

DEPARTMENT OF HEALTH AND HUMAN SERVICES

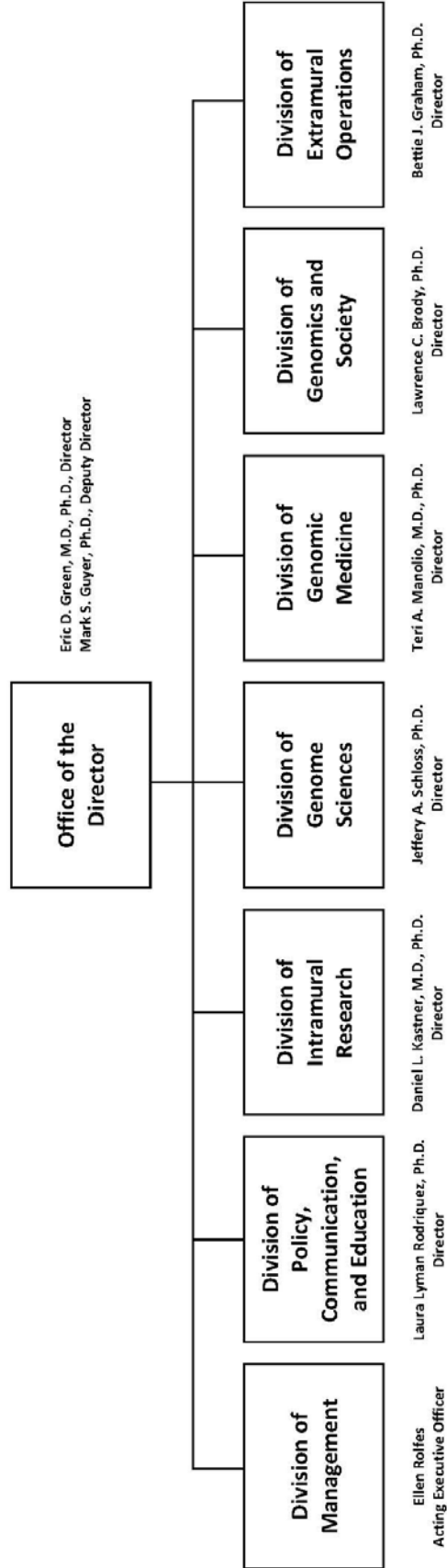
NATIONAL INSTITUTES OF HEALTH

National Human Genome Research Institute (NHGRI)

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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 PHS Act with respect to human genome research, [\$497,813,000] *\$498,451,000*.

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

Amounts Available for Obligation¹
(Dollars in Thousands)

Source of Funding	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Appropriation	\$512,873	\$497,813	\$498,451
Type 1 Diabetes	0	0	0
Rescission	-1,026	0	0
Sequestration	-25,743	0	0
Subtotal, adjusted appropriation	\$486,104	\$497,813	\$498,451
FY 2013 Secretary's Transfer	-2,836	0	0
OAR HIV/AIDS Transfers	0	0	0
Comparative transfers to NLM for NCBI and Public Access	-574	-685	0
National Children's Study Transfers	412	0	0
Subtotal, adjusted budget authority	\$483,107	\$497,128	\$498,451
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	\$483,107	\$497,128	\$498,451
Unobligated balance lapsing	-31	0	0
Total obligations	\$483,076	\$497,128	\$498,451

¹ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2013 - \$26,251 FY 2014 - \$26,414 FY 2015 - \$26,459

**NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute
Budget Mechanism - Total¹**

(Dollars in Thousands)

MECHANISM	FY 2013 Actual		FY 2014 Enacted ²		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
<u>Research Projects:</u>								
Noncompeting	162	\$87,579	162	\$103,250	147	\$98,606	-15	-\$4,644
Administrative Supplements	(15)	2,553	(8)	1,431	(7)	1,510	(-1)	79
<u>Competing:</u>								
Renewal	12	12,132	11	9,690	11	10,517	0	827
New	58	33,234	53	26,546	54	28,812	1	2,266
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	70	\$45,367	64	\$36,236	65	\$39,329	1	\$3,093
Subtotal, RPGs	232	\$135,498	226	\$140,917	212	\$139,445	-14	-\$1,472
SBIR/STTR	25	10,925	26	11,844	28	12,200	2	356
Research Project Grants	257	\$146,423	252	\$152,761	240	\$151,645	-12	-\$1,116
<u>Research Centers:</u>								
Specialized/Comprehensive	31	\$108,071	27	\$130,589	23	\$116,658	-4	-\$13,931
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	23	52,895	22	53,665	26	65,849	4	12,184
Comparative Medicine	0	0	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	54	\$160,967	49	\$184,254	49	\$182,507	0	-\$1,747
<u>Other Research:</u>								
Research Careers	11	\$1,281	11	\$1,419	11	\$1,505	0	\$86
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	400	0	400	0	400	0	0
Other	19	23,910	20	3,732	23	4,239	3	507
Other Research	30	\$25,592	31	\$5,551	34	\$6,144	3	\$593
Total Research Grants	341	\$332,981	332	\$342,566	323	\$340,296	-9	-\$2,270
<u>Ruth L Kirchstein Training Awards:</u>	<u>FTTPs</u>		<u>FTTPs</u>		<u>FTTPs</u>		<u>FTTPs</u>	
Individual Awards	9	\$386	7	\$313	13	\$585	6	\$272
Institutional Awards	159	7,399	134	6,244	163	7,533	29	1,289
Total Research Training	168	\$7,785	141	\$6,557	176	\$8,118	35	\$1,561
Research & Develop. Contracts	7	\$18,067	7	\$18,718	7	\$21,134	0	\$2,416
<i>(SBIR/STTR) (non-add)</i>	<i>(0)</i>	<i>(72)</i>	<i>(0)</i>	<i>(124)</i>	<i>(0)</i>	<i>(124)</i>	<i>(0)</i>	<i>(0)</i>
Intramural Research	239	99,435	239	102,447	239	103,420	0	973
Res. Management & Support	94	24,838	94	25,590	94	25,483	0	-107
<i>Res. Management & Support (SBIR Admin) (non-add)</i>	<i>(0)</i>	<i>(0)</i>	<i>(0)</i>	<i>(0)</i>	<i>(0)</i>	<i>(0)</i>	<i>(0)</i>	<i>(0)</i>
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NHGRI	333	\$483,107	333	\$497,128	333	\$498,451	0	\$1,323

¹ All items in italics and brackets are non-add entries. FY 2013 and FY 2014 levels are shown on a comparable basis to FY 2015.

² The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

Major Changes in Fiscal Year 2015 President's Budget Request

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note that there may be overlap between budget mechanism and activity detail and these highlights will not sum to the total change for the FY 2015 President's Budget request for NHGRI, which is \$1.323 million more than the FY 2014 Enacted level for a total of \$498.451 million.

Research Training (+\$1.561 million, total \$8.118 million):

Support to the NHGRI NRSA training mechanism will be increased by \$1.561 million. The increase will be used to provide funds for an institutional training program in Genomic Medicine. This will increase the number of trainees and develop leaders in genomic sciences who will be crossed-trained in scientific disciplines relevant to genomics. These increases also support Clinical Scientist Development Awards in Genomic Medicine which will provide clinically trained individuals with a mentored genomics research experience that will facilitate their transition to independent research careers.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Summary of Changes¹

(Dollars in Thousands)

FY 2014 Enacted				\$497,128
FY 2015 President's Budget				\$498,451
Net change				\$1,323
CHANGES	FY 2015 President's Budget		Change from FY 2014	
	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2014 pay increase & benefits		\$37,552		\$140
b. January FY 2015 pay increase & benefits		37,552		421
c. Zero more days of pay (n/a for 2015)		37,552		0
d. Differences attributable to change in FTE		37,552		0
e. Payment for centrally furnished services		16,342		162
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		49,526		250
Subtotal				\$973
2. Research Management and Support:				
a. Annualization of January 2014 pay increase & benefits		\$10,794		\$40
b. January FY 2015 pay increase & benefits		10,794		121
c. Zero more days of pay (n/a for 2015)		10,794		0
d. Differences attributable to change in FTE		10,794		0
e. Payment for centrally furnished services		971		10
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		13,718		0
Subtotal				\$171
Subtotal, Built-in				\$1,144

¹ The amounts in the Change from FY 2014 column take into account funding reallocations, and therefore may not add to the net change reflected herein.

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

Summary of Changes - Continued¹

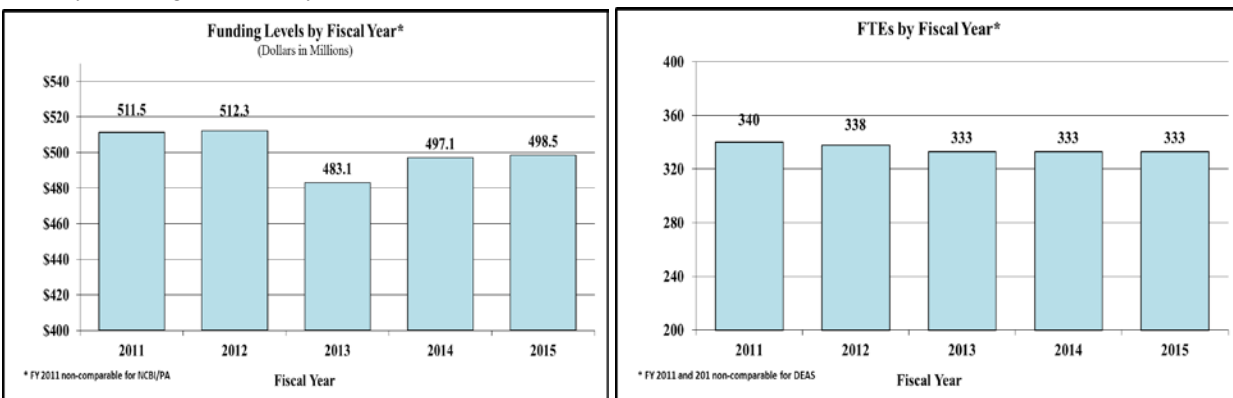
(Dollars in Thousands)

CHANGES	FY 2015 President's Budget		Change from FY 2014	
	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	147	\$100,116	-15	-\$4,565
b. Competing	65	39,329	1	3,093
c. SBIR/STTR	28	12,200	2	356
Subtotal, RPGs	240	\$151,645	-12	-\$1,116
2. Research Centers	49	\$182,507	0	-\$1,747
3. Other Research	34	6,144	3	593
4. Research Training	176	8,118	35	1,561
5. Research and development contracts	7	21,134	0	2,416
Subtotal, Extramural		\$369,548		\$1,707
6. Intramural Research	<u>FTEs</u> 239	\$103,420	<u>FTEs</u> 0	\$0
7. Research Management and Support	94	25,483	0	-278
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, Program	333	\$498,451	0	\$1,429
Total changes				\$1,323

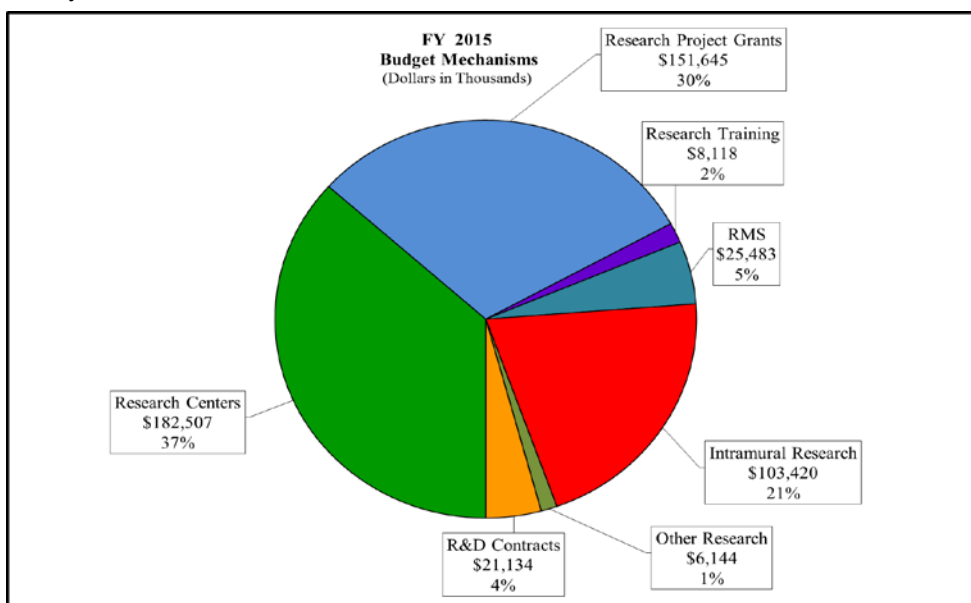
¹ The amounts in the Change from FY 2014 column take into account funding reallocations, and therefore may not add to the net change reflected herein.

Fiscal Year 2015 Budget Graphs

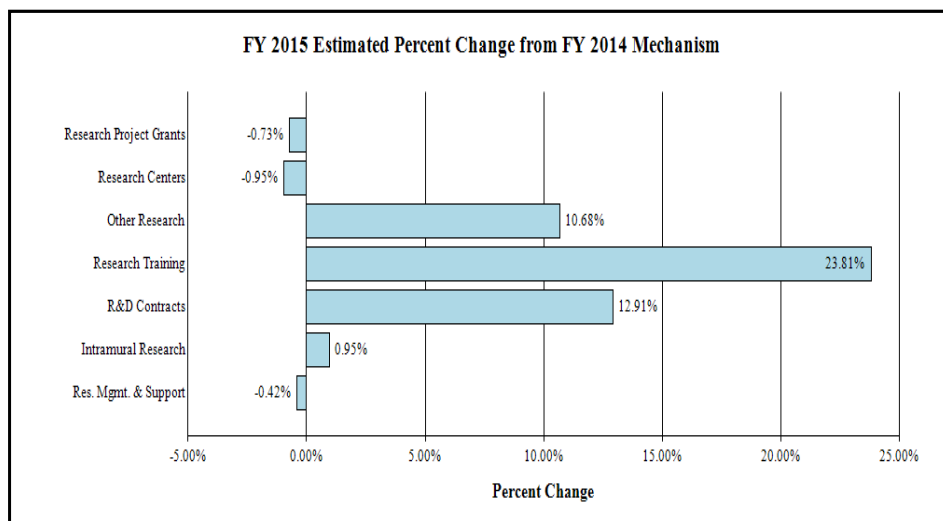
History of Budget Authority and FTEs:



Distribution by Mechanism:



Change by Selected Mechanism:



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

Budget Authority by Activity¹
(Dollars in Thousands)

	FY 2013 Actual		FY 2014 Enacted ²		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Program Activity:								
<u>Detail:</u>								
Understanding the Structure of Genomes		\$31,738		\$27,271		\$27,410		\$139
Understanding the Biology of Genomes		74,854		81,779		82,226		447
Using Genomics to Understand the Biology of Disease		131,833		141,141		141,973		832
Using Genomics to Advance Medical Science		22,563		21,275		21,451		176
Using Genomics to Improve the Effectiveness of Healthcare		9,541		10,840		10,920		80
Bioinformatics and Computational Biology		119,193		115,183		115,777		594
Education and Training		23,251		22,008		22,155		147
Genomics and Society		45,295		50,790		51,056		266
Subtotal, Program Activity*		458,269		470,288		472,968		2,680
<i>Extramural Research (non-add)</i>	<i>0</i>	<i>(358,834)</i>	<i>0</i>	<i>(367,841)</i>	<i>0</i>	<i>(369,548)</i>	<i>(0)</i>	<i>(1,707)</i>
<i>Intramural Research (non-add)</i>	<i>239</i>	<i>(99,435)</i>	<i>239</i>	<i>(102,447)</i>	<i>239</i>	<i>(103,420)</i>	<i>(0)</i>	<i>(973)</i>
Research Management & Support	94	\$24,838	94	\$25,590	94	\$25,483	0	-\$107
TOTAL	333	\$483,107	333	\$497,128	333	\$498,451	0	\$1,323

¹ Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

² The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

* The detail programs listed above include both extramural and intramural funding.

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

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2014 Amount Authorized	FY 2014 Enacted	2015 Amount Authorized	FY 2015 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	\$497,128,000	Indefinite	\$498,451,000
National Human Genome Research Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				\$497,128,000		\$498,451,000

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

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2005 Rescission	\$492,670,000	\$492,670,000	\$496,400,000	\$492,670,000 (\$4,062,000)
2006 Rescission	\$490,959,000	\$490,959,000	\$502,804,000	\$490,959,000 (\$4,910,000)
2007 Rescission	\$482,942,000	\$482,942,000	\$486,315,000	\$486,491,000 \$0
2008 Rescission Supplemental	\$484,436,000	\$493,996,000	\$497,031,000	\$495,434,000 (\$8,655,000) \$2,589,000
2009 Rescission	\$487,878,000	\$504,603,000	\$501,411,000	\$502,367,000 \$0
2010 Rescission	\$509,594,000	\$520,311,000	\$511,007,000	\$516,028,000 \$0
2011 Rescission	\$533,959,000		\$533,127,000	\$516,028,000 (\$4,531,033)
2012 Rescission	\$524,807,000	\$524,807,000	\$505,783,000	\$513,844,000 (\$971,165)
2013 Rescission Sequestration	\$511,370,000		\$512,920,000	\$512,872,835 (\$1,025,746) (\$25,742,690)
2014 Rescission	\$517,319,000		\$513,881,000	\$497,813,000 \$0
2015	\$498,451,000			

Justification of Budget Request

National Human Genome Research Institute

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

Budget Authority (BA):

	FY 2013 <u>Actual</u>	FY 2014 <u>Enacted</u>	FY 2015 President's <u>Budget</u>	FY 2015 +/- <u>FY 2014</u>
BA	\$483,106,792	\$497,128,000	\$498,451,000	+\$1,323,000
FTE	333	333	333	+0

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

Director's Overview

Since the completion of the Human Genome Project (HGP) in 2003, the use of genomic approaches to investigate the role of the genetic code in human health and disease has become pervasive across the biomedical research enterprise. Research funded by the National Human Genome Research Institute (NHGRI) has generated genomic technologies and a growing scientific knowledge base that is enabling today's scientists to conduct basic and translational research to create the foundation for tomorrow's medical breakthroughs. Already, convincing examples are emerging in which a person's genomic information can be used to tailor the treatment for his or her particular disease. In FY 2015, NHGRI's long-standing experience with high-throughput research strategies and technology development will continue to drive genomics-derived progress and innovation throughout the biomedical research community.

Successes emanating from the NHGRI Genome Technology Program have played a major role in the phenomenal decrease in the cost and time needed to sequence a human genome—something that a decade ago would have taken months and millions of dollars can now be accomplished in 1-2 days for a mere \$3,000-5,000.¹ It is now essentially trivial to generate very large datasets of human genome sequences, but this advancement has created the increasingly common circumstance where data analysis and management (not data production) become the bottlenecks in the process to apply genomic information to health care.

The above technological advances and other developments have made genomics a prototypic 'big data' enterprise, bringing major challenges in terms of data management and analysis. To address these new demands, NHGRI has emerged as a leader in data science. For example, the development of readily accessible computational tools is vital for effectively using genome sequence data in basic and clinical research. Such a need is being addressed by NHGRI's

¹ <http://www.genome.gov/sequencingcosts/>

iSeqTools program, which aims to ‘democratize’ access to genome-analysis software by developing and disseminating such tools to biomedical researchers outside of specialist centers. This and other NHGRI data-science programs are synergizing effectively with the broader trans-NIH Big Data to Knowledge (BD2K) initiative.

NHGRI’s extramural research flagship component is the Genome Sequencing Program. A major focus of this program is to accelerate our understanding of how genotype (the genetic constitution of an individual) leads to phenotype (an individual’s physical characteristics, including diseases). For example, the Centers for Mendelian Genomics are investigating the thousands of rare genetic diseases for which the underlying genomic basis remains unknown. In addition to facilitating the rapid and accurate diagnosis of these disorders, the knowledge gained by identifying the genomic defect often leads to new and key insights about more common diseases that involve similar genes or related gene pathways. Meanwhile, investigators at the Large-Scale Sequencing and Analysis Centers are studying more common but also more complicated diseases, often in partnership with investigators supported by other NIH institutes. Notable examples include cancer (in collaboration with the National Cancer Institute), Alzheimer’s disease (in collaboration with the National Institute on Aging), autism (in collaboration with the National Institute for Mental Health), and diabetes (in collaboration with the National Institute of Diabetes and Digestive and Kidney Diseases).

Genomics is still a young field, but it is already positively affecting patient care, for example, in the more precise administration of medications. Indeed, the U.S. Food and Drug Administration now requires ‘pharmacogenomic’ information—where an individual’s particular genomic variation is used to guide drug choice or tailor the drug dose—to appear on the labels of more than 100 medications currently on the market (up from less than ten roughly two decades ago). The number of drugs for which genomic information will help guide the treatment of a patient with that drug should continue to grow.

Thanks to the rapid decrease in the cost for sequencing a human genome, it is becoming increasingly feasible to use genome sequencing as a diagnostic tool. This is being actively piloted by a number of NHGRI-led programs, including the extramural Clinical Sequencing Exploratory Research program and the intramural Undiagnosed Diseases Program. Successes with the latter have led to the establishment of a new NIH Common Fund initiative, the Undiagnosed Diseases Network (for which NHGRI will also play a major leadership role). Also in FY 2015, the Institute will continue to co-fund the Genomic Sequencing and Newborn Screening Disorders research program with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; this innovative program supports integrated research teams of clinicians, scientists, and bioethicists that aim to further the understanding of newborn disorders and to improve treatments for these diseases through the use of genomic information.

To provide more robust resources for studying and treating genetically complex diseases, NHGRI FY 2015 funding will support the Clinical Genome Resource (ClinGen) and, in collaboration with the National Institute on Drug Abuse, the PhenX Project. ClinGen will evaluate and then synthesize published research regarding the clinical relevance of genomic variants into a user-friendly database; this database will be a resource to stimulate further research and could serve as the substrate for developing practice guidelines by relevant clinical

societies. The PhenX Project will develop standard measures related to complex diseases, phenotypes, and environmental exposures to make it simpler for researchers to harmonize data from disparate studies, expanding the data's potential usage beyond the primary research focus.

Finally, it is worth noting that the nation's investment in genomics is delivering benefits, beyond those in science and medicine, to the broader economy. In 2013, the Battelle Technology Partnership Practice published a report, *The Impact of Genomics on the US Economy*,² updating a previous 2011 report. Between 1988 and 2012, the federal government invested \$14.5 billion in genomic research; during that same time frame, this investment generated an estimated economic impact of \$965 billion, creating \$293 billion in personal income. NHGRI will leverage the programs described above as well as the other innovative basic, translational, and clinical efforts that make up the entirety of the Institute's research portfolio to ensure that the promise of genomics will be realized. In doing so, one can anticipate that the economic impact of genomics will continue to grow in FY 2015.

Overall Budget Policy:

The FY 2015 President's Budget request for NHGRI is \$498.451 million, an increase of \$1.323 million or 0.3 percent above the 2014 Enacted level.

Program Descriptions and Accomplishments

Understanding the Structure of Genomes: Research projects that aim to understand the structure of genomes continue to constitute a fundamental part of NHGRI's research portfolio in FY 2015. The Advanced DNA Sequencing Technology Program, a signature technology-development effort of the Institute's Extramural Research Program, has been one of NHGRI's most successful endeavors to date. Launched in 2004, when sequencing the ~3 billion bases in an individual human genome cost tens of millions of dollars, this Program has been responsible for the development of breathtaking new methods for DNA sequencing. The resulting cost reductions have outpaced those seen in the computer industry over the last decade. As a result, the cost of sequencing a human genome has fallen by many orders of magnitude to approximately \$5,000, thereby enabling a multitude of genomic studies to be performed for elucidating important nuances of genome structure. In order to decrease cost further in FY 2015 while also improving data quality, this Program will continue to fund research and development of novel DNA sequencing technologies, with an emphasis on new novel nanopore-based technologies. This technology involves threading single DNA strands through tiny synthetic pores called nanopores. Individual bases—the chemical letters of DNA—are read one at a time as they pass through a nanopore. For perspective, a human hair is 100,000 nanometers in diameter, while a strand of DNA is only two nanometers in diameter. Nanopores being used for these new DNA sequencing methods are 1-2 nanometers in diameter and identify the specific DNA bases by measuring their differential effects on electronic current flowing through the pore.

Budget Policy:

The FY 2015 President's Budget request for Understanding the Structure of Genomes is \$27.410 million, an increase of \$0.139 million or 0.5 percent more than the FY 2014 Enacted level.

² <http://www.battelle.org/site/the-impact-of-genomics-on-the-u-s-economy>

NHGRI will continue to support the development of technologies, exemplified by nanopore sequencing, that have potential to further drive down costs while improving the quality of human genome sequence information that is being obtained for research and clinical uses. The Institute also will continue to fund meritorious investigator-initiated applications to apply these and other technologies toward refining our understanding of genome structure.

Understanding the Biology of Genomes: The development of tools and resources to analyze the structure of individual genomes are also essential for studies that aim to understand how genomes function. An individual's genome sequence can be thought of as the book of instructions required to build all the cells and tissues in that person's body. A high priority for NHGRI is to decipher those instructions through the pursuit of studies that reveal and characterize the various functional elements in the genome. The Encyclopedia of DNA Elements (ENCODE) is the Institute's major program in this area, one that has greatly expanded our understanding of the complex molecular choreography required for converting genomic information into living cells and organisms. In FY 2015, as the current round of ENCODE funding draws to a close, investigators will finalize the generation of ENCODE data and shift their focus to the analysis and publication of this important resource. In order to maximize the impact of ENCODE data, NHGRI will undertake a significant community outreach effort in FY 2015 to define how the nation's investment in ENCODE can be utilized for studying and understanding human health and disease.

Building on earlier ENCODE successes, NHGRI recently launched a new research effort, the Genomics of Gene Regulation (GGR) program, which will be ramping up data production and analysis in FY 2015. While ENCODE is developing a catalog of the genomic elements that play a functional role, GGR aims to establish how those elements are "choreographed" in the assembly and operation of cells and tissues, and specifically focuses on elements involved in regulating the expression of genes—that is, turning genes on and off. GGR is described in greater detail in the Program Portrait below.

Budget Policy:

The FY 2015 President's Budget request for Understanding the Biology of Genomes is \$82.226 million, an increase of \$0.447 million or 0.6 percent more than the FY 2014 Enacted level. The investments in Genomics of Gene Regulation will continue as will efforts to integrate data produced by the ENCODE and GGR projects with those of other projects funded by NHGRI and the NIH Common Fund. By integrating information from these diverse datasets, the research community can build on these existing investments to gain powerful new insights into causes and possible treatments for disease—the ultimate goal of these investments in understanding the biology. Efforts are also being pursued to develop new computational methods that will use these merged data to understand the role of specific DNA sequence changes found in particularly challenging regions of the genes of patients who have specific diseases. The Institute will continue to fund meritorious investigator-initiated applications to develop better tools, models and insights into the relationship between genome structure and biology.

Program Portrait: Genomics of Gene Regulation

FY 2014 Level: \$10.0 million

FY 2015 Level: \$10.0 million

Change: +\$0.0 million

The years since completion of the Human Genome Project have brought about many efforts devoted to understanding how the ~20,000 genes in the human genome are regulated. Gene sequences constitute a mere ~1.5 percent of the ~3-billion-base-long human genome; these are the segments of DNA sequence that code for the proteins that make up the human body. Individual genes and networks of genes are switched on and off by other regions of the genome (called non-coding functional sequences), which do not contain the instructions for making proteins. A thorough understanding of how genes are regulated would allow a scientist to look at a DNA sequence and predict where, when, and how much any gene is expressed.

Researchers have been investigating gene regulation at the level of individual genes for many decades, but the advent of cost-effective and rapid DNA sequencing technologies now provides a previously unimaginable opportunity to conduct detailed analyses of gene regulation in a high-throughput, high-resolution manner. This development has significant relevance to human health—it now appears that the majority of genomic variants that confer risk for common, complex diseases (e.g., diabetes, cardiovascular disease, and mental illness) reside outside of protein-coding sequences and likely in gene-regulatory sequences.

NHGRI's highly successful Encyclopedia of DNA Elements (ENCODE) Project laid a foundation for studying gene regulation in greater detail by cataloging all the regions of the human genome that function in ways beyond coding for proteins, but determining how these functional elements interact with one another to control gene expression was beyond the scope of ENCODE. To that end, NHGRI's new Genomics of Gene Regulation (GGR) initiative is funding a set of demonstration projects that will develop and explore experimental models for investigating how sets of functional genomic elements work in concert to determine when and how individual genes are expressed.

GGR investigators will generate genomic data from a number of different cell types using cutting-edge methods, combining the new information with existing datasets from ENCODE and other public resources. Models of gene-regulatory networks will be developed and used to inform testable hypotheses of how a given stimulus affects the regulation of genes in directing cell development, differentiation, and function. It is anticipated that this process will provide a detailed understanding of the specific gene-regulatory network under study by each GGR project. Through investigating several gene-regulatory networks in this fashion and by organizing the projects in a collaborative research network, the GGR program aims to establish an improved ability to decipher the rules that govern gene regulation, to determine which of these rules are generalizable, and to develop methodologies for expanding this approach to other gene-regulatory pathways.

Using Genomics to Understand the Biology of Disease: NHGRI's largest budgetary investment is in studies that use the tools and strategies associated with genomics research to understand the biology of disease. Work in this research domain builds upon the foundational knowledge provided by the previously described areas (Understanding the Structure of Genomes and Understanding the Biology of Genomes) to advance our understanding of how an individual's genome contributes to his or her health and makes that person susceptible to certain diseases.

There are approximately 7,000 to 9,000 known rare diseases, which are defined as conditions that affect fewer than 200,000 individuals in the U.S.; in aggregate, this group of diseases affects

roughly 25 million Americans. A specific genomic anomaly is the cause of virtually all of these disorders—a given rare disease might be caused by a single letter difference in the ~3 billion letters that make up the human genome sequence. Some of these are relatively well-known conditions, such as cystic fibrosis, but others are extremely rare and may affect only a few families. The genomic bases for upwards of 4,000 of these conditions remain unknown. Thanks to the rapidly decreasing costs for genome sequencing, it is now more feasible than ever to pursue studies aiming to establish the precise genomic variants causing these disorders. Through a combination of NHGRI's extramural Centers for Mendelian Genomics, multiple components of the NHGRI's Intramural Research Program, and the NIH Common Fund's Undiagnosed Diseases Network (a trans-NIH program led by NHGRI), FY 2015 will be a year when there are many studies investigating the genomic origins of phenotypically described rare diseases. Together, these efforts aim to discover the culprit genomic variants, to discover new diseases, and to inform possible treatment strategies.

Another major NHGRI initiative, the Population Architecture using Genomics and Epidemiology (PAGE) Program, focuses on identifying the genomic variants underlying a wide range of common diseases and traits in large, ethnically diverse cohorts. PAGE investigators, in collaboration with the Center for Inherited Disease Research at Johns Hopkins University, are studying ~50,000 participants of non-European descent from well-described cohorts to better understand how ethnic differences in genomic variation relate to human diseases.

Budget Policy:

The FY 2015 President's Budget request for Using Genomics to Understand the Biology of Disease is \$141.973 million, an increase of \$0.832 million or 0.6 percent more than the FY 2014 Enacted level. NHGRI will update and expand the GWAS Catalog to include a standardized naming system of traits that will make the information more readily transportable across databases, and will continue to support whole-exome and whole-genome sequencing for the discovery of disease-related genes and other genomic regions that regulate these genes. The Institute will continue to fund meritorious investigator-initiated applications that will utilize genomics to enhance understanding of disease etiology and pathogenesis as well as differences in responses to environmental exposures.

Using Genomics to Advance Medical Science: In this area, NHGRI seeks to support research studies that aim to translate basic genomic discoveries in order to help make genomic medicine (often called precision medicine) a reality. The Clinical Sequencing Exploratory Research (CSER) Program is a prototypic example of an NHGRI research program that will help to operationalize genomic medicine. In FY 2015, the multidisciplinary groups funded through this program will establish the analysis and interpretation tools, standard operating procedures, and institutional practices necessary to integrate genomic information into medical practice. A significant component of this research program involves examining the ethical and psychosocial implications of reporting and using genomic data in a patient's clinical care. The collaborative and cooperative nature of the CSER Program is designed to facilitate the development and standardization of best practices and common approaches in this area, and to promote their dissemination.

Budget Policy:

The FY 2015 President's Budget request for Using Genomics to Advance Medical Science is \$21.451 million, an increase of \$0.176 million or 0.8 percent more than the FY 2014 Enacted level. NHGRI will continue to apply large-scale genome sequencing to the clinical diagnosis and potential treatment of diseases in programs such as the Undiagnosed Diseases Program and will expand its sequencing efforts into newborns and diseases of the newborn period. Many of these new opportunities are focused on specific diseases and will be pursued in collaboration with other NIH Institutes/Centers. The Institute will continue to fund meritorious investigator-initiated applications that will improve the understanding and application of genomic function in risk assessment, diagnosis, and treatment of human disease.

Using Genomics to Improve the Effectiveness of Healthcare: Research in this area is central to NHGRI's investment in translational science. In addition to the Electronic Medical Records and GENomics (eMERGE) Network described elsewhere in this document, the recently established Implementing Genomics in Practice (IGNITE) Network is incorporating patients' genomic information into electronic medical record systems and developing clinical decision-support tools to make that information accessible and applicable to clinical practice. The clinical sites and coordinating center funded through IGNITE are promoting proven approaches for incorporating genomics into clinical care in a range of clinical settings; these efforts include refining methods for effective implementation, diffusion, and sustainability of genomics in real-world clinical situations. Dissemination of these methods and developing best practices for implementation are key goals of IGNITE, so that the information generated from the Program will find practical applications in patient care.

Budget Policy:

The FY 2015 President's Budget request for Using Genomics to Improve the Effectiveness of Healthcare is \$10.920 million, an increase of \$0.080 million or 0.7 percent more than the FY 2014 Enacted level. NHGRI will expand its support of the IGNITE network in FY 2015 to include new projects related to pharmacogenomics and cross-network projects related to clinician education and participant consent, and will utilize the Clinical Genomics Resource to identify genomic variants with clinical implications and disseminate that information to the scientific community. The Institute also will continue to fund meritorious investigator-initiated applications, and to collaborate with other NIH Institutes/Centers in studying genomic applications to healthcare.

Program Portrait: The Electronic Medical Records and Genomics (eMERGE) Network

FY 2014 Level: \$ 9.0 million

FY 2015 Level: \$15.0 million

Change: +\$6.0 million

The Electronic Medical Records and Genomics (eMERGE) Network is a highly successful translational research initiative that, since 2007, has brought together researchers with expertise in genomics, statistics, bioethics, bioinformatics, and clinical medicine to develop, disseminate, and apply research approaches that combine genome sequence information with electronic medical record (EMR) systems.

eMERGE has several overall goals: to develop the methods and tools necessary to incorporate genomic sequence information into an EMR system; to use that combined information for discovering genomic variants associated with clinical phenotypes; and to investigate how best to utilize state-of-the-art genomic information and methods in delivering precision clinical care.

To enable a future where the use of genomics as a component of clinical care is widespread, intuitive clinical decision-support tools are needed that convey information to clinicians and patients in a robust but convenient manner. In FY 2015, a major new component of eMERGE will use a “targeted sequencing array” to study variation in 85 genes related to drug metabolism, feeding that information back to clinicians to aid in drug-prescribing decisions. Another significant new component will collect information on patients’ views of informed consent and data sharing in genomic research studies.

Bioinformatics, Computational Biology, and Data Science: As it has become increasingly affordable and faster to generate genomic data, the size of generated datasets that researchers have to analyze and interpret has grown enormously. In fact, the deluge of data generated by genomic studies each day makes data management and analysis (not data production) the major bottleneck in genomics research. This “Big Data” challenge is not unique to genomics, but is sweeping across the biomedical research landscape and fostering the emergence of the important new discipline of data science. NHGRI has a strong interest in data science as it pertains to the development of tools, resources, and infrastructure for dealing with genomics data. Programs and projects across the Institute’s research portfolio are involved in the development of bioinformatics and computational biology methods and resources. Publicly accessible data resources (such as those generated by 1000 Genomes, ENCODE, and The Cancer Genome Atlas) are all supported by NHGRI funds, and serve to maximize the nation’s investment in these programs by allowing other biomedical researchers to utilize them in new and innovative ways.

Budget Policy:

The FY 2015 President’s Budget request for Bioinformatics and Computational Biology is \$115.777 million, an increase of \$0.594 million or 0.5 percent more than the FY 2014 Enacted level. The Institute continues to invest in data resources and the development of analysis tools that provide the bedrock for basic and clinically-related genomics research, including participation in support for international data resources, emphasizing the goal of accommodating more data, more diverse data, and a larger community of data and tools users with increasing efficiency. The Institute also will continue to fund meritorious investigator-initiated applications that explore new concepts and develop innovative tools for gathering, analyzing and storing genomic data.

Education and Training: The full benefits of genomics will only be realized if a sufficiently trained and educated workforce exists, one that is able to appropriately apply genomic approaches to biomedical science and medical care. In addition to the new Genomic Science and Genomic Medicine training programs highlighted below, NHGRI has three major extramural research areas that include a training component specifically focused on increasing the diversity of individuals engaged in genomics research: the Centers of Excellence in Genomic Science (CEGS), Large-Scale Genome Sequencing and Analysis Centers, and Model Organism Databases.

Budget Policy:

The FY 2015 President's Budget request for Education and Training is \$22.155 million, an increase of \$0.147 million or 0.7 percent more than the FY 2014 Enacted level. In FY 2015, NHGRI will continue its support for training the next generation of genomics researchers, as well as programs aimed at bringing genomics to healthcare professionals and the general public. NHGRI also plans to increase its support for training in the following areas: bioinformatics, data science, and genomic medicine.

Program Portrait: Genomic Science and Genomic Medicine Training and Career Development

FY 2014 Level: \$0.0 million

FY 2015 Level: \$1.6 million

Change: +\$1.6 million

NHGRI is committed to provide training, resources, and career development for scientists in basic genomic sciences and clinical genomic medicine. To that end, the Institute's Extramural Research Program has developed initiatives for both institutional training grants and individual mentored awards that align with NHGRI's 2011 strategic plan, *Charting a course for genomic medicine from base pairs to bedside*.

Following a 2013 planning workshop, it was recognized that these new training programs must both cover a wide spectrum of genomics research and, at the same time, provide sufficient depth. For instance, providing trainees with a thorough understanding of data science is essential in the era of Big Data, given the vast amounts of data that is readily generated in high-throughput genomics research—data to which trainees must have access. Finally, the development of a professional network for these trainees is highly desirable.

The institutional training program in Genomic Medicine aims to develop the next generation of leaders in the field. Trainees will already have either an M.D. or Ph.D. (or equivalent), and will be trained for two to three years in the key components of genomic medicine as well as the associated ethical, legal, and social implications (ELSI). Similarly, the institutional training program in Genomic Science will develop leaders in genomic sciences who will be cross-trained broadly and deeply in scientific disciplines relevant to genomics, with an emphasis on developing strong credentials in data science.

Clinical Scientist Development Awards in Genomic Medicine will provide clinically trained individuals with a mentored genomics research experience that will facilitate their transition to independent research careers. As with the institutional program, trainees will receive ELSI training in addition to their clinical genomics research experience.

Career Awards in Genomic Sciences will provide opportunities to individuals with a biological Ph.D. to cross-train in another discipline relevant to genomic sciences; previously, such awards were limited to researchers with backgrounds in mathematics, physics, chemistry, and computer and engineering sciences.

Realizing NHGRI's vision of a future where the use of genomics in clinical care is widespread requires a diverse, well-trained, and highly creative workforce. These programs will equip the next generation of genomic scientists and clinicians with the skills and experience needed to lead their fields in the 21st century.

Genomics and Society: Since its inception, NHGRI has dedicated roughly five percent of its research funding to examine the ethical, legal, and social implications (ELSI) of genomic advances and the increasing availability of genomic information in society. This research area continues to be a vital component of the Institute's strategic vision. In FY 2015, the Program will continue to explore issues that arise in the design and conduct of genomics research, particularly those related to the clinical applications of genomics. Questions of particular interest include those related to informed consent for genomics research, privacy issues arising from the use of large research databases, when and how to return individual genomic findings to research participants and patients, and whether and how to provide information about unanticipated health-related genomic findings to participants.

In addition to multiple standing funding announcements to stimulate ELSI research, several major NHGRI research programs incorporate ELSI research as a critical component, including

CSER, eMERGE, and the recently launched Genomic Sequencing and Newborn Screening Research Program (in collaboration with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development).

Within the Institute's Intramural Research Program, the Social and Behavioral Research Branch will continue in FY 2015 to conduct leading-edge research that tests the effectiveness of strategies for communicating information about genetic risks; to develop and evaluate behavioral interventions relevant to genomics; to analyze how to use genomic discoveries in clinical practice; and to explore the social, ethical, and policy implications of genomics research.

Budget Policy:

The FY 2015 President's Budget request for Genomics and Society is \$51.056 million, an increase of \$0.266 million or 0.5 percent more than the FY 2014 Enacted level. In FY 2015, NHGRI will continue to support the ELSI program extramurally and the Social and Behavioral Research Branch intramurally, to study, analyze, and anticipate the social, behavioral, ethical, and legal issues that may result from the use of new DNA sequencing technologies and the genomic information those technologies generate.

Research Management and Support: NHGRI's Division of Policy, Communications, and Education uses Research Management and Support funds to provide key leadership for a number of ongoing initiatives, including educational and outreach activities associated with the joint NHGRI-Smithsonian National Museum of Natural History exhibition, *Genome: Unlocking Life's Code*, as well as community-focused genomics programs. In FY 2015, this Division will conduct public engagement and education activities around the country as the exhibition begins to travel across North America. NHGRI also continues to provide leadership in the area of genomics education for healthcare professionals. The Inter-Society Coordinating Committee for Physician Education in Genomics (ISCC) was recently formed to facilitate interactions among physician professional societies and to exchange practices and resources for genomics education and clinical care. By identifying the needs of the societies and clinicians with respect to current evidence and knowledge gaps, the ISCC aims in FY 2015 to offer partnerships and available expertise to guide the development of educational initiatives that will foster the maturation of genomic medicine.

Budget Policy:

The FY 2015 President's Budget estimate for the Research Management and Support program is \$25.483 million, a decrease of \$0.107 million or 0.4 percent less than the FY 2014 Enacted level. In FY 2015, NHGRI will continue to seek strategic solutions to manage the diverse and cutting-edge NHGRI research portfolio. Policy, outreach, and communications activities will be utilized to complement and extend discussions about the ethical, legal, and social implications of genomics research, working in close collaboration with all research divisions across the Institute. Critical analyses and evaluations of research and other Institute programs will inform leadership's management of the research portfolio and development of future directions.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Budget Authority by Object Class¹
(Dollars in Thousands)

	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Total compensable workyears:			
Full-time employment	333	333	0
Full-time equivalent of overtime and holiday hours	0	0	0
Average ES salary	\$180	\$180	\$0
Average GM/GS grade	12.4	12.4	0.0
Average GM/GS salary	\$102	\$103	\$1
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	\$105	\$105	\$0
Average salary of ungraded positions	\$137	\$137	\$0
OBJECT CLASSES	FY 2014	FY 2015	FY 2015
Personnel Compensation			
11.1 Full-Time Permanent	\$15,736	\$15,893	\$157
11.3 Other Than Full-Time Permanent	16,056	16,216	160
11.5 Other Personnel Compensation	232	234	2
11.7 Military Personnel	792	801	9
11.8 Special Personnel Services Payments	4,390	4,434	44
11.9 Subtotal Personnel Compensation	\$37,206	\$37,578	\$372
12.1 Civilian Personnel Benefits	\$9,921	\$10,268	\$347
12.2 Military Personnel Benefits	495	500	5
13.0 Benefits to Former Personnel	0	0	0
Subtotal Pay Costs	\$47,622	\$48,346	\$724
21.0 Travel & Transportation of Persons	\$1,957	\$1,942	-\$15
22.0 Transportation of Things	133	132	-1
23.1 Rental Payments to GSA	3	3	0
23.2 Rental Payments to Others	16	16	0
23.3 Communications, Utilities & Misc. Charges	561	551	-10
24.0 Printing & Reproduction	2	2	0
25.1 Consulting Services	\$266	\$265	-\$1
25.2 Other Services	16,746	16,517	-229
25.3 Purchase of goods and services from government accounts	\$60,904	\$62,643	\$1,739
25.4 Operation & Maintenance of Facilities	\$245	\$243	-\$2
25.5 R&D Contracts	4,610	4,476	-134
25.6 Medical Care	3,004	2,995	-9
25.7 Operation & Maintenance of Equipment	2,032	2,033	1
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal Other Contractual Services	\$87,807	\$89,172	\$1,365
26.0 Supplies & Materials	\$6,270	\$6,270	\$0
31.0 Equipment	3,634	3,603	-31
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	349,123	348,414	-709
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	0	0	0
44.0 Refunds	0	0	0
Subtotal Non-Pay Costs	\$449,506	\$450,105	\$599
Total Budget Authority by Object Class	\$497,128	\$498,451	\$1,323

¹ Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

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

**Salaries and Expenses
(Dollars in Thousands)**

OBJECT CLASSES	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Personnel Compensation			
Full-Time Permanent (11.1)	\$15,736	\$15,893	\$157
Other Than Full-Time Permanent (11.3)	16,056	16,216	160
Other Personnel Compensation (11.5)	232	234	2
Military Personnel (11.7)	792	801	9
Special Personnel Services Payments (11.8)	4,390	4,434	44
Subtotal Personnel Compensation (11.9)	\$37,206	\$37,578	\$372
Civilian Personnel Benefits (12.1)	\$9,921	\$10,268	\$347
Military Personnel Benefits (12.2)	495	500	5
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	\$47,622	\$48,346	\$724
Travel & Transportation of Persons (21.0)	\$1,957	\$1,942	-\$15
Transportation of Things (22.0)	133	132	-1
Rental Payments to Others (23.2)	16	16	0
Communications, Utilities & Misc. Charges (23.3)	561	551	-10
Printing & Reproduction (24.0)	2	2	0
Other Contractual Services:			
Consultant Services (25.1)	266	265	-1
Other Services (25.2)	16,746	16,517	-229
Purchases from government accounts (25.3)	48,490	47,709	-781
Operation & Maintenance of Facilities (25.4)	245	243	-2
Operation & Maintenance of Equipment (25.7)	2,032	2,033	1
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services (25.0)	\$67,779	\$66,767	-\$1,012
Supplies & Materials (26.0)	\$6,270	\$6,270	\$0
Subtotal Non-Pay Costs	\$76,718	\$75,680	-\$1,038
Total Administrative Costs	\$124,340	\$124,026	-\$314

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

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2013 Actual			FY 2014 Est.			FY 2015 Est.		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Extramural Operations									
Direct:	15		15	15		15	15		15
Reimbursable:	2		2	2		2	2		2
Total:	17		17	17		17	17		17
Division of Genome Sciences									
Direct:	11		11	11		11	11		11
Reimbursable:	2		2	2		2	2		2
Total:	13		13	13		13	13		13
Division of Genomic Medicine									
Direct:	12		12	12		12	12		12
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	12		12	12		12	12		12
Division of Genomics and Society									
Direct:	3		3	3		3	3		3
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	3		3	3		3	3		3
Division of Intramural Research									
Direct:	204	8	212	204	8	212	204	8	212
Reimbursable:	26	1	27	26	1	27	26	1	27
Total:	230	9	239	230	9	239	230	9	239
Division of Management									
Direct:	32		32	32		32	32		32
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	32		32	32		32	32		32
Division of Policy, Communications and Education									
Direct:	11		11	11		11	11		11
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	11		11	11		11	11		11
Office of the Director									
Direct:	6		6	6		6	6		6
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	6		6	6		6	6		6
Total	324	9	333	324	9	333	324	9	333
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and Development Agreements.	0	0	0	0	0	0	0	0	0
FISCAL YEAR	Average GS Grade								
2011	12.1								
2012	12.3								
2013	12.4								
2014	12.4								
2015	12.4								

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Detail of Positions

GRADE	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	180,000	180,000	180,000
GM/GS-15	31	31	31
GM/GS-14	24	24	24
GM/GS-13	57	57	57
GS-12	45	45	45
GS-11	13	13	13
GS-10	2	2	2
GS-9	5	5	5
GS-8	15	15	15
GS-7	1	1	1
GS-6	1	1	1
GS-5	0	0	0
GS-4	0	0	0
GS-3	1	1	1
GS-2	1	1	1
GS-1	0	0	0
Subtotal	196	196	196
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	5	5	5
Senior Grade	3	3	3
Full Grade	1	1	1
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	9	9	9
Ungraded	148	148	148
Total permanent positions	206	206	206
Total positions, end of year	354	354	354
Total full-time equivalent (FTE) employment, end of year	333	333	333
Average ES salary	180,000	180,000	180,000
Average GM/GS grade	12.4	12.4	12.4
Average GM/GS salary	101,359	102,373	103,396

Includes FTEs whose payroll obligations are supported by the NIH Common Fund.