

STORIES OF DISCOVERY

Completion of the Human Genome Sequence

April 2003 witnessed the announcement by the International Human Genome Sequencing Consortium, led by the NIH, of the successful completion of the Human Genome Project, more than two years ahead of schedule and under budget. With the essential completion of the sequence of the three billion DNA letters in the human genome, all the goals of the Human Genome Project were completed successfully. This landmark initiative essentially launches the genome era.

The finished sequence covers about 99 percent of the human genome's gene-containing regions, and the deposited sequence has an accuracy of greater than 99.99 percent. The project's new research strategies and experimental technologies have generated a steady stream of ever-larger and more complex genomic data sets that have poured into public databases and have transformed the study of virtually all life processes. The genomic approach of technology development and large-scale generation of community resource data sets has introduced an important new dimension into biological and biomedical research. Interwoven advances in genetics, comparative genomics, high-throughput biochemistry, and bioinformatics are providing biologists with a markedly improved repertoire of research tools that will allow analysis and understanding of health and disease at an unprecedented level of molecular detail. Genome sequences, the bounded sets of information that guide biological development and function, lie at the heart of this revolution. In short, genomics has become a central and cohesive discipline of biomedical research.

April 2003 also witnessed the publication of the National Human Genome Research Institute's (NHGRI) landmark scientific report laying out a vision for the future of the field of genomics, and describing the role that the NHGRI, the NIH, and other government agencies will play in enabling that future. The proposed initiatives outlined in this new vision build upon the advances in biology provided by the human sequence.

A scientific paper will be published in early 2004 to provide a summary of how the sequence was completed, a detailed validation of its quality, an analysis of what can be learned that was not apparent from the draft sequence, and a revised gene count. Beyond this initial overview paper, other papers, several of which have already been published, will detail the analysis and gene annotation of each chromosome. These analyses will greatly assist biomedical researchers throughout the world, who are using the sequence to make breakthroughs in disease research.

Collins FS, Green ED, Guttmacher, AE, Guyer, MS: A vision for the future of genomics research. Nature 422: 835-847, 2003.

SCIENCE ADVANCES

Discovering the Gene for Hutchinson-Gilford Progeria Syndrome and its Implication for Aging

A team of scientists in the National Human Genome Research Institute (NHGRI) has discovered the genetic basis of a disorder that causes the most dramatic form of premature aging, a finding that promises to shed new light on this rare disease, as well as on normal human aging.

In 2001, the Progeria Research Foundation (PRF) co-hosted a workshop with various institutes and centers of the National Institutes of Health (NIH), including the National Institute on Aging and the Office of Rare Diseases. The workshop brought together leading scientists from around the world to identify promising areas of research in Hutchinson-Gilford progeria syndrome (HGPS). This partnership eventually led to increased funding for progeria research, derived from the Greek word for old age, "geras," and the formation of the PRF Genetics Consortium, a group of 20 scientists whose common goal is to find the genetic cause of progeria and to develop ways of treating the disease.

As a result of the PRF workshop, a team of NHGRI researchers began studying the genetic basis for HGPS in order to find the genetic link to this rare syndrome. Children with this condition usually appear normal at birth; however, by the age of two years they stop growing, lose their hair, and show skin changes and loss of subcutaneous tissue that resemble the ravages of old age. They rarely live past adolescence, dying almost always of advanced cardiovascular disease - heart attack and stroke. The classic syndrome has never been observed to recur in families, making it particularly challenging to locate the gene, since scientists often depend on familial recurrence to track the genetic culprit. Progeria is estimated to affect one in 4 million newborns worldwide, and there had previously been no diagnostic test or treatment for the progressive, fatal disorder.

Using an array of genomic technologies, such as whole-genome scans and high-throughput sequencing of targeted DNA regions, as well as the recently completed human genome sequence, researchers determined that the most common cause of HGPS is a single letter misspelling in a gene on chromosome 1 that codes for lamin A (*LMNA*), a protein that is a key component of the membrane surrounding the cells' nucleus. Specifically, the researchers found that 18 out of the 20 children with classic HGPS harbored exactly the same misspelling in the *LMNA* gene. In every instance, the parents were found to be normal, indicating that the misspelling was a new, or de novo, mutation in the child.

Researchers are now looking at the *LMNA* genes of people who are exceptionally long-lived to see if there are any variants of the gene associated with longevity. Other studies will focus on determining whether repeated damage to the *LMNA* gene over the course of a lifetime may influence the rates at which people age. The implications of this work may extend far beyond progeria to each and every human being. What is learned about the molecular basis of this model of premature aging may provide a better understanding of what occurs in the body as we all grow older.

Eriksson M, Brown WT, Gordon LB, Glynn MW, Singer J, Scott L, Erdos MR, Robbins CM, Moses TY, Berglund P, Dutra A, Pak E, Durkin S, Csoka AB, Boehnke M, Glover TW, Collins FS (2003) Recurrent de novo point mutations in lamin A cause Hutchinson-Gilford progeria syndrome. *Nature* 423:293-8.

Comparative Genomics to Understand the Human Genome

Background: One of the most powerful approaches for unlocking the secrets of the human genome is comparative genomics - i.e., comparing genome sequences across many organisms to determine similar patterns. While a definitive goal of the Human Genome Project was to finish the sequence of the human genome, a goal that still lies ahead is to interpret its biological meaning and function. The genome includes the blueprints for genes and proteins, the regulatory elements that ensure proper function of all genes, the structural elements that govern chromosome behavior, and the rich records of our evolutionary history. Some of these features can be easily recognized in the human sequence, but many are subtle and difficult to discern.

The current NHGRI-supported, large-scale sequencing centers have built a considerable capacity for, and expertise in, sequencing entire genomes. Sequencing the genomes of the human, mouse, rat, and a wide variety of other organisms - from yeast to chimpanzees - is driving the development of this exciting new field of biological research which will help determine the function of the human genome.

Advance: A concerted effort to sequence the entire mouse genome was started in October 2000. In December 2002, a publication reported the results of this effort, including the production of a high quality, highly ordered, representative assembly of the genome. Another important organism for use in physiological studies is the rat. In February 2001 NHLBI and NHGRI funded the Rat Genome Sequencing Project, which led to the November, 2002 announcement by the Rat Genome Sequencing Consortium of the completion and assembly of the draft DNA sequence of the laboratory rat. A publication describing the initial analysis of this assembly is forthcoming.

In the summer of 2003, a team led by NHGRI researchers reported results that demonstrate how such comparisons reveal functionally important parts of the human genome beyond the genes themselves. The research team compared the sequence of the same large genomic region in 13 vertebrate species: human, chimpanzee, baboon, cat, dog, cow, pig, rat, mouse, chicken, zebrafish, and two species of pufferfish (*Fugu*, *Tetraodon*). Their results provided dramatic new insights into the functional elements present in this region. In fact, about two-thirds of the most important components had been previously unrecognized by any other method.

Implications: The large-scale sequencing centers supported by NHGRI have just undergone a competitive review process. Their combined capacity is expected to yield the equivalent of about 20 additional draft vertebrate genomes in the next three years. These additional species sequences will provide exciting new insights into the function of the human genome. These discoveries will assist the efforts of genome scientists to translate the basic findings of the Human Genome Project into tangible applications such as the diagnosis, prevention, and treatment of disease.

Thomas JW, Touchman JW, Blakesley RW, et al: Comparative analysis of multi-species sequences from targeted genomic regions. *Nature* 424: 788-793, 2003.

Mouse Genome Sequencing Consortium: Initial sequencing and comparative analysis of the mouse genome. *Nature* 420: 520-562, 2002.

Safer Methods for Gene Therapy

Background: Gene therapy is a promising scientific field that offers fundamentally new ways of curing human diseases. A decade of clinical studies has demonstrated the complexity of the biology behind gene therapy and exposed a number of technical challenges. A new study, conducted by NHGRI researchers, provides insight into one of the most serious current technical hurdles for gene therapy, and suggests ways to surmount it.

Advance: This study demonstrates for the first time that the genetically engineered mouse virus used in many gene therapy trials tends to insert itself at the beginning of genes in the target cell, potentially disrupting the genes' normal function. This discovery may lead to safer gene therapy techniques by re-engineering the virus, or using a different vector. In January 2003, the U.S. Food and Drug Administration (FDA) placed a "clinical hold" on 27 gene therapy studies after two children being treated by French researchers for a form of severe combined immunodeficiency disease developed a leukemia-like condition. These children were treated with an experimental gene therapy using Moloney murine Leukemia Virus (MoMuLV), which presumably integrated randomly into the genome of target cells. But scientists lacked the means to study these integration events in a large-scale fashion.

A team from the NHGRI Genome Technology Branch and the AIDS Vaccine Program of the National Cancer Institute developed a laboratory technique that allowed them to sort through the entire genome of hundreds of individual cells rapidly to see where the retroviruses inserted. They found that MoMuLV does not insert its genes randomly, as had been previously thought. It tends to insert at the beginning of a gene, potentially affecting the way the gene works. The virus is eight times more likely to land at the beginning of a gene than would occur at random. While not clear yet why this occurs, this insight will clearly help scientists determine how best to use MoMuLV for gene therapy. In addition to targeting the beginning of genes, MoMuLV seems to prefer more actively expressed genes. That may explain why the two French gene therapy patients with leukemia showed signs that the vector had integrated next to the LMO2 gene, a gene that is turned on in bone marrow cells to promote the growth of white blood cells. Current evidence suggests that the activation of LMO2 by the viral insertion is responsible for the leukemic state in these two children.

Implications: This work has shown that, by capturing and then sequencing a small bit of the human genome immediately adjacent to where the retrovirus inserts, a laboratory test can easily identify the insertion site in gene therapy. Now that a high-quality, finished copy of the human genome is available in public databases, it only takes the sequence of 30 base pairs (the chemical subunits, or letters, that make up the human genome) to know exactly where in the genome that sequence resides. This exemplifies the laboratory applications for which the finished genome sequence was intended, applications that will soon improve the practice of medicine.

Wu X, Li Y, Crise B, Burgess SM: Transcription Start Regions in the Human Genome Are Favored Targets for MLV Integration. *Science* 300: 1749-1751, 2003.

The Genetic Basis of Maleness: Detailed Analysis of the Human Y Chromosome

Background: The 23 pairs of chromosomes in the human genome bear the three billion DNA letters that carry the genetic blueprint for human life. The analysis of individual chromosomes is an integral part of the Human Genome Project, as they provide the foundational information for the structure, organization, and evolution of the human genome. However, without the highly accurate sequence data produced by the Human Genome Project made freely available to researchers everywhere in the world, such analyses were impossible.

Advance: Researchers from the International Human Genome Sequencing Consortium performed and published in the journal *Nature* a detailed analysis of the reference sequence of the Y chromosome - the chromosome present in males but not in females. The careful analysis revealed an unexpected and a novel mechanism by which this chromosome maintains its genetic integrity.

Unlike all other chromosomes that occur in pairs and preserve genetic integrity by exchanging information with matching genes on the homologous chromosome (a process called "crossing over"), the Y chromosome is unpaired and thus lacks that option. Instead, the Y appears to exchange genes within itself, between two copies of repeated sequences that lie near each other as mirror images. This phenomenon, called gene conversion - the non-reciprocal transfer of genetic information from one DNA molecule to another -- has been previously observed on a small scale over long evolutionary timescales between repeated sequences on the same chromosome, but not at the dramatic frequency apparently employed by the Y chromosome.

Implications: Researchers would not have been able to understand the unusual genetic structure of the Y chromosome without the availability of a highly accurate finished human sequence. Such analyses will speed the discovery of genes and our understanding of how they relate to human health and disease.

With the completion of the Human Genome Project, researchers plan to publish a separate analysis on each completed chromosome over the next year or so. In addition to the Y chromosome, researchers with the International Human Genome Sequencing Consortium have already published analyses of chromosomes 6, 7, 14, 20, 21, and 22.

Skaletsky H, Kuroda-Kawaguchi T, Minx P, et al: The male-specific region of the human Y chromosome is a mosaic of discrete sequence classes. *Nature* 423: 825-837, 2003.

NIH ROADMAP

The NHGRI is very enthusiastic about the initiatives included in the NIH Roadmap and is deeply involved in the implementation plans for Molecular Libraries and Molecular Imaging, Biological Pathways and Networks, Structural Biology, Nanomedicine, Computational Biology, Interdisciplinary Networks, and Public-Private Partnerships. Here we will focus on just one of those initiatives.

Molecular Libraries (“Chemical Genomics”)

As part of the NHGRI *Vision for the Future of Genomics Research*, and now also in partnership with multiple other NIH Institutes as part of NIH’s new Roadmap for Medical Research, the NHGRI will take a lead role in developing the small molecule approach that will offer public sector researchers access to high throughput screens for small organic molecules. These small molecules can be used as chemical probes to study cellular pathways in greater depth. This resource will provide new ways to explore the functions of major components of the cell in health and disease. In addition, it is hoped this initiative will speed the development of new drugs and agents to detect and treat common and rare diseases by providing early stage compounds that encompass a broad range of novel targets and activities.

Three key technological advances drive the NIH’s foray into chemical genomics. First, the successful completion of the Human Genome Project has provided an enormous cache of biological information and identified a wealth of potential new drug targets. Second, developments in combinatorial chemistry have given academic researchers potential access to compounds previously available only to researchers in private sector pharmaceutical and biotechnology companies. Third, advances in robotic technology and informatics now allow investigators to screen hundreds of thousands of compounds in a single day, orders of magnitude greater than was possible a decade ago.

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 chemically diverse small molecules, of both known and unknown activities. Over time, this collection will be expanded and modified to provide a working set of compounds that will target larger domains of “biological space,” the total set of biomolecular surface domains that are capable of interacting with a small molecule. Investigators who have developed assays suitable for high throughput screening will apply for access to the screening centers. After peer review, suitable assays will be run through a screen of 500,000 or more compounds, and the “hits” subjected to a first pass of medicinal chemistry optimization to generate useful compounds. We anticipate that this new resource will be a useful research tool for many academic investigators.

NHGRI INITIATIVES

ENCODE – ENCYClopedia Of DNA Elements

For the scientific community to make the best use of the tremendous resource provided by the Human Genome Project, the identities and precise locations of all sequence-based functional elements in the genome must be determined. To address this issue, the NHGRI has launched a project called the ENCyclopedia Of DNA Elements (ENCODE) to identify comprehensively the functional elements in the human genome.

The ENCODE project begins as a pilot effort that will evaluate methods for the exhaustive identification and verification of functional sequence elements in 30 megabases, or about one percent, of human genomic DNA. This will require access to information, resources, ideas, expertise, and technology beyond the scope of what any single group can currently provide. Therefore, the pilot will be carried out by a consortium of investigators with diverse backgrounds and expertise working cooperatively to (1) evaluate rigorously the relative merits of each of a varied set of computational and experimental techniques, technologies, and strategies for identifying all of the functional elements in human genomic sequence, (2) test the capabilities of such methods to scale up efficiently so that it will ultimately be feasible to use them to analyze all of the functional elements encoded in the entire human genome sequence, and (3) identify and fill gaps in our ability to annotate genomic sequence.

The ENCODE project is intended 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 sequence. A fully annotated human genome sequence will be an integrated information resource that will enable the efforts of the entire research community in both basic and clinical research. On October 9, 2003, the NHGRI announced the first ENCODE grants (www.genome.gov).

It is obvious, however, that current technology is not capable of achieving all of the aims of even the initial phase of the ENCODE project. Therefore, at the same time that high-throughput efforts are being initiated using well-developed technologies, a parallel effort has started to develop new technologies. Simultaneously with the announcement of the ENCODE awards, the NHGRI announced the first set of grants for a companion project intended to expand the repertoire of tools that can be applied to the ENCODE or similar projects in the future. It is envisioned that when such a “tool box” of technologies is available, it will be possible to annotate the human genome with biologic information that will serve as a platform for more in-depth, detailed studies of biological function.

\$1000 Genome Sequence

Completion of the DNA sequence of the human genome and near-completion of several other organisms has clearly demonstrated the value of comparative genomics for understanding the structure and function of the human genome. But current sequencing costs are too high to collect the number and quality of genome sequences that are needed to achieve the desired level of

knowledge. Similarly, understanding the role in disease of DNA sequence variation between different individual humans would be greatly facilitated by completely sequencing the genomes of many individuals, and using DNA sequence information for care of individual patients clearly is not possible given the current costs. Therefore, NHGRI is launching an aggressive program, based on the *Vision for the Future of Genomic Research*, to develop technologies to dramatically lower the cost of DNA sequencing.

In 2004, NHGRI will initiate parallel programs to advance DNA sequencing technology. The goal of the first program is, in five years, to develop the capability to produce a high quality draft sequence for a large complex (e.g., mammalian) genome for \$100,000. The second program has the goal of producing a genome sequence for \$1000; we predict it will take ten years to reach this goal. Achieving those goals would represent 2-3 and 4-5 orders of magnitude reduction, respectively, from current (2003) costs. Different technological approaches will likely be needed to achieve these different goals, and the opportunity costs of skipping the \$100,000 genome, if it can be achieved five years earlier than the \$1000 genome, are large. Therefore, NHGRI believes it is crucial to launch both programs, the \$100,000 genome and the \$1000 genome, at the same time.

Achieving truly inexpensive and distributed sequencing capability would completely change the nature of biomedical research and ultimately health care. The issues are speed, integration and accuracy, each of which has hidden costs. To address the large market that is possible, the sequencing instrument should cost about \$1,000 and work at the appropriate scale. It should integrate much of the “expertise” needed to prepare and analyze the DNA so that the technology will be much more widely accessible than today, (where cost-effective sequencing can only be done in very large, well equipped and well organized sequencing “factories”). Several revolutionary sequencing methods are currently in commercial development. Most of these offer potential to yield large numbers of sequenced DNA base pairs very rapidly from very small volume reactions, in highly integrated systems. Some of these, if successful, could achieve the desired cost and process integration. But they are based on ideas that still need a lot of development.

Once achieved, a \$1000 genome analysis would be of great interest to the health care market for correlating genotype information with health outcomes. This includes determining genes in each individual that predispose that individual, upon interaction with that person’s environment, to specific diseases; and assessing which drugs are likely to elicit an adverse reaction, so that they can be avoided and alternative pharmaceuticals administered.

Informatics Resources for the Human Genome

The NHGRI recognizes the need for investigators studying human biology to have access to information that would link biological function and expression of genes to the human genome sequence. Currently, certain Model Organism Databases (MODs) play this important role for information concerning, for example, yeast, fruit fly, roundworm and mouse. Currently, there is no centralized information resource from which investigators can obtain such information about the human. To discuss the need for such a centralized resource, NHGRI and the Wellcome Trust sponsored a workshop on informatics resources for the human genome on September 22-23, 2003 in Bethesda, MD. While there was a wide difference of opinions among the workshop

attendees about the need for a single “Human Base” that would be strictly comparable to a MOD where the “model organism” was the human, they did recognize the importance of integrating available resources and providing high quality data linking biology to the human genome. The workshop recommended a different concept for a Human Base, in which the central resource would play more of a hub-like and biologically based role, coordinating existing research database sources and adding value to genome-based information by curating additional information from the literature and direct submissions. This hub model would leverage information from existing sources, such as Online Mendelian Inheritance in Man, National Center for Biotechnology Information, and Ensembl Genome Browser, without duplicating those efforts and also provide new sources of high quality information needed by the scientific community. To be successful, Human Base would have to focus on user needs and have a clear-cut commitment to, and mechanisms for being responsive to, the needs of the scientific community. The NHGRI will work with the research community to develop this resource.

Centers for Excellence for 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) that will bring investigators from multiple disciplines together to address new ELSI issues resulting in the advances in genetics and genomics.

The CEER program is designed to support the development of research groups that will identify and investigate genetic and genomic ELSI research related to questions that can best be approached through intensive and extended collaboration among investigators from multiple disciplines, using diverse methodologies. The investigators in a CEER 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 issues.

Intellectual Property Rights in Genetics and Genomics Research

The NHGRI has worked on issues of intellectual property related to genetic and genomic data, and as these issues continue to play themselves out in the broader arena, the NHGRI has developed new initiatives to address them.

The NHGRI ELSI program has proposed 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 to help build the research base necessary to inform the rational development of future policy options regarding intellectual property, genetics, and genomics. Examples of the types of topics that may fall under this initiative include: application issues, ownership issues, licensing issues, enforcement issues, international issues, and impact issues.

The NHGRI, along with several other NIH Institutes, has also recently agreed to provide funds for a National Academy of Sciences' study entitled "Intellectual Property in Genomic and Protein Research and Innovation." This 18-month study, which will involve experts from law, public policy and genomic sciences, will address such important questions as: What is the impact of intellectual property (IP) and licensing on genetic and proteomic research? What are the policy options that should be addressed in this area? How have other areas of the world, e.g. Europe and Asia, addressed these issues? In the end, it is hoped that this study will provide some direction on how to address the complex issues surrounding the interface of IP, biomedical research, and patient care.

Social and Behavioral Research Branch

The NHGRI has just formed a new Social and Behavioral Genetics Research Branch within its intramural research program. The main focus of the Branch will be 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 improve interventions for preventive disease and promoting health and well-being; 2) apply social, behavioral, and communication theories to understand the essential elements of communicating genetic risk effectively; 3) develop and refine evidence-based methods of communicating genetic risk to affected 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. In its first year the Branch will identify priorities for a research agenda consistent with its mission, help plan for the development of a Social & Behavioral Science Center at the NIH, and recruit new faculty and trainees.

OTHER AREAS OF INTEREST

International HapMap Project

One use of the human genome sequence has been to study the role that genetic variation plays in health and disease. There are at least 10 million DNA sites where people commonly differ in their DNA sequences, and some of these variations affect an individual's risk for disease or response to drugs. To study genetic variation more effectively across the genome, the NHGRI and a team of international partners has launched the International HapMap project.

The NHGRI has taken a leadership role in the development of the HapMap, a catalog of common haplotype blocks and the single nucleotide polymorphisms (SNPs) that tag them. The goal of the International HapMap Project is to determine the common patterns of DNA sequence variation in the human genome (i.e. haplotype blocks) and to make this information freely available in the public domain. An 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 parts of 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 www.hapmap.org.

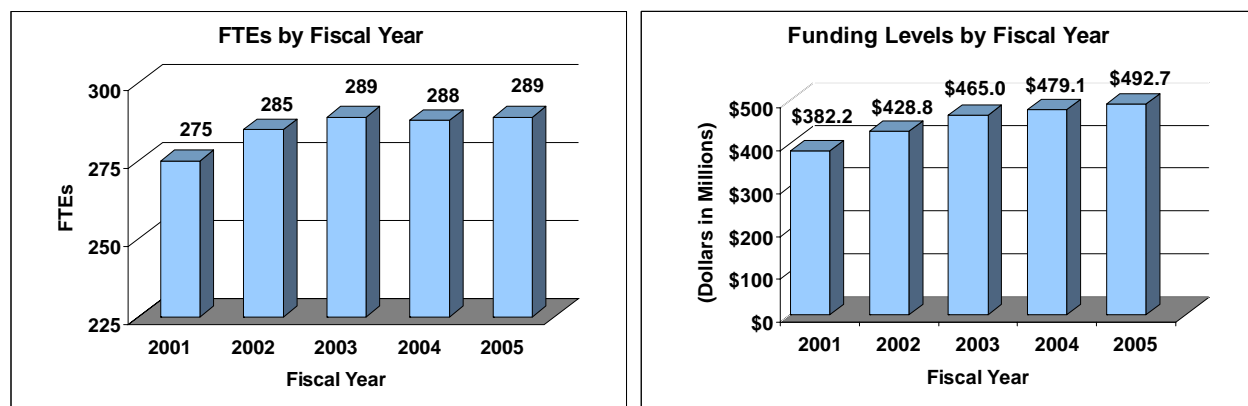
Direct-to-Consumer Marketing of Genetic Tests

The 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 begun researching this issue with studies focusing on printed materials and the Internet. So far, researchers have found that many direct-to-consumer (DTC) advertisements exaggerate the scientific basis of the claims made and/or fail to effectively communicate the limitations of the specific genetic knowledge discussed. In particular, the Internet has provided a powerful medium for the construction of "informational" resources through which DNA analysis is often linked to the ability 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 from Myriad, was piloted in two metropolitan areas in the last year. The NHGRI will continue to track DTC marketing through continuing research on the limitations and implications of this new marketing approach, as well as through dialogues with Food and Drug Administration staff, Federal Trade Commission staff, and the Secretary's Advisory Committee on Genetics Health and Society (SACGHS).

BUDGET POLICY

The Fiscal Year 2005 budget request for the NHGRI is \$492,670,000, an increase of \$13,842,000 and 2.9 percent over the FY 2004 Final Conference Level. Also included in the FY 2005 request, is NHGRI's support for the trans-NIH Roadmap initiatives, estimated at 0.63% of the FY 2005 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of FTEs and Funding Levels for NHGRI are shown in the graphs below. Note that the Fiscal Year 2001 FTE figure is not comparable to the figures in the succeeding years due to NIH's consolidation of its Human Resources function in FY 2003.

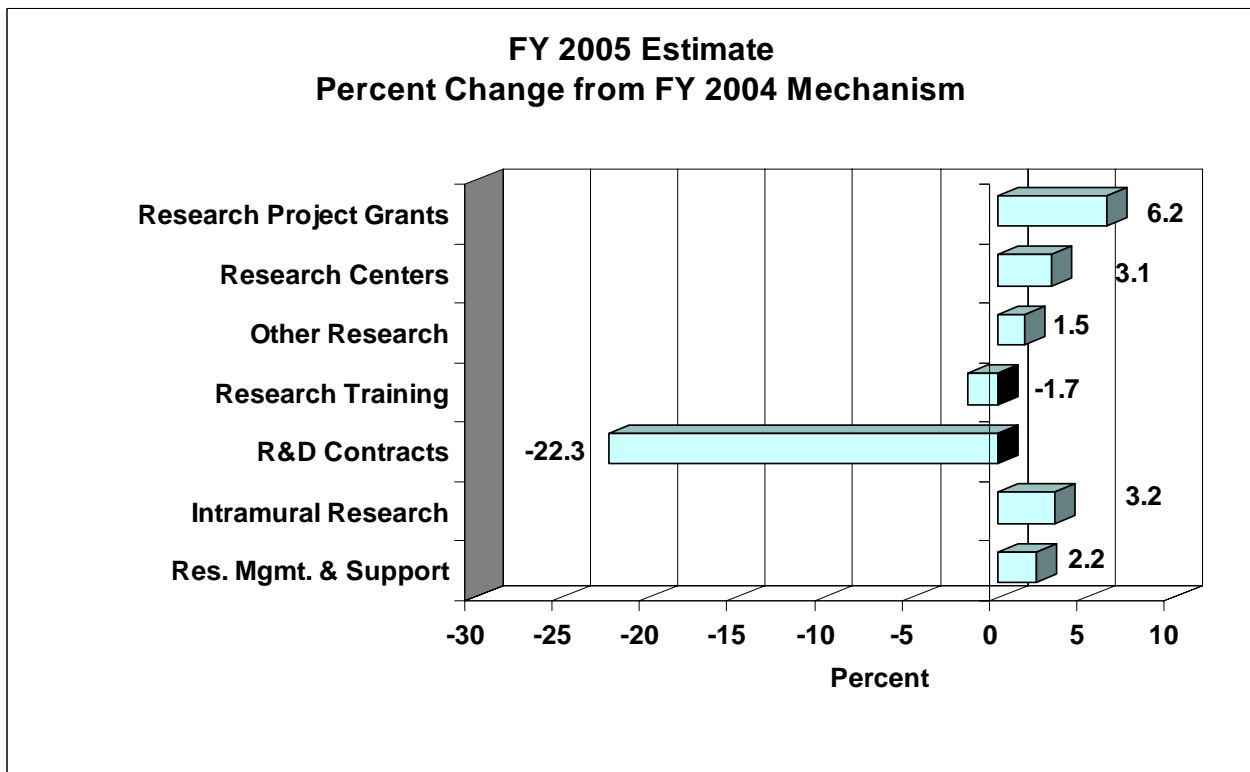
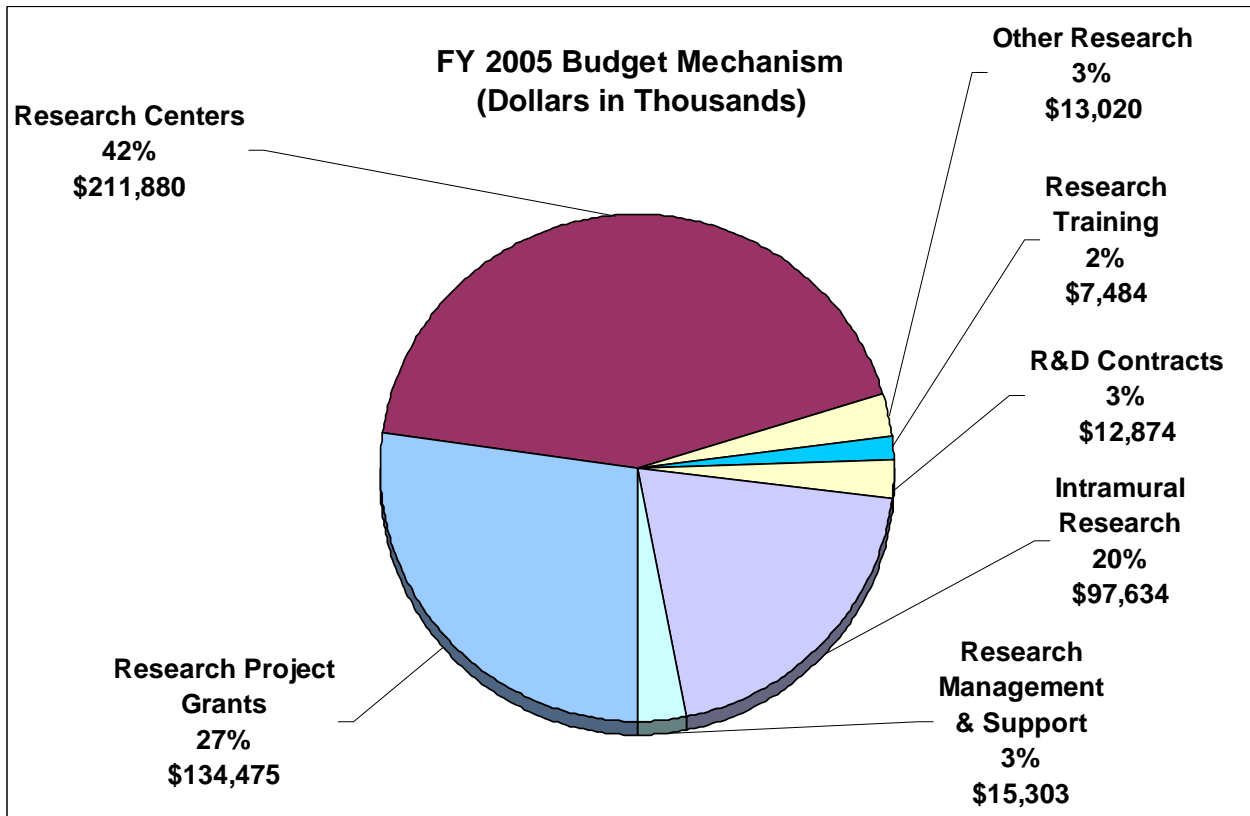


NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. The FY 2005 NIH request provides for an aggregate 1.3 percent increase in average cost for Research Project Grants, consistent with the Gross Domestic Product deflator. The NHGRI is providing an average cost increase of 1.9 percent for direct recurring costs in noncompeting continuation awards. Competing RPGs are based on an average cost increase of 1 percent.

Advancement in medical research is dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2005 request, NHGRI will support 157 pre- and postdoctoral trainees in full-time training positions. Stipend levels for pre-doctoral and post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will remain at FY 2004 levels.

The Fiscal Year 2005 request includes funding for 31 research centers, 46 other research grants and 20 R&D contracts. Intramural Research and Research Management and Support receive increases to support increased pay and estimated inflationary increases in FY 2005. Additional funding of \$89,000 for the Clinical Center portion of Obesity Clinical Research was also added to Intramural Research.

The mechanism distribution by dollars and percent change are displayed below:



NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Budget Mechanism - Total

MECHANISM	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
<u>Research Projects:</u>						
Noncompeting	76	\$60,001,000	107	\$70,008,000	137	\$77,124,000
Administrative supplements	(17)	1,395,000	(17)	1,643,000	(17)	1,656,000
Full funded	0	0	0	0	0	0
Single year	75	43,196,000	76	44,846,000	76	45,289,000
Subtotal, competing	75	43,196,000	76	44,846,000	76	45,289,000
Subtotal, RPGs	151	104,592,000	183	116,497,000	213	124,069,000
SBIR/STTR	36	9,487,000	36	10,144,000	36	10,406,000
Subtotal, RPGs	187	114,079,000	219	126,641,000	249	134,475,000
<u>Research Centers:</u>						
Specialized/comprehensive	20	192,161,000	19	177,887,000	19	183,335,000
Clinical research	0	0	0	0	0	0
Biotechnology	10	22,299,000	12	27,693,000	12	28,545,000
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	86,000	0	0	0	0
Subtotal, Centers	30	214,546,000	31	205,580,000	31	211,880,000
<u>Other Research:</u>						
Research careers	32	5,949,000	29	6,227,000	28	6,318,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0
Biomedical research support	0	0	0	9,000	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	28	6,314,000	18	6,593,000	18	6,702,000
Subtotal, Other Research	60	12,263,000	47	12,829,000	46	13,020,000
Total Research Grants	277	340,888,000	297	345,050,000	326	359,375,000
<u>Research Training:</u>	<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>	
Individual awards	20	862,000	20	896,000	20	896,000
Institutional awards	137	6,384,000	140	6,721,000	137	6,588,000
Total, Training	157	7,246,000	160	7,617,000	157	7,484,000
Research & development contracts (SBIR/STTR)	10 (0)	12,769,000 (0)	10 (0)	16,572,000 (0)	20 (0)	12,874,000 (0)
<u>Intramural research</u>	<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>	
Intramural research	226	91,709,000	222	94,615,000	223	97,634,000
Research management and support	63	11,773,000	66	14,974,000	66	15,303,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NHGRI	289	464,385,000	288	478,828,000	289	492,670,000
(RoadMap Support)		(0)		(1,645,000)		(3,103,000)
(Clinical Trials)		(8,832,000)		(9,066,000)		(9,326,000)

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
<u>Extramural Research:</u>								
Human Genome Research		\$360,903		\$369,239		\$379,733		\$10,494
Subtotal, Extramural research		360,903		369,239		379,733		10,494
Intramural research	226	91,709	222	94,615	223	97,634	1	3,019
Res. management & support	63	11,773	66	14,974	66	15,303	0	329
Total	289	464,385	288	478,828	289	492,670	1	13,842

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Summary of Changes

FY 2004 Final Conference		\$478,828,000		
FY 2005 Estimated Budget Authority		492,670,000		
Net change		13,842,000		
CHANGES	FY 2004 Budget Base		Change from Base	
	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase				
		\$25,717,000		\$387,000
b. Annualization of January 2004 pay increase				
		25,717,000		264,000
c. January 2005 pay increase				
		25,717,000		296,000
d. One less day of pay				
		25,717,000		(99,000)
e. Payment for centrally furnished services				
		14,778,000		443,000
f. Increased cost of laboratory supplies, materials, and other expenses				
		54,120,000		1,639,000
Subtotal				2,930,000
2. Research Management and Support:				
a. Within grade increase				
		6,740,000		119,000
b. Annualization of January 2004 pay increase				
		6,740,000		69,000
c. January 2005 pay increase				
		6,740,000		78,000
d. One less day of pay				
		6,740,000		(26,000)
e. Payment for centrally furnished services				
		1,015,000		30,000
f. Increased cost of laboratory supplies, materials, and other expenses				
		7,219,000		59,000
Subtotal				329,000
Subtotal, Built-in				3,259,000

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Summary of Changes--continued

CHANGES	FY 2004 Budget Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	107	\$71,651,000	30	\$7,129,000
b. Competing	76	44,846,000	0	443,000
c. SBIR/STTR	36	10,144,000	0	262,000
Total	219	126,641,000	30	7,834,000
2. Research centers	31	205,580,000	0	6,300,000
3. Other research	47	12,829,000	(1)	191,000
4. Research training	160	7,617,000	(3)	(133,000)
5. Research and development contracts	10	16,572,000	10	(3,698,000)
Subtotal, extramural		369,239,000		10,494,000
6. Intramural research	<u>FTEs</u> 222	94,615,000	<u>FTEs</u> 1	3,019,000
7. Research management and support	66	14,974,000	0	329,000
Subtotal, program		478,828,000		13,842,000
Total changes	288		1	17,101,000

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Budget Authority by Object

	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	288	289	1
Full-time equivalent of overtime & holiday hours	2	2	0
Average ES salary	\$131,342	\$131,342	\$0
Average GM/GS grade	10.8	10.8	0.0
Average GM/GS salary	\$65,677	\$66,662	\$985
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	\$67,990	\$69,009	\$1,019
Average salary of ungraded positions	74,208	75,321	1,113
OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	\$10,915,000	\$11,334,000	\$419,000
11.3 Other than Full-Time Permanent	11,755,000	12,206,000	451,000
11.5 Other Personnel Compensation	384,000	399,000	15,000
11.7 Military Personnel	0	0	0
11.8 Special Personnel Services Payments	3,106,000	3,106,000	0
Total, Personnel Compensation	26,160,000	27,045,000	885,000
12.1 Civilian Personnel Benefits	6,193,000	6,433,000	240,000
12.2 Military Personnel Benefits	104,000	108,000	4,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	32,457,000	33,586,000	1,129,000
21.0 Travel & Transportation of Persons	1,203,000	1,219,000	16,000
22.0 Transportation of Things	233,000	237,000	4,000
23.1 Rental Payments to GSA	3,000	3,000	0
23.2 Rental Payments to Others	334,000	344,000	10,000
23.3 Communications, Utilities & Miscellaneous Charges	410,000	425,000	15,000
24.0 Printing & Reproduction	128,000	130,000	2,000
25.1 Consulting Services	857,000	868,000	11,000
25.2 Other Services	14,916,000	14,823,000	(93,000)
25.3 Purchase of Goods & Services from Government Accounts	40,408,000	40,549,000	141,000
25.4 Operation & Maintenance of Facilities	6,522,000	6,660,000	138,000
25.5 Research & Development Contracts	9,508,000	6,424,000	(3,084,000)
25.6 Medical Care	814,000	818,000	4,000
25.7 Operation & Maintenance of Equipment	1,853,000	1,880,000	27,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	74,878,000	72,022,000	(2,856,000)
26.0 Supplies & Materials	9,480,000	9,652,000	172,000
31.0 Equipment	8,013,000	8,192,000	179,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	351,688,000	366,859,000	15,171,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	1,000	1,000	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	446,371,000	459,084,000	12,713,000
Total Budget Authority by Object	478,828,000	492,670,000	13,842,000

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Salaries and Expenses

OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	\$10,915,000	\$11,334,000	\$419,000
Other Than Full-Time Permanent (11.3)	11,755,000	12,206,000	451,000
Other Personnel Compensation (11.5)	384,000	399,000	15,000
Military Personnel (11.7)	0	0	0
Special Personnel Services Payments (11.8)	3,106,000	3,106,000	0
Total Personnel Compensation (11.9)	26,160,000	27,045,000	885,000
Civilian Personnel Benefits (12.1)	6,193,000	6,433,000	240,000
Military Personnel Benefits (12.2)	104,000	108,000	4,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	32,457,000	33,586,000	1,129,000
Travel (21.0)	1,203,000	1,219,000	16,000
Transportation of Things (22.0)	233,000	237,000	4,000
Rental Payments to Others (23.2)	334,000	344,000	10,000
Communications, Utilities and Miscellaneous Charges (23.3)	410,000	421,000	11,000
Printing and Reproduction (24.0)	128,000	130,000	2,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	857,000	868,000	11,000
Other Services (25.2)	14,916,000	14,823,000	(93,000)
Purchases from Govt. Accounts (25.3)	22,607,000	25,605,000	2,998,000
Operation & Maintenance of Facilities (25.4)	6,522,000	6,660,000	138,000
Operation & Maintenance of Equipment (25.7)	1,853,000	1,880,000	27,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	46,755,000	49,836,000	3,081,000
Supplies and Materials (26.0)	9,479,000	9,651,000	172,000
Subtotal, Non-Pay Costs	58,542,000	61,838,000	3,296,000
Total, Administrative Costs	90,999,000	95,424,000	4,425,000

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Significant Items in House and Senate Appropriations Committee Reports

The following section represents FY 2004 Congressional requirements for reports and significant items derived from Senate Report 108-10 and House Report 108-188. These actions discussed below are contingent on inclusion of similar language and funding in the final FY 2004 appropriation and related reports. Additional items may be transmitted at a later date as a result of the final Conference report.

Item

Gene-Environment Interactions – The NHGRI is commended for its partnerships with other institutes and the Office of Behavioral and Social Sciences Research to push the frontier of genetics research forward by examining gene-environment interactions. Research on the environmental stimuli (such as behaviors, experience of stress, or exposure to certain physical conditions) that lead to the expression of genes is critical if science is to reap the benefits of the mapped genome. The NHGRI is encouraged to work with OBSSR on multidisciplinary training programs to increase the number of skilled scientists who can bridge the behavioral and genetic realms.

Action taken

The NHGRI sees integrative research that advances the understanding of how environmental factors affect gene expression in health and disease as an area of great importance. Because of recent advances in genomics that have resulted from the availability of the completed sequence of the human genome, there is great promise in the ability to address these issues. In 2001, the NHGRI and the NIH Office of Behavioral and Social Sciences Research (OBSSR), formed the trans-NIH Working Group on Interactions among Genetic, Behavioral, and Social Factors. The working group includes representatives of numerous NIH institutes and centers and enables the NIH to coordinate its efforts on these matters. In its intramural program, the NHGRI has just created a new Branch on Behavioral and Social Science Research. The NIH is proposing that the NHGRI's BSSR Branch be the nucleus of a trans-NIH Social & Behavioral Science Center (SBSC), which will also help coordinate efforts to address such issues as gene-environment interactions. Over the past few years, several Institute of Medicine expert panels commissioned by NIH have concurred in suggesting that understanding social and behavioral factors will be essential to maintaining and further promoting public health improvements. These reports have called for expanded research at the nexus of the complex array of factors - from psychological and inter-personal to the larger social forces - that contribute to health and wellbeing. Following up on these recommendations will be one of the important functions of the new center, which will involve researchers from NHGRI, OBSSR and other parts of the NIH. The new center will also serve as an ideal training ground for new investigators wanting to study gene-environment interactions. Finally, the NHGRI has been working with OBSSR on a new NIH Roadmap Initiative, "Interdisciplinary Research Teams of the Future." The OBSSR has developed a new

RFA that hopes to attract proposals that create new ways to provide individuals previously trained in one discipline with formal course work and laboratory training in a second discipline. This training initiative will be ideal for the cross-disciplinary approach needed to address the complex issues of genetics and environmental interaction.

Item

ENCODE– The Committee commends NHGRI for creating the ENCyclopedia Of Data Elements [ENCODE] project, which has a long-term goal of identifying and locating all protein-coding genes, non-protein coding genes and other sequence-based functional elements contained in human DNA sequence. This significant undertaking will help scientists mine and fully utilize the human sequence, gain a deeper understanding of human biology, predict potential disease risk and stimulate new strategies for the prevention and treatment of disease. The Committee would like to receive a report on the progress of this effort prior to next year’s hearings, with emphasis on the project's place within the Institute's plan for future activities.

Action taken

On October 9, 2003 the National Human Genome Research Institute (NHGRI) announced the first grants in a three-year, \$36 million scientific reconnaissance mission aimed at discovering all parts of the human genome that are crucial to biological function through the ENCODE project.

The ENCODE project will be carried out by an international consortium made up of scientists in government, industry and academia. A major aspect of this initiative is a three-year pilot project in which research groups will work cooperatively to test efficient, high-throughput methods for identifying, locating and fully analyzing all of the functional elements contained in a set of DNA target regions that covers approximately 30 megabases, or about 1 percent of the human genome. If the pilot effort proves successful, the project will be expanded to cover the entire genome.

The NHGRI will provide a full report on the ENCODE project to the committee prior to next year’s hearings.

**NATIONAL INSTITUTES OF HEALTH
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Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2004 Amount Authorized	2004 Final Conference	2005 Amount Authorized	2005 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	\$471,211,000	Indefinite	\$485,186,000
National Human Genome Research Institute	Section 401	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487	42§288	<u>a/</u>	7,617,000	<u>b/</u>	7,484,000
Total, Budget Authority				478,828,000		492,670,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.

b/ Reauthorizing legislation will be submitted.

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation ^{1/}
1996	166,678,000 ^{2/}	170,041,000	163,943,000 ^{2/}	169,041,000
Rescission				(266,000)
1997	177,788,000 ^{2/}	189,267,000	180,807,000 ^{2/}	189,657,000 ^{3/}
1998	202,197,000 ^{2/}	211,772,000	218,851,000	217,704,000
1999	236,275,000 ^{2/4/}	246,111,000	249,891,000	264,892,000
Rescission				(185,000)
2000	271,536,000 ^{2/}	308,012,000	337,322,000	337,322,000
Rescission				(1,795,000)
2001	353,427,000 ^{2/}	386,410,000	385,888,000	382,384,000
Rescission				(192,000)
2002	426,739,000 ^{2/}	423,454,000	440,448,000	429,515,000
Rescission				(757,000)
2003	458,182,000	458,182,000	468,037,000	468,037,000
Rescission				(3,042,000)
2004	478,072,000	478,072,000	482,372,000	482,222,000
Rescission				(3,149,000)
2005	492,670,000			

^{1/} Reflects enacted supplementals, rescissions, and reappropriations.

^{2/} Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.

^{3/} Excludes enacted administrative reductions of \$ 128,000

^{4/} Excludes reductions of \$721,000 for the budget amendment for bioterrorism.

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute**

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Office of the Director	7	6	6
Office of Administrative Management	16	16	16
Office of Policy, Communications and Education	14	14	14
Division of Intramural Research	226	222	223
Division of Extramural Research	26	30	30
Total	289	288	289
FTEs supported by funds from Cooperative Research and Development Agreements	(2)	(2)	(2)
FISCAL YEAR	Average GM/GS Grade		
2001	10.7		
2002	10.9		
2003	10.8		
2004	10.8		
2005	10.8		

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Detail of Positions

GRADE	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
ES-6			
ES-5			
ES-4			
ES-3			
ES-2			
ES-1	1	1	1
Subtotal	1	1	1
Total - ES Salary	\$131,342	\$131,342	\$131,342
GM/GS-15	18	18	18
GM/GS-14	10	10	11
GM/GS-13	28	29	30
GS-12	37	36	34
GS-11	28	29	29
GS-10	3	3	3
GS-9	19	18	20
GS-8	11	13	12
GS-7	15	13	13
GS-6	5	4	5
GS-5	3	4	3
GS-4	3	2	2
GS-3	1	1	1
GS-2	1	1	1
GS-1	1	1	1
Subtotal	183	182	183
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	1	1	1
Senior Grade	1	1	1
Full Grade			
Senior Assistant Grade	1	1	1
Assistant Grade			
Subtotal	3	3	3
Ungraded	109	109	109
Total permanent positions	154	153	154
Total positions, end of year	296	295	296
Total full-time equivalent (FTE) employment, end of year	289	288	289
Average ES level	ES-1	ES-1	ES-1
Average ES salary	\$131,342	\$131,342	\$131,342
Average GM/GS grade	10.8	10.8	10.8
Average GM/GS salary	\$63,089	\$65,677	\$66,662

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New Positions Requested

	FY 2005		
	Grade	Number	Annual Salary
Roadmap Staff Scientist	Title 42	1	\$155,000
Total Requested		1	