

DEPARTMENT OF HEALTH AND HUMAN SERVICES

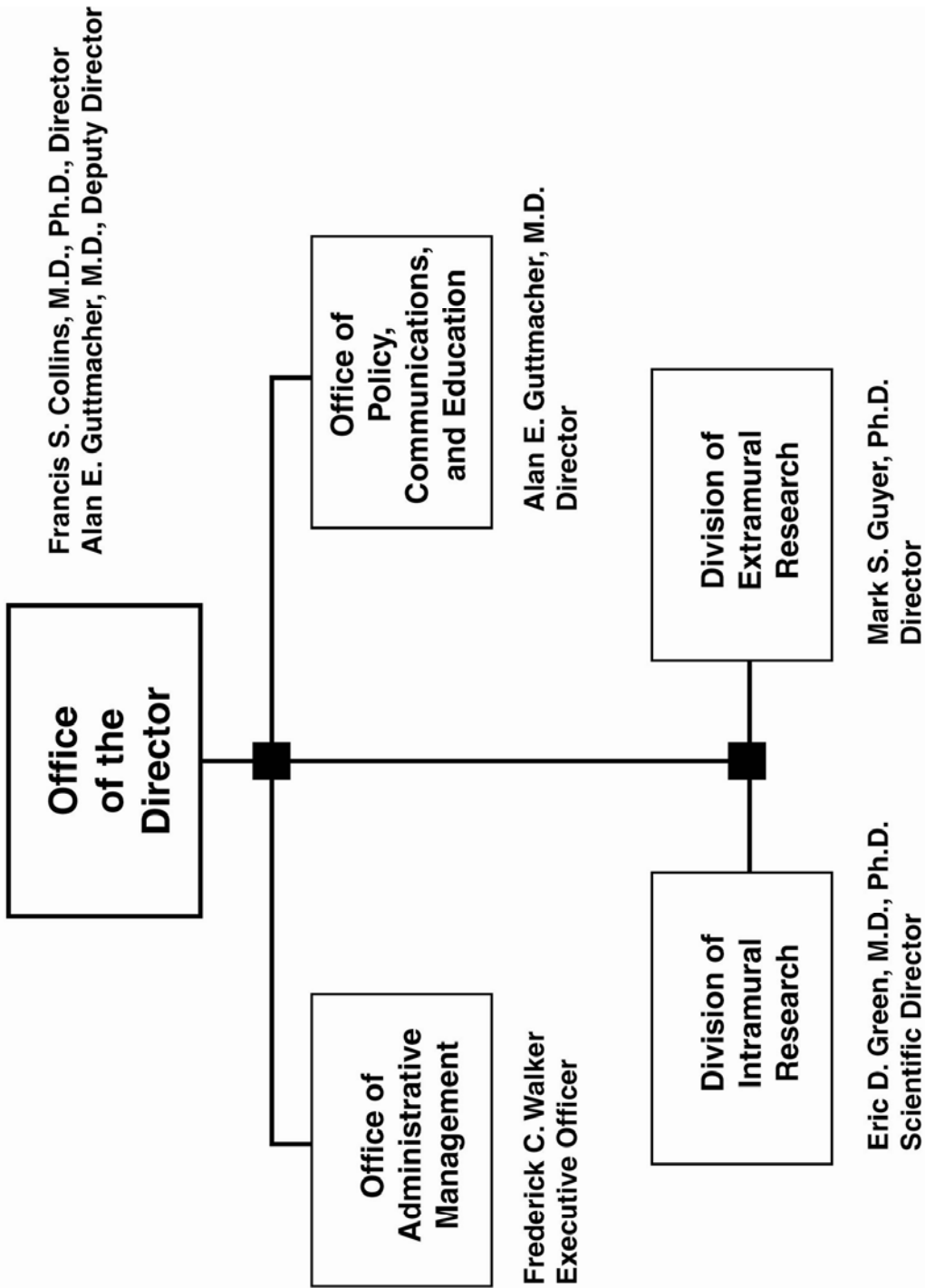
NATIONAL INSTITUTES OF HEALTH

National Human Genome Research Institute

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# NATIONAL HUMAN GENOME RESEARCH INSTITUTE

## Organizational Structure



**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, [~~\$490,959,000~~] *\$482,942,000*.

[Department of Health and Human Services Appropriations Act, 2006]

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

**Amounts Available for Obligation 1/**

Source of Funding	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Appropriation	\$492,670,000	\$490,959,000	\$482,942,000
Enacted Rescissions	(4,062,000)	(4,910,000)	0
Subtotal, Adjusted Appropriation	488,608,000	486,049,000	482,942,000
Real transfer under NIH Director's one-percent transfer authority for Roadmap	(3,089,000)	(4,343,000)	
Comparative transfer from OD for NIH Roadmap	3,089,000	4,343,000	
Subtotal, adjusted budget authority	488,608,000	486,049,000	482,942,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	488,608,000	486,049,000	482,942,000
Unobligated balance lapsing	(19,000)	0	0
Total obligations	488,589,000	486,049,000	482,942,000

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

FY 2005 - \$15,613,000    FY 2006 - \$16,626,000    FY 2007 - \$17,616,000

Excludes \$45,000 in FY 2006 and \$125,000 in FY 2007 for royalties.

## Justification

### National Human Genome Research Institute

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Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.

Budget Authority:

FY 2005		FY 2006		FY 2007		Increase or	
Actual		Appropriation		Estimate		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>
275	\$488,608,000	286	\$486,049,000	288	\$482,942,000	+2	-\$3,107,000

This document provides justification for the Fiscal Year 2007 activities of the National Human Genome Research Institute, including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2007 HIV/AIDS activities can be found in the NIH section entitled “Office of AIDS Research (OAR).” Detailed information on the NIH Roadmap for Medical Research may be found in the Overview section.

## INTRODUCTION

In April 2003, an international consortium of scientists, led by the National Human Genome Research Institute (NHGRI), announced the completion of the sequence of the human genome, with all of the data from this historic effort placed in the public domain. On October 26, 2005, a different international consortium of dedicated scientists from six countries, again led by the NHGRI, announced the production of a very different map of the human genome, one that may prove even more powerful, because of its medical applications. This is the “HapMap,” and once again all of the data has been placed in the public domain.

The Genome Project spelled out the letters of the DNA code that we all share. The HapMap provides detailed knowledge of the variation in the genome. The HapMap investigates those spelling differences in the human instruction book that predispose some people to diabetes, others to heart disease, and others to cancer. The HapMap reveals the way in which this genetic variation is organized into chromosomal neighborhoods, and now we can use it to uncover the heritable causes of virtually any common disease.

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

This project could not have succeeded without the dedicated efforts of more than 2,000 scientists across the world who delivered on every promise of the HapMap. In fact, in its brief three-year life, this project produced a HapMap three times more detailed than originally thought possible. This detailed HapMap will greatly speed the progress of science and medicine and is a major accomplishment. The NHGRI will build on this success to better understand both the genetic and environmental factors that cause disease and to develop more tools that will benefit all of science and humankind.

## Stories of Discovery: The Development of the HapMap

Understanding how genetic variation is inherited in DNA “haplotypes” (or blocks of related DNA) can provide considerable savings in time, effort, and cost in uncovering hereditary factors in disease. The NHGRI played a major leadership role in the development of the HapMap (haplotype map), a catalog of haplotype blocks and the markers of genetic variation, called single nucleotide polymorphisms (SNPs) that tag them. The HapMap provides overwhelming evidence that variation in the human genome is organized into local neighborhoods, called haplotypes that usually are inherited as intact blocks of information. The project was successfully completed in October of 2005, and achieved a diversity of coverage three times the originally projected level. Researchers have already used the HapMap to find the genes and variants that contribute to common diseases like macular degeneration, Parkinson’s disease, cardiac arrhythmia, and celiac disease; in addition, it is a powerful resource for studying the genetic factors contributing to variation in individual response to disease, to drugs, and to vaccines.

At the outset of the project in October 2002, the International HapMap Consortium set an ambitious goal of creating a human haplotype map, or HapMap, within three years. In a paper in the October 27, 2005 issue of the journal *Nature*, more than 200 researchers from Canada, China, Japan, Nigeria, the United Kingdom and the United States described the initial results from this public-private effort to chart the patterns of genetic variation common in the world’s population. The *Nature* paper marks the attainment of that goal with its detailed description of the Phase I HapMap, consisting of more than 1 million SNPs. In record time, the Consortium has also generated the data for Phase II of HapMap, containing nearly three times more markers than the initial version, and enabling researchers to focus their gene searches even more precisely on specific regions of the genome.

In addition to its intended function as a resource for studies of human health and disease, the Phase I HapMap has yielded fascinating clues into how our species evolved over time and specific forces that were important as the human population spread around the globe. The HapMap consortium, made up of the six contributing countries, found that genes involved in immune response and neurological processes are more likely to recombine than those for DNA repair, DNA packaging, or cell division. Researchers speculate the difference might be due to natural selection shaping human population in ways that favor increased diversity for genes that influence the body’s interactions with the environment, such as those involved in immune response, but not in genes involved in core cellular processes.

The Consortium found evidence that a very small subset of human genetic variation may be related to selection pressures related to geographic or environmental factors, such as microorganisms that cause infectious diseases. This evidence appears as significant differences in genetic variation patterns in particular genomic regions among the populations studied. While more follow-up study is needed to explore the differences, researchers say some of the most striking examples merely serve to confirm well-known genetic differences among populations, such as the Duffy blood group, which plays a role in response to malaria, and the lactase gene, which influences the ability to digest milk products.

As was the case with all of the data generated by the Human Genome Project, HapMap data are being made swiftly and freely available in public databases. Researchers can access this data through the HapMap Data Coordination Center ([www.hapmap.org](http://www.hapmap.org)).

The International HapMap Consortium: A haplotype map of the human genome. *Nature* 437, 1299-1320, 2005. <http://www.nature.com/nature/journal/v437/n7063/full/nature04226.html>  
Press Release: <http://genome.gov/17015412>

## Insights from the Chimpanzee Genome and Multiple Genome Comparisons

The first comprehensive comparison of the genetic blueprints of humans and chimpanzees shows our closest living non-human relatives share identity with 96 percent of the human DNA sequence. In a paper published in the September 1, 2005 issue of the journal *Nature*, the Chimpanzee Sequencing and Analysis Consortium, which is supported by the National Human Genome Research Institute (NHGRI), describes its landmark analysis comparing the genome of the chimp (*Pan troglodytes*) with that of human (*Homo sapiens*). The chimp sequence draft represents the first non-human primate genome and the fourth mammalian genome (after human, mouse, and rat) described in a major scientific publication.

The consortium found that the chimp and human genomes are very similar and encode very similar proteins. The DNA sequences that can be directly compared between the two genomes are almost 99 percent identical. When DNA insertions and deletions are taken into account, humans and chimps still share 96 percent of their sequence. At the protein level, 29 percent of chimp genes code for the same amino sequences in chimps and humans. In fact, the typical human protein has accumulated just one unique change since chimps and humans diverged from a common ancestor about 6 million years ago. To put this into perspective, the number of genetic differences between humans and chimps is approximately 60 times less than that seen between human and mouse and about 10 times less than between the mouse and rat. On the other hand, the number of genetic differences between a human and a chimp is about 10 times more than between any two humans.

The researchers involved in the chimp genome project discovered that a few classes of genes are changing unusually quickly in both humans and chimpanzees, compared with other mammals. These classes include genes involved in perception of sound, transmission of nerve signals, production of sperm, and cellular transport of electrically charged molecules called ions. Researchers suspect the rapid evolution of these genes may have contributed to the special characteristics of primates. Among the genetic changes that researchers will look for in the coming years are those related to such human-specific features as walking upright on two feet, a greatly enlarged brain, and complex language skills.

In a related study published in the July 22 issue of the journal *Science*, a team of 25 scientists from the United States, France, and Singapore compared the organization of the chromosomes of eight mammalian species: human, mouse, rat, cow, pig, dog, cat, and horse. The team used sophisticated computer software to align and compare the mammals' genetic material, or genomes. This alignment of the chromosomes showed that they tend to separate in the same places as species evolve, resulting in rearrangements of their DNA. It had been thought that such breaks in chromosomes occurred at random, but this work showed these breaks occur consistently across many species. Such insights will enable scientists to learn a great deal more about how the human genome works and affects our growth and development.

The Chimpanzee Sequencing and Analysis Consortium: Initial sequence of the chimpanzee genome and comparison with the human genome. *Nature* 437: 69-87, 2005.

<http://www.nature.com/nature/journal/v437/n7055/full/nature04072.html>

Press Release: <http://genome.gov/15515096>

Murphy WJ, et al: Dynamics of mammalian chromosome evolution inferred from multispecies comparative maps. *Science* 309: 613-7, 2005.

[http://www.sciencemag.org/cgi/content/full/309/5734/613?maxtoshow=&HITS=10&hits=10&RESULTFORM AT=&titleabstract=Dynamics+of+mammalian+chromosome+evolution+inferred+from+multispecies+comparati v&searchid=1130426562433\\_7407&stored\\_search=&FIRSTINDEX=0&fdate=3/1/2005&tdate=10/31/2005](http://www.sciencemag.org/cgi/content/full/309/5734/613?maxtoshow=&HITS=10&hits=10&RESULTFORM AT=&titleabstract=Dynamics+of+mammalian+chromosome+evolution+inferred+from+multispecies+comparati v&searchid=1130426562433_7407&stored_search=&FIRSTINDEX=0&fdate=3/1/2005&tdate=10/31/2005)

Press Release: <http://genome.gov/15015042>



## SCIENCE ADVANCES

### **Analysis of the X Chromosome**

*Background:* One of the central goals of the effort to analyze the human genome is the identification of all genes, which are generally defined as stretches of DNA that code for particular proteins. Therefore, obtaining the complete DNA sequence of the human X chromosome, and carrying out a detailed analysis of its content, will greatly add in the effort to understand the hundreds of human diseases that are inherited in an X-linked fashion.

*Advance:* In March 2005, the NIH announced the first comprehensive analysis of the sequence of the human X chromosome, providing sweeping new insights into the evolution of sex chromosomes and the biological differences between males and females. A detailed analysis of the X chromosome's DNA sequence and a survey of its gene activity were published in the journal *Nature*. This analysis confirmed the existence of 1,098 protein-coding genes on the X chromosome. Only 54 of the 1,098 genes have functional counterparts on the much smaller Y chromosome, which has been described as an "eroded" version of the X chromosome. The X chromosome's gene density is among the lowest for the human chromosomes analyzed to date.

*Implications:* Despite its relatively low gene density, the X chromosome holds a prominent place in the study and understanding of human disease. This arises from the fact that any defects in genes on the X chromosome are often apparent in males because the Y does not carry corresponding genes to compensate (males have both an X and a Y chromosome, while females have two X chromosomes). More than 300 diseases already have been mapped to the X chromosome, and though the X chromosome contains only 4 percent of all human genes, it accounts for almost 10 percent of inherited diseases caused by a single gene (often referred to as "Mendelian" disorders). Such "X-linked" disorders include red-green color blindness, hemophilia, varied forms of mental retardation, and Duchenne muscular dystrophy.

### **A Big Leap Forward in Genome Sequencing Technology**

*Background:* Current DNA sequencing technology, which enables a detailed description of the order of the chemical building blocks, or bases, in a given stretch of DNA, relies on a method introduced decades ago by Fred Sanger of the Laboratory of Molecular Biology in Cambridge, U.K. In "Sanger sequencing," bacteria are used to amplify the DNA and costly reagents or chemicals label DNA bases for identification. The cost of this sequencing method has dropped by several orders of magnitude in the past ten years, from more than \$1 to less than a 10th of a cent per base. But the cost of high volume sequencing, for example, the sequencing of an individual's whole genome for medical purposes, remains prohibitively high.

*Advance:* Two publications in the August 2005 volume of the journal *Science* announced bold new advances in sequencing technology by NHGRI-funded researchers. Both of the two new technologies described in those publications eliminate the need for bacteria. They attach DNA to aqueous beads encased in oil, and copy DNA by chemical reactions. As thousands of these reactions are performed in tiny amounts, the cost of sequencing is decreased by reductions in personnel and equipment, and by the reduced cost of reagents.

*Implications:* While both experimental techniques require an increase in accuracy and in the length of the DNA sequence “read” (the amount of sequence generated in a single reaction), they hold promise to decrease the cost of DNA sequencing dramatically and thus to bring medical sequencing beyond the laboratory and firmly into the practice of medicine.

### **Anti-Cancer Drugs May Hold Promise for Premature Aging Disorder**

*Background:* There are currently no treatments for the rare genetic disorder progeria. When they are born, children with progeria appear normal. But, as they grow older, they experience growth retardation and show dramatically accelerated symptoms of aging – such as, hair loss, skin wrinkling, and fat loss. Accelerated cardiovascular disease also ensues, typically causing death from heart attack or stroke by about the age of 12.

*Advance:* Building upon their success in identifying the gene that causes progeria, researchers at the NHGRI have discovered that drugs originally developed for cancer also can reverse the dramatic nuclear structure abnormalities that are the hallmark of cells from children with progeria. This is a serendipitous surprise, rather like finding out that the key to your house also works in the ignition of your car. The new work that provided this surprise involved using farnesyl transferase inhibitors (FTIs) to treat skin cells taken from progeria patients.

*Implications:* If upcoming studies in a mouse model validate the results of the cell experiments and translate into improvements in the animals’ conditions, a clinical trial of FTIs in children with progeria may begin as early as next year. This work also has important implications for understanding the aging processes that all people experience.

### **Rapid New Test Developed for Inherited Immune Deficiency**

*Background:* Babies born with Severe Combined Immunodeficiency (SCID) fail to develop a normal immune system. SCID babies can be infected by a wide range of viruses, bacteria, and fungi that are normally controlled by a healthy baby’s immune system. Although a rare disease, SCID is known to the public from media accounts - and a made-for-TV movie starring John Travolta - about David, “the Bubble Boy,” a Texas boy who spent his entire life in a germ-free environment, ultimately dying at age 12, in 1984, after a failed bone marrow transplant. If undetected and untreated, SCID typically leads to death before the baby’s first birthday. However, if SCID is diagnosed in time, there are now often effective treatments. One form of the disease can be treated with an injectable medication. All forms of the disorder can be cured through the transplantation of bone marrow if a matching donor can be identified. And finally, SCID may be treated through human gene therapy, in which a normal copy of the defective gene is inserted into the patient’s own blood-forming cells. The first gene therapy experiments in history were carried out at NIH in 1990 in two young Ohio girls with SCID. Today the girls are alive, continue to do well, and are involved in ongoing research at the NHGRI.

*Advance:* Researchers at the NHGRI have developed a new laboratory method that rapidly identifies babies born with inherited forms of SCID. The new genetic test, which still must be validated before widespread use, could someday be added to the panel of tests that already

screens newborns for a variety of disorders. Developed in the NHGRI Division of Intramural Research (DIR), the new test can use the same dried blood samples already collected from newborns, and would provide the first accurate, high-throughput screen for immune deficiencies.

*Implications:* Prior efforts to identify this disorder by counting white blood cells in newborns proved unreliable and expensive. Many babies are diagnosed with SCID so late that they develop fatal infections before their condition is recognized. It is, therefore, critical to identify affected children immediately after birth and since the babies lack overt clinical symptoms for some time, a molecular test is a good approach. No one knows exactly how many babies are born with SCID. Current estimates suggest that 1 in every 50,000 to 100,000 births may be affected.

## NIH ROADMAP

### **Chemical Genomics and the Molecular Libraries and Imaging Initiative of the NIH Roadmap**

The NHGRI has taken a lead role in developing a chemical genomics initiative that will offer public-sector researchers access to high throughput screens for small organic molecules that can be used as chemical probes to study the functions of genes, cells, and biochemical pathways. This will provide novel ways to explore the functions of major components of the cell in health and disease. This initiative will also facilitate the development of new drugs by providing early stage compounds that will enable public and private sector researchers to validate new drug targets, which could then move into the drug-development pipeline. This would be particularly helpful for rare diseases, which may not otherwise be attractive for pursuit by the private sector. This resource is both a component of the 2003 NHGRI Vision for the Future of Genomics Research, and a prominent part of the NIH Roadmap for Medical Research.

The Molecular Libraries and Imaging Roadmap group, co-led by NHGRI and the National Institute of Mental Health (NIMH), has achieved a number of important milestones. In June, the nine extramural centers of the Molecular Libraries Screening Center Network (MLSCN) were funded, and the intramural MLSCN center, the NIH Chemical Genomics Center (NCGC) housed in the NHGRI Intramural Program, had its first birthday. Individual investigators from many academic centers have already submitted chemical assays (tools used for screening or analyzing compounds). The NCGC (<http://www.ncgc.nih.gov/>) ran its first full screen of chemical assays in May, and since then has completed 10 more screens on assays submitted by the research community, generating over 1,000,000 data points. The NCGC now has 20 staff members, and has multiple robotic screening platforms operational, including an ultra-high throughput system capable of screening over 1 million chemical compounds per day. The NCGC's first compound and assay result data are now in PubChem, a new division of NCBI's Entrez databases built as part of the Molecular Libraries and Imaging Roadmap (<http://pubchem.ncbi.nlm.nih.gov/>). In September 2005, the Molecular Libraries and Imaging Roadmap funded seven new grant programs for individual investigators in cheminformatics research, chemical diversity, novel assay technologies, HTS instrumentation, predictive ADME-Toxicology, and imaging probe technology.

## NEW INITIATIVES

### **Cancer Genome Atlas**

The National Cancer Institute (NCI) and the NHGRI, recognizing the benefit that a comprehensive collection of genetic and epigenetic components for major cancers could provide to the cancer community, have agreed to examine the best approaches to build a comprehensive collection and analysis of genetic mutations found in human cancers. That would include determining genome sequence, copy number changes, epigenetic alterations, gene expressions data, and even proteomic information on thousands of individual tumors from dozens of different tissue types.

The NCI and the NHGRI sponsored a workshop in July 2005 to seek input from members of the scientific community who have expertise in cancer and clinical research, genomics, technology development, bioinformatics and bioethics, as well as those from the public, non-profit, advocacy and private sectors. Attendees were asked to provide guidance and expertise on a number of issues, including the types of cancer that should be studied, optimal technology strategies, and bioethical issues.

A pilot program, which will determine the feasibility and usefulness of a full-scale effort, is scheduled to begin in fiscal year 2006 and is expected to take at least three years to complete. The NCI and the NHGRI will jointly fund the pilot project, and the management structure for the pilot will take advantage of the scientific knowledge and management expertise of both Institutes. In addition, an external scientific committee of experts has been established to provide guidance on all aspects of the design and evaluation of the pilot project. The committee will work with NCI and NHGRI staff to evaluate progress and revise scientific strategies, where necessary, to meet pilot project goals and milestones.

The pilot project is a major undertaking and will require considerable preparation to address all of the technical and scientific issues. It also will establish parameters that will demonstrate the feasibility of a large-scale project. Although the recommendation proposed to the National Cancer Board in February 2005 included cost projections, the NIH has not at this time determined the exact cost of the pilot project. The NCI and the NHGRI have recently committed to contribute up to \$50 million each over three years for the pilot. A set of Requests for Applications will be issued following the necessary institute approvals. The applications will be evaluated by a rigorous peer-review process and then funded according to standard NIH procedures.

### **Medical Sequencing**

With the completion of the Human Genome Project, and the acquisition of the genomic sequences of a number of other organisms for the purpose of aiding the annotation of the human sequence, the NHGRI now intends to harness the power of its large-scale sequencing program to reach the long-range objective of making human DNA sequencing a tool for both research and routine medical practice. As more is learned about the genetic contribution to disease, and as the cost of sequencing decreases, genomic sequence information will become ever more important

both for biomedical research and for providing medically relevant information to individuals. When it becomes affordable for an individual's genome to be fully sequenced, the information obtained will allow estimates of future disease risk, and improve the prevention, diagnosis, and treatment of disease.

The institute is particularly interested in defining a sequencing program that will both drive technology and produce data useful to biomedical research at all stages along the way. NHGRI has convened a Medical Sequencing Working Group (MSWG) to help it chart a course towards these aims. The MSWG is charged with providing both general advice on how the program should evolve and specific advice about projects that NHGRI should pursue in the near term with its existing sequencing capacity. The MSWG is also charged with providing guidance on setting policies for ethical, legal, and social issues arising from the program. The MSWG has identified three broad realms of interest: rare single gene disorders; complex disorders; and normal human variation. Within those realms, the MSWG has made proposals in three areas: uncloned mapped, rare single gene disorders; X-linked chromosome disorders; and multi-gene common diseases. It should be emphasized that the medical sequencing program is still in a formative stage: efforts in each of these proposed areas will likely have to be initiated at small scale, and results evaluated, before proceeding with larger-scale projects. The institute is now seeking input from the scientific community about how best to proceed in this area.

### **Knockout Mouse Project**

The technology to “knockout” or remove genes in mouse embryonic stem cells was developed in the late 1980s and has led to many insights into human biology and disease. However, knockout mice have so far been published and made available to the research community for only about 10 percent of the estimated 25,000 mouse genes. Recognizing the wealth of information that mouse knockouts can provide, the NHGRI coordinated a 2003 meeting to enable members of the genomics community to discuss the feasibility of a dedicated project to produce knockout mice for every mouse gene and make these mice available as a community resource. These discussions resulted in a coordinated, cooperative plan.

In March 2005, the NIH held a workshop to discuss the current status of the mouse knockout field, what international initiatives are planned to produce more mice, and what role the NIH should play to ensure that the mouse knockout resource envisioned by the meeting is realized. In preparation for the March 2005 meeting, the NIH gathered information about existing knockouts from the Mouse Genome Database and gene trap sequence data submitted to the NIH database GenBank, and conducted an inventory of available but unreported knockout mice. This showed that mutations have been constructed in at least 8,188 unique genes, though not all of these resources are generally available. The meeting heard from a European group that hopes to generate a large resource of mutations in embryonic stem (ES) cells of mice and learned that other knockout mice programs are planned elsewhere.

The workshop endorsed: 1) The importance of constructing a freely-accessible set of ES cells carrying null mutations with reporters as recommended by the meeting participants. The addition of 10,000 more nulls with a reporter would complete the resource, with a null for each gene in the mouse genome. Such a resource would complement the set of conditional mutants

that other projects plan to generate; 2) Efforts should be supported to develop the specific C57BL/6 ES cell lines as a system for generation of knockout mutants in an experimentally tractable genetic background; 3) “Repatriation” (collection) of existing ES cells and mice to repositories as an alternative to remaking the null mutants needs to be considered. However, issues such as quality control, relative expense, and other potential restrictions must be carefully evaluated before a decision is made; and 4) International mouse knockout efforts need to be coordinated to avoid overlap.

## **OTHER AREAS OF INTEREST**

### **\$100,000 and \$1,000 Genome Initiatives**

In August 2005, the NHGRI awarded grants totaling more than \$32 million to advance the development of innovative sequencing technologies intended to reduce the cost of DNA sequencing, and expand the use of genomics in biomedical research and health care. These efforts are aimed at speeding the rate at which the next generation of sequencing technologies become available in the scientific lab and the medical clinic. Over the past decade, DNA sequencing costs have fallen more than 100-fold, fueled in large part by tools, technologies, and process improvements developed as part of the successful effort to sequence the human genome. However, it still costs about \$10 million to sequence 3 billion base pairs - the amount of DNA found in the genomes of humans and other mammals.

The NHGRI’s near-term goal is to lower the cost of sequencing a mammalian-sized genome to \$100,000, which would enable researchers to sequence the genomes of hundreds or even thousands of people as part of studies to identify genes that contribute to common, complex diseases. Ultimately, the NHGRI’s vision is to cut the cost of whole-genome sequencing to \$1,000 or less, which will enable the sequencing of individual genomes as part of routine medical care. The ability to sequence an individual genome cost-effectively could enable health care professionals to tailor diagnosis, treatment, and prevention to each person’s unique genetic profile.

### **Minority Outreach Activities**

The NHGRI has been at the forefront of ensuring that minority scientists and students are equipped to meet the new challenges of genome research for the 21<sup>st</sup> century. New programs have been developed to increase the number of underrepresented minority genome scientists by: (1) providing opportunities for established minority scientists to conduct genome and genetic disease research at the NIH; (2) making training opportunities available at all career levels; (3) increasing awareness about genome and genetic research through NHGRI presentations at workshops, courses, and symposia and by supporting minority faculty and students to attend relevant workshops, courses, and symposia; and (4) increasing the diversity of the NHGRI staff.

Some of the specific activities of the institute regarding minority outreach stem from its Minority Action Plan, which was developed in 2002, and modified as the needs of the Institute have changed. The Plan requires grantees who receive significant research funds from the NHGRI to

provide opportunities for members of underrepresented minority groups to receive genomics training in their laboratories. The types of activities that are currently supported include curriculum development and teacher training for grades K-12; high school and undergraduate summer research internships; and graduate, postgraduate, and faculty fellowships. The number of underrepresented minorities receiving genomics training has increased significantly as a result of this initiative.

Another activity sponsored by the institute is the Current Topics in Genomic Research Short Course. This week-long summer intensive course on genetics attracts faculty and students from minority-serving institutions. It aims to update participants' knowledge in genetics and help them develop curriculum for their use, as well as to promote relationships and collaborations among groups that could continue those relationships and collaborations back at their schools, well beyond the Short Course.

To better inform the Latino community, the NHGRI, the National Council of La Raza's Institute for Hispanic Health (NCLR/IHH), and the NIH's Office of Rare Diseases (ORD), have established a one-year pilot project partnership to develop effective and efficient ways to reach Latino communities with information about family health history and access to services for genetic and rare diseases. The information will be taken directly to the community through the development of a training module specific to the needs of "promotores de salud," (lay health worker). The module will be used initially by the two partner community-based organizations involved with this project: La Clínica de la Raza in Oakland, CA and La Clínica del Pueblo in Washington, DC. In addition, the organizations involved will share the processes, outcomes, and challenges with a network of more than 300 community-based organizations throughout the nation.

### **Family History Initiative**

The history of illness within one's family is a resource of genetic information that can help more accurately determine an individual's risk for specific diseases. However, to date, this resource has been underutilized in health. To address this, the U.S. Surgeon General has established the U.S. Surgeon General's Family History Initiative, a collaborative effort between a number of Department of Health and Human Services agencies, including NHGRI, in cooperation with non-governmental groups. The purpose of the Initiative is to increase awareness of the utility of family history in health care and disease prevention, to encourage and enable individuals to compile their own family histories, and to promote family history as a tool in health maintenance and disease prevention. U.S. Surgeon General Richard Carmona has declared Thanksgiving Day, the day when many American families traditionally gather, as National Family History Day. Families are encouraged to share and discuss their family medical history on Thanksgiving Day and throughout the year. The first annual National Family History Day was celebrated on Thanksgiving 2004.

A software tool called "My Family Health Portrait" has been developed to help individuals compile family history information. Version I of the tool is downloadable in English or Spanish from the HHS web site, and to date there have been over 250,000 downloads of the tool. Free print versions are also available in both languages. Version II was launched just prior to

Thanksgiving 2005 as an improved, web-based tool. One of many new features of Version II is the ability for users to change the focus of the pedigree report to enable efficient sharing of the data with family members. It is hoped that this initiative will have an impact on patient-healthcare provider interaction, facilitating the development of more accurate family history information for patient medical records and leading to more personalized and effective disease prevention and treatment strategies.

## **INNOVATIONS IN MANAGEMENT AND ADMINISTRATION**

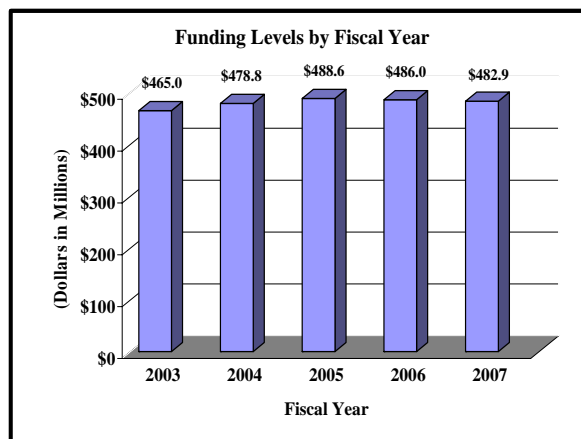
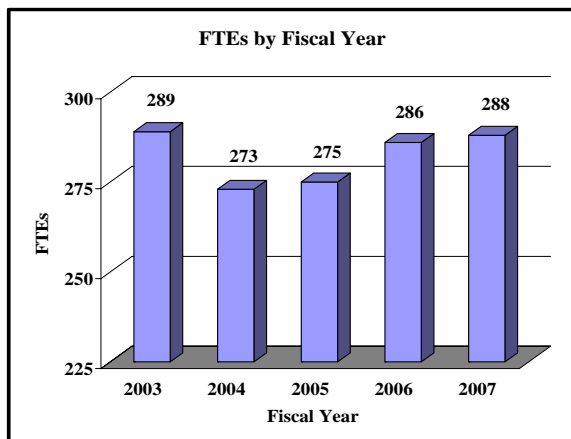
In an effort to offset the mandatory increases in Research Management and Support as well as Intramural Research, NHGRI is looking at: 1) changing the way that corporate administrative services such as IT, ethics, budget and finance, and management analysis are funded. This shift requires developing algorithms so such services can be funded appropriately by the programs utilizing these services; 2) revising the budget planning process so that operational and programmatic needs can be identified and accommodated early in the fiscal year to ensure that the requirement is funded appropriately; 3) reviewing how administrative services are being delivered with an eye towards recalibrating the balance between IC-wide management and local autonomy. The potential centralization of some administrative processes may result in a modest cost savings through economies of scale; 4) analyzing administrative processes and looking for ways to streamline and insert best practices into business practices. This process may improve the efficiency of business operations, and therefore, may result in a modest cost savings; and 5) reviewing Blackberry and cell phone usage to ensure that they are issued to the appropriate personnel as well as being used appropriately. NHGRI's goal is to decrease the issuance of telecommunications devices by 10 percent.

## **BUDGET POLICY**

The Fiscal Year 2007 budget request for the NHGRI is \$482,942,000, a decrease of \$3,107,000 and -0.6 percent below the FY 2006 Appropriation. Included in the FY 2007 request is NHGRI's support for the trans-NIH Roadmap initiatives, estimated at 1.2 percent of the FY 2007 budget request. 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 as the result of several administrative restructurings in recent years, FTE data is non-comparable.



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 pursuing new research opportunities. We estimate that the average cost of competing RPGs will be \$625,000 in FY 2007. While no inflationary increases are provided for direct recurring costs in noncompeting RPGs, where the NHGRI has committed to a programmatic increase for an award, such increases will be provided.

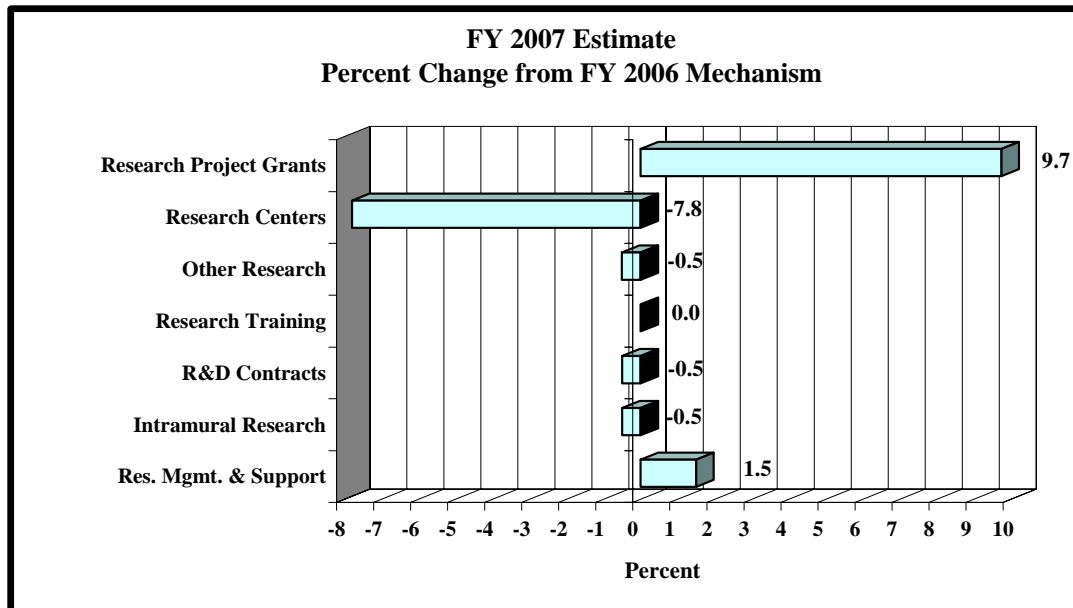
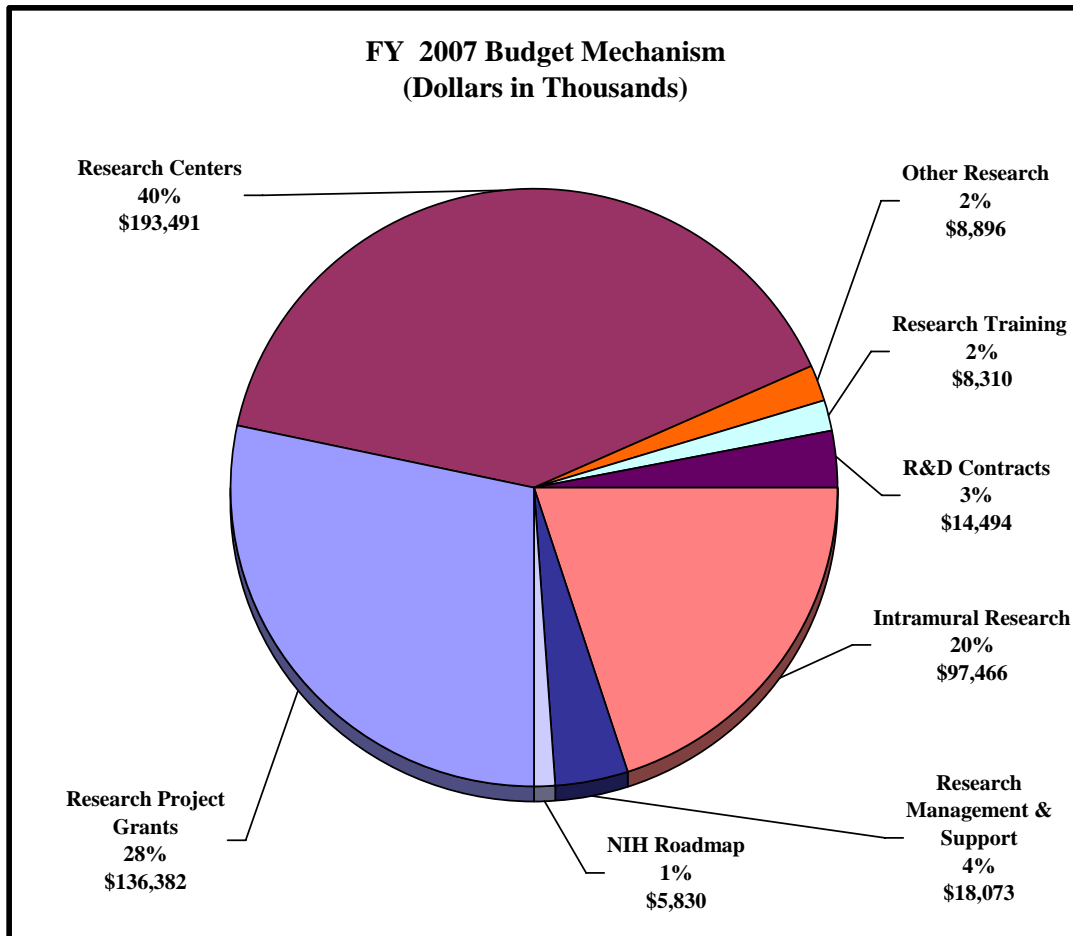
NIH must nurture a vibrant, creative research workforce, including sufficient numbers of new investigators with new ideas and new skills. In the FY 2007 budget request for NHGRI, \$270,000 will be used to support 3 awards for the new K/R "Pathway to Independence" program.

NHGRI will also support the Genes, Environment, and Health Initiative (GEHI) to: 1) accelerate discovery of the major genetic factors associated with diseases that have a substantial public health impact and; 2) accelerate the development of innovative technologies and tools to measure dietary intake, physical activity, and environmental exposures, and to determine an individual's biological response to those influences. The FY 2007 request includes \$825,000 to support this project.

In the FY 2007 request, stipend levels for trainees supported through the Ruth L. Kirschstein National Research Service Awards will remain at the FY 2006 levels.

The FY 2007 request includes funding for 30 research centers, 47 other research grants, including 21 career awards, and 20 R&D contracts. Intramural Research decreases by 0.5 percent. Research Management and Support increases by 1.5 percent.

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 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
<u>Research Projects:</u>						
Noncompeting	137	\$73,009,000	125	\$67,044,000	129	\$79,415,000
Administrative supplements	(25)	9,657,000	(23)	6,579,000	(23)	6,448,000
Competing:						
Renewal	6	12,032,000	8	5,002,000	8	5,001,000
New	45	19,867,000	57	35,638,000	57	35,627,000
Supplements	0	0	0	0	0	0
Subtotal, competing	51	31,899,000	65	40,640,000	65	40,628,000
Subtotal, RPGs	188	114,565,000	190	114,263,000	194	126,491,000
SBIR/STTR	36	10,281,000	36	10,014,000	35	9,891,000
Subtotal, RPGs	224	124,846,000	226	124,277,000	229	136,382,000
<u>Research Centers:</u>						
Specialized/comprehensive	24	184,740,000	21	182,401,000	21	168,186,000
Clinical research	0	0	0	0	0	0
Biotechnology	17	27,743,000	9	27,450,000	9	25,305,000
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	41	212,483,000	30	209,851,000	30	193,491,000
<u>Other Research:</u>						
Research careers	22	4,218,000	28	4,174,000	21	4,153,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	24	4,818,000	26	4,767,000	26	4,743,000
Subtotal, Other Research	46	9,036,000	54	8,941,000	47	8,896,000
<b>Total Research Grants</b>	<b>311</b>	<b>346,365,000</b>	<b>310</b>	<b>343,069,000</b>	<b>306</b>	<b>338,769,000</b>
<u>Research Training:</u>	<u>FTEPs</u>		<u>FTEPs</u>		<u>FTEPs</u>	
Individual awards	16	736,000	17	728,000	15	728,000
Institutional awards	156	7,663,000	151	7,582,000	151	7,582,000
Total, Training	172	8,399,000	168	8,310,000	166	8,310,000
Research & development contracts (SBIR/STTR)	21 (0)	14,528,000 (23,000)	21 (0)	14,567,000 (0)	20 (0)	14,494,000 (0)
Intramural research	<u>FTEs</u> 207	98,505,000	<u>FTEs</u> 208	97,954,000	<u>FTEs</u> 210	97,466,000
Research management and support	63	17,722,000	64	17,806,000	64	18,073,000
NIH Roadmap for Medical Research	5	3,089,000	14	4,343,000	14	5,830,000
Total, NHGRI	275	488,608,000	286	486,049,000	288	482,942,000
(Clinical Trials)		(9,758,000)		(9,682,000)		(9,590,000)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

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

**Budget Authority by Activity**  
**(dollars in thousands)**

ACTIVITY	FY 2005		FY 2006		FY 2007		Change	
	Actual		Appropriation		Estimate			
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
<u>Extramural Research:</u>								
Human Genome Research		\$369,292		\$365,946		\$361,573		(\$4,373)
Subtotal, Extramural research		369,292		365,946		361,573		(4,373)
Intramural research	207	98,505	208	97,954	210	97,466	2	(488)
Res. management & support	63	17,722	64	17,806	64	18,073	0	267
NIH Roadmap for Medical Research	5	3,089	14	4,343	14	5,830	0	1,487
Total	275	488,608	286	486,049	288	482,942	2	(3,107)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

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

**Summary of Changes**

FY 2006 Estimate		\$486,049,000		
FY 2007 Estimated Budget Authority		482,942,000		
Net change		(3,107,000)		
CHANGES	FY 2006 Appropriation		Change from Base	
	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		\$28,582,000		\$433,000
b. Annualization of January 2006 pay increase		28,582,000		222,000
c. January 2007 pay increase		28,582,000		487,000
d. Payment for centrally furnished services		15,699,000		235,000
e. Increased cost of laboratory supplies, materials, and other expenses		53,673,000		1,195,000
Subtotal				2,572,000
2. Research Management and Support:				
a. Within grade increase		9,057,000		163,000
b. Annualization of January 2006 pay increase		9,057,000		70,000
c. January 2007 pay increase		9,057,000		155,000
d. Payment for centrally furnished services		1,416,000		21,000
e. Increased cost of laboratory supplies, materials, and other expenses		7,333,000		155,000
Subtotal				564,000
Subtotal, Built-in				3,136,000

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

**Summary of Changes--continued**

CHANGES	FY 2006			
	Appropriation		Change from Base	
	No.	Amount	No.	Amount
<b>B. Program:</b>				
1. Research project grants:				
a. Noncompeting	125	\$73,623,000	4	\$12,240,000
b. Competing	65	40,640,000	0	(12,000)
c. SBIR/STTR	36	10,014,000	(1)	(123,000)
Total	226	124,277,000	3	12,105,000
2. Research centers	30	209,851,000	0	(16,360,000)
3. Other research	54	8,941,000	(7)	(45,000)
4. Research training	168	8,310,000	(2)	0
5. Research and development contracts	21	14,567,000	(1)	(73,000)
Subtotal, extramural				(4,373,000)
6. Intramural research	<u>FTEs</u> 208	97,954,000	<u>FTEs</u> 2	(3,060,000)
7. Research management and support	64	17,806,000	0	(297,000)
8. NIH Roadmap for Medical Research	14	4,343,000	0	1,487,000
Subtotal, program		486,049,000		(6,243,000)
Total changes	286		2	(3,107,000)

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

**Budget Authority by Object**

	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	286	288	2
Full-time equivalent of overtime & holiday hours	1	1	0
Average ES salary	\$145,193	\$149,549	\$4,356
Average GM/GS grade	11.8	11.8	0.0
Average GM/GS salary	\$80,057	\$81,818	\$1,761
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	\$75,492	\$76,775	\$1,283
Average salary of ungraded positions	115,882	117,852	1,970
<b>OBJECT CLASSES</b>	<b>FY 2006 Appropriation</b>	<b>FY 2007 Estimate</b>	<b>Increase or Decrease</b>
Personnel Compensation:			
11.1 Full-Time Permanent	\$12,542,000	\$13,396,000	\$854,000
11.3 Other than Full-Time Permanent	12,776,000	13,167,000	391,000
11.5 Other Personnel Compensation	600,000	651,000	51,000
11.7 Military Personnel	235,000	290,000	55,000
11.8 Special Personnel Services Payments	4,056,000	4,302,000	246,000
<b>Total, Personnel Compensation</b>	<b>30,209,000</b>	<b>31,806,000</b>	<b>1,597,000</b>
12.0 Personnel Benefits	7,254,000	7,496,000	242,000
12.2 Military Personnel Benefits	176,000	183,000	7,000
13.0 Benefits for Former Personnel	0	0	0
<b>Subtotal, Pay Costs</b>	<b>37,639,000</b>	<b>39,485,000</b>	<b>1,846,000</b>
21.0 Travel & Transportation of Persons	1,804,000	1,851,000	47,000
22.0 Transportation of Things	321,000	336,000	15,000
23.1 Rental Payments to GSA	0	0	0
23.2 Rental Payments to Others	24,000	26,000	2,000
23.3 Communications, Utilities & Miscellaneous Charges	540,000	555,000	15,000
24.0 Printing & Reproduction	166,000	171,000	5,000
25.1 Consulting Services	640,000	643,000	3,000
25.2 Other Services	10,532,000	10,552,000	20,000
25.3 Purchase of Goods & Services from Government Accounts	53,229,000	50,820,000	(2,409,000)
25.4 Operation & Maintenance of Facilities	3,139,000	3,153,000	14,000
25.5 Research & Development Contracts	2,403,000	2,412,000	9,000
25.6 Medical Care	746,000	748,000	2,000
25.7 Operation & Maintenance of Equipment	1,810,000	1,813,000	3,000
25.8 Subsistence & Support of Persons	0	0	0
<b>25.0 Subtotal, Other Contractual Services</b>	<b>72,499,000</b>	<b>70,141,000</b>	<b>(2,358,000)</b>
26.0 Supplies & Materials	10,269,000	10,334,000	65,000
31.0 Equipment	7,063,000	7,132,000	69,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	351,379,000	347,079,000	(4,300,000)
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	2,000	2,000	0
44.0 Refunds	0	0	0
<b>Subtotal, Non-Pay Costs</b>	<b>444,067,000</b>	<b>437,627,000</b>	<b>(6,440,000)</b>
<b>NIH Roadmap for Medical Research</b>	<b>4,343,000</b>	<b>5,830,000</b>	<b>1,487,000</b>
<b>Total Budget Authority by Object</b>	<b>486,049,000</b>	<b>482,942,000</b>	<b>(3,107,000)</b>

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

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

**Salaries and Expenses**

OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
<b>Personnel Compensation:</b>			
Full-Time Permanent (11.1)	\$12,542,000	\$13,396,000	\$854,000
Other Than Full-Time Permanent (11.3)	12,776,000	13,167,000	391,000
Other Personnel Compensation (11.5)	600,000	651,000	51,000
Military Personnel (11.7)	235,000	290,000	55,000
Special Personnel Services Payments (11.8)	4,056,000	4,302,000	246,000
<b>Total Personnel Compensation (11.9)</b>	<b>30,209,000</b>	<b>31,806,000</b>	<b>1,597,000</b>
Civilian Personnel Benefits (12.1)	7,254,000	7,496,000	242,000
Military Personnel Benefits (12.2)	176,000	183,000	
Benefits to Former Personnel (13.0)	0	0	0
<b>Subtotal, Pay Costs</b>	<b>37,639,000</b>	<b>39,485,000</b>	<b>1,846,000</b>
Travel (21.0)	1,804,000	1,851,000	47,000
Transportation of Things (22.0)	321,000	336,000	15,000
Rental Payments to Others (23.2)	24,000	26,000	2,000
Communications, Utilities and Miscellaneous Charges (23.3)	540,000	555,000	15,000
Printing and Reproduction (24.0)	166,000	171,000	5,000
<b>Other Contractual Services:</b>			
Advisory and Assistance Services (25.1)	640,000	643,000	3,000
Other Services (25.2)	10,532,000	10,552,000	20,000
Purchases from Govt. Accounts (25.3)	38,662,000	37,151,000	(1,511,000)
Operation & Maintenance of Facilities (25.4)	3,139,000	3,153,000	14,000
Operation & Maintenance of Equipment (25.7)	1,810,000	1,813,000	3,000
Subsistence & Support of Persons (25.8)	0	0	0
<b>Subtotal Other Contractual Services</b>	<b>54,783,000</b>	<b>53,312,000</b>	<b>(1,471,000)</b>
Supplies and Materials (26.0)	10,269,000	10,334,000	65,000
<b>Subtotal, Non-Pay Costs</b>	<b>67,907,000</b>	<b>66,585,000</b>	<b>(1,322,000)</b>
<b>Total, Administrative Costs</b>	<b>105,546,000</b>	<b>106,070,000</b>	<b>524,000</b>



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

**Significant Items in House and Senate Appropriations Committee Reports**

FY 2006 House Appropriations Committee Report Language (Report No. 109-143)

Item

***Genome strategic plan*** -- The Committee commends the Institute's efforts to contribute to the future possibility that comprehensive genome sequence information could become a part of each American's individual health care plan. NIH has assembled significant resources of well-characterized populations to enable the testing and validation of genotyping and genome sequencing in diseases that are known to have a strong genetic basis, such as diabetes, hypertension, and several others. The Committee urges NHGRI to work together with other appropriate Institutes in this regard to develop models for the new era of molecular medicine. (p. 94)

Action taken or to be taken

2005 witnessed the announcement by the International HapMap Consortium, a collaborative effort led by the National Institutes of Health (NIH), of the successful completion of the "Haplotype" Map. The HapMap reveals the way in which genetic variation is organized into chromosomal neighborhoods, and this will enable researchers to uncover the heritable causes of virtually any common disease. This detailed HapMap will greatly speed the progress of science and medicine and is a major accomplishment. Already the NHGRI, in collaboration with several other NIH institutes, is planning activities to use the HapMap to identify, in well-characterized populations, the major genetic susceptibility factors for a number of diseases of substantial public health impact, including diabetes, heart disease, stroke, cancer, and Alzheimer's disease.

Virtually all diseases have a hereditary component, which is transmitted from parent to child through the three billion DNA letters that make up the human genome. Within that massive instruction book, there are about 10 million alternate spellings, or "variants," where the DNA sequence commonly differs between individuals. Most of these variants are simple one-letter substitutions, called "single nucleotide polymorphisms," or "SNPs." While most SNPs are biologically unimportant, a small fraction significantly changes the function of a gene. Finding these disease-causing variants is one of the highest priorities of current biomedical research. The HapMap Project has greatly sped up the effort of identifying potential hereditary factors in virtually any common disease, by allowing researchers to conduct a HapMap-based "genome-wide association studies." The success of this approach was recently demonstrated by its use in finding a major causative gene for macular degeneration, the leading cause of blindness in the elderly. This discovery immediately opened new pathways to drug development and prevention never before even contemplated in a condition that, until now, was believed to be largely irreversible. Discovery of disease genes like this allows development of new models for molecular medicine, and eventually the interaction of this information into better preventive medicine for all Americans.

FY 2006 Senate Appropriations Committee Report Language (Report No. 109-103)

Item

***Basic Behavioral and Social Sciences Research*** -- The Committee encourages NHGRI to participate in trans-institute initiatives organized by OBSSR or another institute to strengthen basic behavioral research and enhance opportunities for behavioral science research training. (p. 149)

Action taken or to be taken

The NHGRI is an active participant in the efforts of the Office of Behavioral and Social Science Research (OBSSR) to coordinate and enhance behavioral research at the NIH. The Institute is represented on the OBSSR Coordinating Committee as well as the on the NIH's Health Disparities Planning Committee and Health Disparities Policy Subcommittee. The NHGRI also has a representative on the Methodological Innovations in the Behavioral and Social Sciences Initiative, which is part of the NIH Roadmap. The NHGRI is participating in an OBSSR self-evaluation working group that will culminate in a forward-looking research agenda as OBSSR celebrates its 10<sup>th</sup> anniversary. Under the leadership of OBSSR, the NHGRI also contributed to the recent commissioning of an IOM Report on gene and environment interactions to catalyze research in this area. In addition, the NHGRI has been working with the National Institute for General Medical Science (NIGMS) and its Behavioral Science-Biology Interface Training Program Planning Group.

Besides such NIH wide efforts, the NHGRI has developed a Social and Behavioral Research Branch within its own intramural program and recruited a distinguished Branch Chief and two tenure-track investigators. This new Branch's overarching objective is to conduct research on the social and behavioral aspects of translating genomic discoveries into improved health, thus assisting in the translation of basic biomedical research discoveries into practical behavioral interventions related to genetic disorders. The Branch has already formed productive collaborations with other components of the NIH that work on behavioral research.

Item

***Chromosome Abnormalities*** -- The Committee commends the NIH for its efforts over the past year to encourage new scientific work into molecular, genetic, clinical and therapeutic aspects of chromosome abnormalities. Because of the multi-systemic consequences of a chromosome abnormality, multidisciplinary and multi-Institute support by NIH will be required in order to make progress that will be meaningful to those affected. The Committee continues to urge NIH to seek ways to expand and intensify such research, especially studies involving the syndromes of chromosome 18. (p. 149)

Action taken or to be taken

Several NIH institutes fund projects that investigate chromosomal abnormalities. This includes work that specifically focuses on chromosome 18, such as research that looks at chromosome 18q deletion syndromes in human and mouse, research investigating dosage sensitive regions on

chromosome 18, research that examines chromosome 18 as a model for chromosomal instability, and studies that look at genomic imprinting on chromosome 18. In September of 2005, the NHGRI funded investigators published a detailed analysis of the finished sequence of chromosome 18, identifying 337 genes and a variety of other features of direct relevance to human disorders including deletions or duplications of this chromosome. (*Nature* 437:551-5, 2005)

NHGRI funds many projects that seek to increase our understanding of chromosomal structure, both normal and abnormal, in general. These include development of technology to allow identification of chromosomal insertions and deletions, research to examine the causes of genome instability, research that investigates chromosomal interactions, and studies that aim to identify all of the functional elements of the human genome and to understand their function.

The NIH will continue its efforts to expand the understanding of chromosome abnormalities.

#### Item

***Targeting Disease Prevention*** -- The Committee commends NHGRI for its leadership of the international haplotype mapping [HapMap] project. The HapMap will provide a powerful new public resource to gain a deeper understanding of human biology, and discover the genetic and environmental factors that contribute to disease, predict potential disease risk, optimize drug prescribing for individuals, and identify and validate critical new targets for therapeutic development. These new developments also suggest that a large-scale population-based cohort study in the United States could provide a critical path toward improved genome-based public health and the Committee urges NHGRI to explore the feasibility of commencing such a study. (p. 149)

#### Action taken or to be taken

On October 26, 2005, an international consortium of dedicated scientists from six countries, led by the NHGRI, announced the production of a new map of the human genome, one that may prove even more powerful than the human genome sequence, because of its medical applications. This is the "HapMap". Once again all of the data has been placed in the public domain.

The Genome Project spelled out the letters of the DNA code that we all share. The HapMap provides detailed knowledge of the variation in the genome. The HapMap reveals the way in which this genetic variation is organized into chromosomal neighborhoods, and now we can use it to uncover the heritable causes of virtually any common disease. This detailed HapMap will greatly speed the progress of science and medicine and is a major accomplishment. The NHGRI will build on this success to understand better the genetic and environmental factors that cause disease and to develop more tools that will benefit all of science and humankind.

The need for a large-scale population study to understand the biological processes and pathways leading to common diseases has become increasingly clear. To gain such understanding would require gathering and integrating information about pertinent genetic and environmental factors

that influence health, disease, and response to treatment. To obtain an unbiased picture of the spectrum of factors that contribute to common diseases, it would be important to study a large representative sample of the population within the United States, and to follow these individuals prospectively over many years. Effectively studying diseases with general population prevalence as low as one percent will require studying hundreds of thousands of people. The NHGRI has begun discussing the possibility of such a study with the NIH Director and other NIH institutes and centers. The NHGRI convened a working group in summer 2004 with outside experts to explore this possible project. The report of the working group is now available on the Web at: <http://www.genome.gov/Pages/About/OD/ReportsPublications/PotentialUSCohort.pdf>.

In FY 2006-2007, the NHGRI plans to support community consultations to obtain views from the public on what the design of large-scale U.S.-based studies of genes and environment in health should look like.

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

**Authorizing Legislation**

	PHS Act/ Other Citation	U.S. Code Citation	2006 Amount Authorized	FY 2006 Appropriation	2007 Amount Authorized	FY 2007 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
National Human Genome Research Institute	Section 401	42§285b	Indefinite	\$477,739,000	Indefinite	\$474,632,000
National Research Service Awards	Section 487(d)	42§288	a/	8,310,000		8,310,000
<b>Total, Budget Authority</b>				<b>486,049,000</b>		<b>482,942,000</b>

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

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

**Appropriations History**

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation <u>1/</u>
1998	202,197,000 <u>2/</u>	211,772,000	218,851,000	217,704,000
1999	236,275,000 <u>2/ 3/</u>	246,111,000	249,891,000	264,892,000
Rescission				(185,000)
2000	271,536,000 <u>2/</u>	308,012,000	337,322,000	337,322,000
Rescission				(1,795,000)
2001	353,427,000 <u>2/</u>	386,410,000	385,888,000	382,384,000
Rescission				(192,000)
2002	426,739,000	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	492,670,000	496,400,000	492,670,000
Rescission				(4,062,000)
2006	490,959,000	490,959,000	502,804,000	490,959,000
Rescission				(4,881,000)
2007	482,942,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

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

3/ Reflects a decrease 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 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Office of the Director	6	6	6
Office of Administrative Management	18	18	18
Office of Policy, Communications and Education	12	12	12
Division of Intramural Research	212	223	225
Division of Extramural Research	27	27	27
<b>Total</b>	<b>275</b>	<b>286</b>	<b>288</b>
Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research			
FTEs supported by funds from Cooperative Research and Development Agreements	(2)	(2)	(2)
FISCAL YEAR	Average GM/GS Grade		
2003	10.8		
2004	11.6		
2005	11.8		
2006	11.8		
2007	11.8		

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**Detail of Positions**

GRADE	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Total - ES Positions	1	1	1
Total - ES Salary	\$142,346	\$145,193	\$149,549
GM/GS-15	22	22	22
GM/GS-14	11	11	11
GM/GS-13	38	38	38
GS-12	41	41	41
GS-11	21	22	22
GS-10	3	2	2
GS-9	9	10	10
GS-8	10	9	9
GS-7	10	13	13
GS-6	1	0	0
GS-5	0	0	0
GS-4	0	0	0
GS-3	1	1	1
GS-2	0	0	0
GS-1	0	0	0
Subtotal	167	169	169
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	1	1	1
Senior Assistant Grade			
Assistant Grade			
Subtotal	3	3	3
Ungraded	125	126	128
Total permanent positions	167	169	169
Total positions, end of year	296	299	301
Total full-time equivalent (FTE) employment, end of year	275	286	288
Average ES salary	\$142,346	\$145,193	\$149,549
Average GM/GS grade	11.8	11.8	11.8
Average GM/GS salary	\$77,392	\$80,057	\$81,818

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research



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**New Positions Requested**

	FY 2007		
	Grade	Number	Annual Salary
Tenure-Track Investigator	Title 42	2	\$100,000
Total Requested		2	