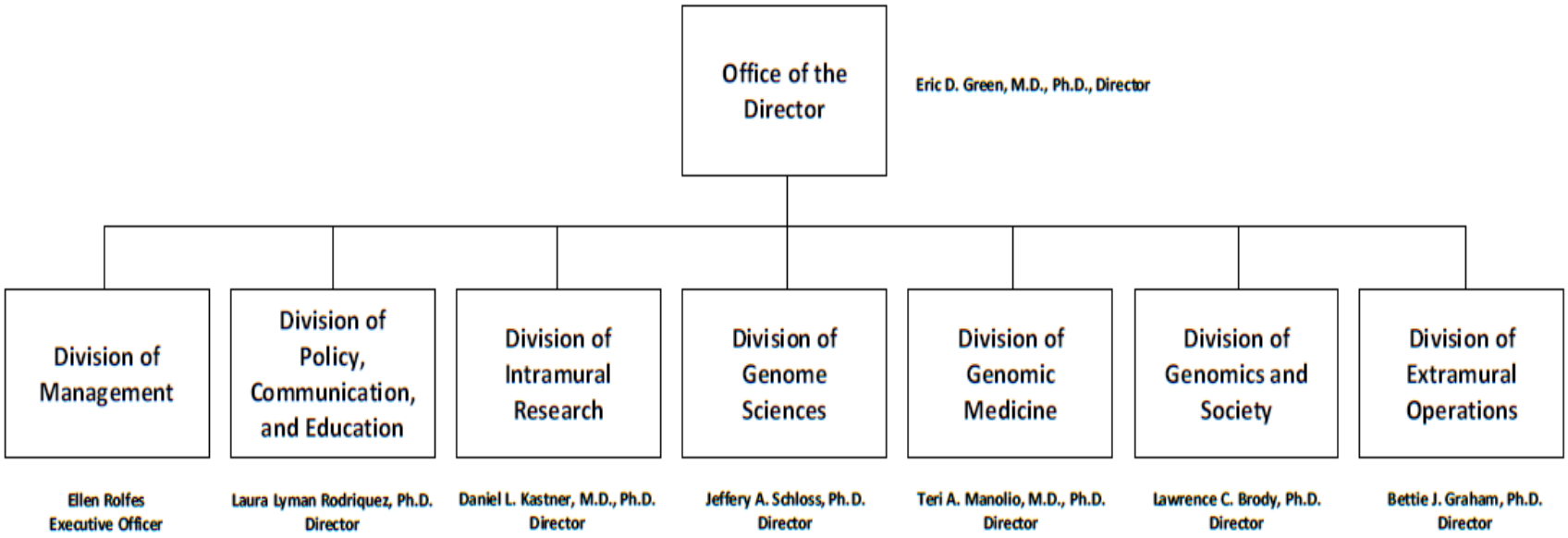
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Human Genome Research Institute (NHGRI)

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, [$499,356,000]*$515,491,000*.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Amounts Available for Obligation[1]
(Dollars in Thousands)

Source of Funding	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Appropriation	$497,813	$499,356	$515,491
Type 1 Diabetes	0	0	0
Rescission	0	0	0
Sequestration	0	0	0
FY 2014 First Secretary's Transfer	-1,250	0	0
FY 2014 Second Secretary's Transfer	-98	0	0
Subtotal, adjusted appropriation	$496,465	$499,356	$515,491
OAR HIV/AIDS Transfers	0	-679	0
National Children's Study Transfers	1,636	0	0
Subtotal, adjusted budget authority	$498,101	$498,677	$515,491
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$498,101	$498,677	$515,491
Unobligated balance lapsing	-25	0	0
Total obligations	$498,076	$498,677	$515,491

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2014 - $28,326 FY 2015 - $37,000 FY 2016 - $37,600

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National Human Genome Research Institute

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY 2015	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	171	$104,740	144	$91,205	153	$96,835	9	$5,630
Administrative Supplements	*(15)*	2,279	*(6)*	2,128	*(11)*	16,022	*(5)*	13,894
Competing:								
Renewal	18	10,827	24	17,353	9	19,000	-15	1,647
New	32	13,579	42	21,763	59	118,999	17	97,236
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	50	$24,407	66	$39,116	68	$137,999	2	$98,883
Subtotal, RPGs	221	$131,426	210	$132,449	221	$250,856	11	$118,407
SBIR/STTR	28	11,880	31	12,438	34	13,422	3	984
Research Project Grants	249	$143,306	241	$144,887	255	$264,278	14	$119,391
Research Centers:								
Specialized/Comprehensive	27	$133,039	29	$127,220	16	$28,201	-13	-$99,019
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	25	60,142	26	62,353	32	52,532	6	-9,821
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	52	$193,180	55	$189,573	48	$80,733	-7	-$108,840
Other Research:								
Research Careers	10	$1,252	11	$1,384	13	$1,778	2	$394
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	3,131	23	4,068	18	2,973	-5	-1,095
Other Research	29	$4,783	34	$5,852	31	$5,151	-3	-$701
Total Research Grants	330	$341,270	330	$340,312	334	$350,162	4	$9,850
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	6	$252	7	$301	10	$453	3	$152
Institutional Awards	155	5,667	153	5,722	184	6,995	31	1,273
Total Research Training	161	$5,919	160	$6,023	194	$7,448	34	$1,425
Research & Develop. Contracts	6	$21,319	6	$19,620	6	$22,139	0	$2,519
(SBIR/STTR) (non-add)	*(0)*	*(59)*	*(0)*	*(59)*	*(0)*	*(59)*	*(0)*	*(0)*
Intramural Research	226	103,386	226	104,435	226	106,816	0	2,381
Res. Management & Support	104	26,208	106	28,287	106	28,926	0	639
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NHGRI	330	$498,101	332	$498,677	332	$515,491	0	$16,814

[1] All items in italics and brackets are non-add entries.

Major Changes in Fiscal Year 2016 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 2016 President's Budget request for NHGRI, which is $16.814 million more than the FY 2015 Enacted level for a total of $515.491 million.

Research Project Grants (RPGs) (+$119.391 million, total $264.278 million):
The NHGRI Genome Sequencing Program (GSP) has been a central component of NHGRI's Extramural Research Program since the Institute's inception and has capitalized on new opportunities throughout its existence. This program has previously been funded within the Research Centers budget mechanism, with the funding period of the current GSP grants ending in FY 2015. However, beginning in FY 2016, it is anticipated that these grants will be funded from the RPG pool. This is not a change in the type of activities funded, but only a shift in the mechanism in which the activities are categorized. The renewal of this important NHGRI program includes the establishment of the Centers for Common Disease Genomics and the continuation of the Centers for Mendelian Genomics. These programs will emphasize strongly the use of genome sequencing for studying human disease and for developing resources for multiple common and Mendelian disease research communities. The program has the potential to facilitate rapid and accurate diagnosis of many disorders, enhance prognostic precision, suggest novel treatments, and, possibly, point to actions for preventing disease. Several of the grants supporting the ENCylopedia of DNA Elements (ENCODE) program are also moving from the Research Centers budget mechanism to the RPG pool. NHGRI will also continue to support new investigator-initiated research within the RPG pool.

Research Centers (-$108.840 million, total $80.733 million):
This decrease represents the movement of several large ongoing NHGRI initiatives from the Research Centers budget mechanism line to the RPG mechanism. There is a balancing increase in the funding for RPGs.

Using Genomics to Advance Medical Science (+$3.335 million; total $24.502 million):
This increase to resources will be used to support the clinical validation components of the NIH Precision Medicine Cohort, a national research cohort of one million or more Americans to propel our understanding of health and disease and create innovative and forward-looking ways to engage participants in research and enable open, respectful data sharing. Participants who voluntarily choose to join this effort will be able to share their genomic data, biological specimens, and behavioral data, and, if they choose, link it to their electronic health records (EHRs), taking advantage of the latest in social media and mobile applications, and with appropriate privacy protections in place. Bona fide researchers from across the country will have access to data voluntarily provided, thereby crowdsourcing rich data to the brightest minds in biomedical research. The cohort will be built largely by linking existing cohorts together taking advantage of infrastructure, data security and expertise already in place. NIH will help to connect these existing cohorts, but the current sponsors of the cohorts will maintain their ownership and management. Research on this scale promises to lead to new prevention strategies, novel therapeutics and medical devices, and improvements in how we prescribe drugs – on an *individual* and *personalized basis*. The NIH Precision Medicine Cohort addresses the fourth and fifth areas of NHGRI's strategic plan in

equal proportions. The clinical validation components use genomics to advance medical science by assessing outcomes after using genetics to direct therapy, identifying causes of rare or undiagnosed diseases, and validating drug targets to develop improved therapeutic agents.

Using Genomics to Improve the Effectiveness of Healthcare (+$3.107 million; total $14.061 million):
This increase in resources will be used to support the clinical implementation components of the NIH Precision Medicine Cohort described above. The NIH Precision Medicine Cohort addresses the fourth and fifth areas of NHGRI's strategic plan in equal proportions. The clinical implementation components improve the effectiveness of healthcare by developing processes for performing genetic testing and using results in care, including clinical informatics systems for reporting genomic results, education of clinicians and patients in clinical use of genomic results, and dissemination of information on actionable clinical variants.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Summary of Changes

(Dollars in Thousands)

FY 2015 Enacted	$498,677
FY 2016 President's Budget	$515,491
Net change	$16,814

CHANGES	FY 2016 President's Budget		Change from FY 2015	
	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2015 pay increase & benefits		$38,120		$130
b. January FY 2016 pay increase & benefits		38,120		390
c. One more day of pay (n/a for 2015)		38,120		151
d. Differences attributable to change in FTE		38,120		0
e. Payment for centrally furnished services		17,055		416
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		51,642		1,294
Subtotal				$2,381
2. Research Management and Support:				
a. Annualization of January 2015 pay increase & benefits		$12,193		$41
b. January FY 2016 pay increase & benefits		12,193		124
c. One more day of pay (n/a for 2015)		12,193		48
d. Differences attributable to change in FTE		12,193		0
e. Payment for centrally furnished services		1,370		33
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		15,363		392
Subtotal				$639
Subtotal, Built-in				$3,020

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

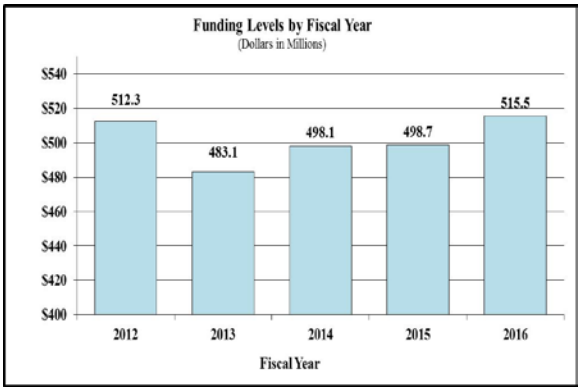
Summary of Changes - Continued

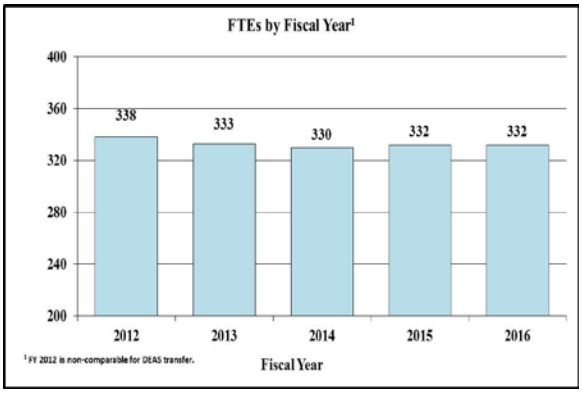
(Dollars in Thousands)

CHANGES	FY 2016 President's Budget		Change from FY 2015	
	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	153	$112,857	9	$19,524
b. Competing	68	137,999	2	98,883
c. SBIR/STTR	34	13,422	3	984
Subtotal, RPGs	255	$264,278	14	$119,391
2. Research Centers	48	$80,733	-7	-$108,840
3. Other Research	31	5,151	-3	-701
4. Research Training	194	7,448	34	1,425
5. Research and development contracts	6	22,139	0	2,519
Subtotal, Extramural		$379,749		$13,794
	FTEs		FTEs	
6. Intramural Research	226	$106,816	0	$0
7. Research Management and Support	106	28,926	0	0
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, Program	332	$515,491	0	$13,794
Total changes				$16,814

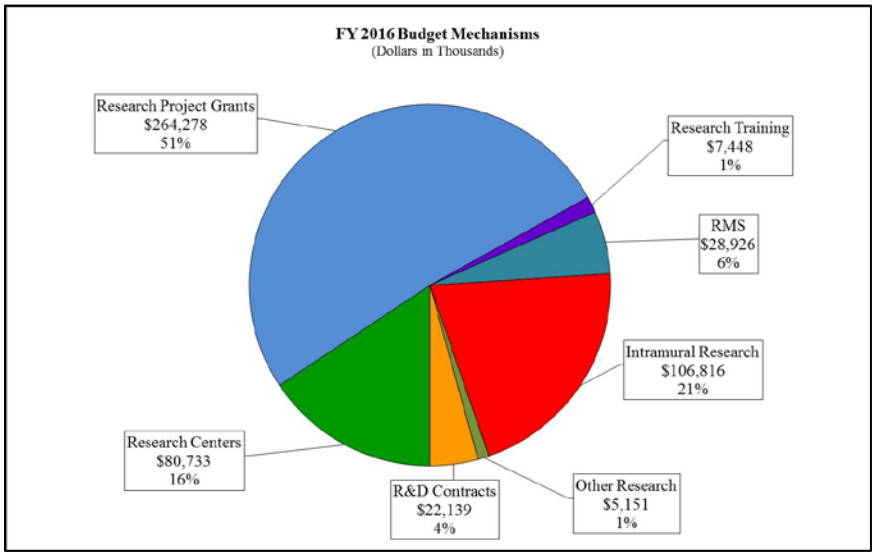
Fiscal Year 2016 Budget Graphs

History of Budget Authority and FTEs:

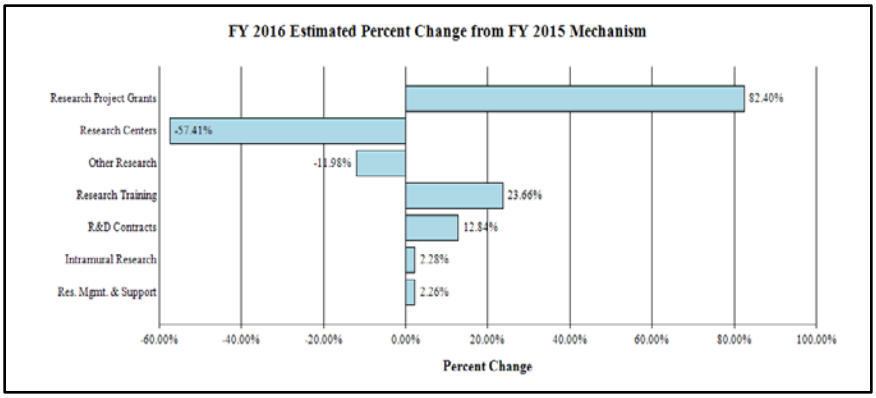




Distribution by Mechanism:



Change by Selected Mechanism:



NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Budget Authority by Activity[1]
(Dollars in Thousands)

	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY 2015	
Program Activity:	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Understanding the Structure of Genomes		$39,277		$39,049		$39,313		$264
Understanding the Biology of Genomes		77,210		76,914		77,588		674
Using Genomics to Understand the Biology of Disease		136,747		136,424		143,695		7,271
Using Genomics to Advance Medical Science		21,038		21,167		24,502		3,335
Using Genomics to Improve the Effectiveness of Healthcare		10,924		10,954		14,061		3,107
Bioinformatics and Computational Biology		122,720		122,082		122,980		898
Education and Training		19,881		19,903		20,176		273
Genomics and Society		44,096		43,897		44,250		353
Subtotal, Program Activity*		**$471,893**		**$470,390**		**$486,565**		**$16,175**
Extramural Research (non-add)	*(0)*	*(368,508)*	*(0)*	*(365,955)*	*(0)*	*(379,749)*	*(0)*	*(13,794)*
Intramural Research (non-add)	*226*	*(103,386)*	*226*	*(104,435)*	*226*	*(106,816)*	*(0)*	*(2,381)*
Research Management & Support	**104**	**$26,208**	**106**	**$28,287**	**106**	**$28,926**	**0**	**$639**
TOTAL	**330**	**$498,101**	**332**	**$498,677**	**332**	**$515,491**	**0**	**$16,814**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.
* 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	2015 Amount Authorized	FY 2015 Enacted	2016 Amount Authorized	FY 2016 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$498,677,000	Indefinite	$515,491,000
National Human Genome Research Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$498,677,000		$515,491,000

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2006	$490,959,000	$490,959,000	$502,804,000	$490,959,000
Rescission				($4,910,000)
2007	$482,942,000	$482,942,000	$486,315,000	$486,491,000
Rescission				$0
2008	$484,436,000	$493,996,000	$497,031,000	$495,434,000
Rescission				($8,655,000)
Supplemental				$2,589,000
2009	$487,878,000	$504,603,000	$501,411,000	$502,367,000
Rescission				$0
2010	$509,594,000	$520,311,000	$511,007,000	$516,028,000
Rescission				$0
2011	$533,959,000		$533,127,000	$516,028,000
Rescission				($4,531,033)
2012	$524,807,000	$524,807,000	$505,783,000	$513,844,000
Rescission				($971,165)
2013	$511,370,000		$512,920,000	$512,872,835
Rescission				($1,025,746)
Sequestration				($25,742,690)
2014	$517,319,000		$513,881,000	$497,813,000
Rescission				$0
2015	$498,451,000			$499,356,000
Rescission				$0
2016	$515,491,000			

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 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
BA	$489,101,000	$498,677,000	$515,491,000	+$16,184,000
FTE	330	332	332	+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 in 2003, the National Human Genome Research Institute (NHGRI) has funded and conducted research to uncover the role that the genome plays in human health and disease. This research has occurred across a spectrum: basic research to shed light on the structure and function of the genome; translational research to decipher the molecular bases of human diseases; and clinical research to establish how to use genomic information to advance medical care. Additionally, NHGRI has supported exploration of the complex ethical, legal, and social implications of genomics, and is committed to ensuring that the knowledge and benefits generated from genomics research are disseminated widely, both to current and future researchers and to the general public to ensure genomic literacy.

A signature technology-development program led by the Division of Genome Sciences has yielded powerful new methods for DNA sequencing, driving down the cost of genome sequencing at an exponential rate. At the end of the Human Genome Project in 2003, it cost more than $1,300 to sequence a million bases of DNA (the human genome totals 3 billion bases); by 2014, that cost had fallen to a mere five cents.[1] In addition to empowering research on the human genome in previously unimaginable ways, such new genomic methods can be readily applied to track and combat infectious microbes. For instance, these "next-generation" DNA sequencing methods enabled public health scientists to elucidate rapidly the precise origin and transmission route of the viral strain responsible for the 2014 African Ebola virus outbreak. With real-time ability to identify and monitor the (often rapid) evolution of viral and bacterial outbreaks, DNA sequencing methods provide valuable data for tracing the spread of an infectious agent and, therefore, for informing healthcare decisions.

Scientists are now unraveling many of life's mysteries through a deeper understanding of our genome, a direct consequence of the dramatic decrease in the cost of sequencing DNA and the

[1] http://www.genome.gov/sequencingcosts

consequent uptake of genomic approaches throughout the biomedical research enterprise. In FY 2016, multiple laboratories within NHGRI's Intramural Research Program will continue their genomic studies of rare diseases; many of these studies capitalize effectively on the outstanding medical infrastructure of the NIH Clinical Center and the state-of-the-art genomics capabilities of the NIH Intramural Sequencing Center. Such efforts illustrate the power of the robust bench-to-bedside capabilities of the NIH Intramural Research Program.

Supported by NHGRI's Extramural Research Program for more than a decade, the ENCylopedia of DNA Elements (ENCODE) Project is cataloging all the "functional elements" (or biologically important working parts) of both the human and mouse genomes. Such functional elements include the stretches of DNA that act as "on or off" switches to dictate when, where, and how much our genes are used to manufacture proteins. ENCODE's results help to explain how human cells can develop into many specialized cell types despite having the identical genome sequence. ENCODE data now represents a fundamental resource for the wider biomedical and biological research communities, especially for efforts aiming to understand human biology and disease.

In FY 2016, the extramurally supported IGNITE (Implementing GeNomics In pracTicE) Network will investigate how to best integrate genomic information into clinical practice. Specifically, IGNITE researchers are developing and sharing best practices for using genomic medicine in diverse clinical settings, for example by tackling challenges associated with integrating genomic and family history information into electronic medical records. The IGNITE and the other NHGRI genomic medicine initiatives represent the leading edge of clinical applications of genomics.

The early successes of the Intramural Undiagnosed Diseases Program have resulted in its expansion beyond the NIH Clinical Center to six additional clinical sites across the country (as well as a coordinating center and two DNA sequencing facilities) through the support of the NIH Common Fund. The new Undiagnosed Diseases Network (UDN), which is being led by NHGRI, is designed to conduct genomics-based investigations of undiagnosed diseases and to provide answers to patients about their undiagnosed conditions. Such undiagnosed diseases represent true medical mysteries for which diagnoses have eluded even skilled physicians, often because they are extremely rare or previously unknown conditions.

As with IGNITE (and many of the other programs led by the Division of Genomic Medicine), the participating UDN groups will collaborate to develop best practices for the use of genomics in clinical care. Towards that end, and recognizing that the realization of genomic medicine requires healthcare professionals to understand how best to apply genomics to patient care, NHGRI founded the Intersociety Coordinating Committee for Practitioner Education in Genomics (ISCC) and continues to catalyze the widespread adoption and integration of genomic medicine into clinical practice through partnerships with professional societies and other NIH institutes/centers.

NHGRI is also funding the development and refinement of computational tools and data resources for use by the wider biomedical community. This ongoing effort to democratize the use of genomic approaches beyond highly specialized centers is important for fully realizing the promise of the Nation's investment in genomics. In addition, NHGRI's commitment to preparing

a diverse and talented biomedical research workforce with strong genomics expertise also contributes to this goal. NHGRI's Diversity Action Plan involves training scientists from diverse backgrounds, as well as conducting extensive outreach aimed at underrepresented minorities to inform them about the opportunities in genomics and associated disciplines.

From the inception of the Human Genome Project, NHGRI has funded research to examine the ethical, legal, and social implications (ELSI) of genomic advances and the increasing availability of genomic information. FY 2016 will see continued growth of ELSI research questions and the integration of ELSI research studies with broader genomics initiatives, especially those that are piloting genomic approaches in clinical settings, all led by the Division of Genomics and Society. NHGRI remains a leader in bioethics research at NIH and, indeed, in the world. Funding of extramural programs, such as the multi-disciplinary Centers of Excellence in ELSI Research (CEERs), together with the Institute's intramural social and behavioral research efforts have placed NHGRI at the forefront of bioethics research and training.

Through these initiatives and the ones described in the program portraits to follow, NHGRI will fund and conduct research in FY 2016 that extends our knowledge about how the human genome works, how variation among our genomes contributes to human disease, and how best to apply that information to advance the health of United States citizens.

Overall Budget Policy:
The FY 2016 President's Budget request for NHGRI is $515.491 million, an increase of $16.814 million or 3.4 percent above the FY 2015 Enacted level.

Program Descriptions and Accomplishments

Understanding the Structure of Genomes: Studies that aim to understand the structure of genomes will continue to comprise a fundamental part of NHGRI's research portfolio in FY 2016. A signature program in this effort is the Advanced Sequencing Technology Program. This effort supports innovative research for developing new technologies to sequence DNA; in FY 2016, NHGRI will be close to achieving its original goal of reducing the cost of sequencing a human genome to $1000; the Institute remains committed to supporting the research necessary to achieve that goal (and beyond). A major emphasis of the program in FY 2016 is on novel nanopore-based technologies, which involve threading 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 the nanopore. For perspective, a human hair is around 100,000 nanometers in diameter, while a strand of DNA is around 2 nanometers in diameter. Nanopores being used with these new DNA sequencing methods are around 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 2016 President's Budget request for Understanding the Structure of Genomes is $39.313 million, an increase of $0.264 million or 0.7 percent more than the FY 2015 Enacted level. NHGRI will continue to support the development of technologies 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. These technologies will also be applied to the

sequencing of genomes, to expand the catalog of publicly-available genome sequence information for the human population and model organisms. 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: Developing tools and resources for analyzing the structure of genomes provides a vital foundation for studies aimed at understanding how genomes function. Each individual's genome sequence can be thought of as the instructions – written in DNA – required to build all the cells and tissues in a person's body. Studies that decipher those instructions are a high priority for NHGRI.

Building on ENCODE's success (described above) is the Genomics of Gene Regulation (GGR) program. Whereas ENCODE seeks to catalog the functional elements of the genome, GGR intends to uncover the choreography of those genomic elements that determines how genes are used by different cells (i.e., their regulation). More than 90 percent of the genetic variants associated with human disease (as identified by genome-wide association studies) are located outside of the protein-coding sequences, and many are thought to reside in regulatory sequences (the functional elements cataloged by ENCODE). A fuller understanding of how networks of genes are regulated will enable a much better understanding of how variation in non-coding regions of our genome influences our biology and the role that gene regulation plays in causing disease.

Budget Policy:
The FY 2016 President's Budget request for Understanding the Biology of Genomes is $77.588 million, an increase of $0.674 million or 0.9 percent more than the FY 2015 Enacted level. The investments in GGR and ENCODE will continue in FY 2016, as will efforts to integrate data produced by these projects with those of other projects funded by NHGRI and the NIH Common Fund. This research will be extended by computational research (that includes a validation component) to predict which, among the many changes in genome regulatory sequences that occur in nature, do in fact have consequences for the characteristics of an organism, such as whether a particular disease state is likely to result from those changes. By integrating information from these diverse approaches, the research community can gain powerful new insights into causes and possible treatments for disease—the ultimate goal of these investments in understanding the basic biology. 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: Centers for Mendelian Genomics

FY 2015 Level: $9.7 million
FY 2016 Level: $10.0 million
Change : +$0.3 million

More than 25 million Americans suffer from rare diseases, which are caused (in most cases) by a mutation in a single gene (these are also known as Mendelian diseases). Some of these disorders may affect only a handful of families worldwide, while others may afflict more than a hundred thousand individuals; collectively, rare diseases are more common than cancer. While the genomic bases for several thousand rare diseases have been established, this is not yet the case for the remaining 2000-4000 known rare diseases. Due to the profound decrease in DNA sequencing costs over the last decade, it is now more feasible than ever to determine the genomic bases of these latter rare diseases, thereby providing new insights about their underlying causes.

The Centers for Mendelian Genomics (CMGs), a component of NHGRI's large-scale genome sequencing program, use DNA sequencing and computational approaches to discover the genes and variants that underlie Mendelian diseases. The discoveries from the Centers can lead to rapid and accurate diagnoses of Mendelian disorders, and might lead to new therapeutic approaches. Importantly, findings about rare disorders also can provide insight into common and more complex conditions (i.e., those caused by multiple genomic variants acting weakly and in concert with environmental influences), which affect many more people.

Using Genomics to Understand the Biology of Disease: The research studies within this area build upon the foundational knowledge provided by better understanding the structure of genomes and their biology, specifically by examining how an individual's genome contributes to their health and susceptibility to disease. In FY 2016, research to decipher the genomic bases of rare and common human diseases will represent NHGRI's largest budgetary investment. Key examples of the work within this research domain are discussed in greater detail in two of the Program Portraits, specifically the "Centers for Mendelian Genomics," and "Common Disease Genomics."

Budget Policy:
The FY 2016 President's Budget request for Using Genomics to Understand the Biology of Disease is $143.695 million, an increase of $7.271 million or 5.3 percent more than the FY 2015 Enacted level. NHGRI will continue efforts to identify the genetic causes of Mendelian diseases and facilitate collaborations in Mendelian genomics world-wide. The Institute will also re-direct its large-scale sequencing program to focus a major effort on identifying genomic contributors to common, complex diseases-- those caused by the interaction of many genetic variants and environmental factors acting together. NHGRI will use the tremendous recent advances in sequencing technology to detect rare variants (carried by less than 1% of the population) that increase the risk of these diseases and will use them to understand disease biology and identify potential treatment strategies. 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: NHGRI is at the forefront of pioneering clinical research to translate genomic discoveries into advances in medicine, which is key for the implementation of genomic medicine (often called "individualized" or "precision" medicine). In

FY 2016, the Institute will fund a number of such research studies. The Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) program – funded in collaboration with the *Eunice Kennedy Shriver* National Institute for Child Health and Human Development – features pilot research projects investigating the implications, challenges, and opportunities associated with the use of genome sequence information in the newborn period. NSIGHT investigators are conducting clinical research that is advancing knowledge about specific disorders that are identifiable via genome sequencing in newborns, as well as the related ethical, legal, and psychosocial implications of generating, storing, and using such genomic information in the newborn period.

The integration of genomic medicine into routine clinical practice will depend upon an open and accessible knowledgebase of genomic variants – differences in the genomes among people – and their clinical consequences. The recently launched Clinical Genome Resource (ClinGen) is designed to collect relevant clinical information about genomic variants, develop a consensus approach to defining the clinical relevance of those variants, and disseminate clinically relevant information about those variants to researchers and clinicians. This resource will be essential to advance the goals of implementing and improving the application of genomics in clinical care. Resources such as ClinGen are central to NHGRI's commitment to ensure that knowledge generated through genomics research is disseminated widely to benefit human health.

Budget Policy:
The FY 2016 President's Budget request for Using Genomics to Advance Medical Science is $24.502 million, an increase of $3.335 million or 15.8 percent more than the FY 2015 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 Electronic Medical Records and Genomics (eMERGE) Network and the Undiagnosed Diseases Program. It will also work to expand identification of genetic variants influencing individual reactions to drugs in collaboration with other NIH Institutes/Centers and to develop electronic tools to assist clinicians in using this information seamlessly and effectively in the regular course of providing patient care. 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: Programs in this last research domain represent NHGRI's most clinically oriented genomic studies. FY 2016 will bring significant maturation of the Implementing Genomics in Practice (IGNITE) Network, which will develop and disseminate the best approaches for implementing genomic medicine. This set of groups are tackling challenges such as incorporating patients' genomic information into electronic medical records and developing clinical decision-support tools for using that information for clinical management. Through a number of demonstration projects, the program is taking sophisticated genomic-based interventions developed in highly specialized centers and disseminating them to diverse settings, including military and VA hospitals as well as those focused on underserved populations. IGNITE, like other NHGRI projects, is an example of how federally funded biomedical research is exploring how to harness data and technology to improve human health.

Budget Policy:
The FY 2016 President's Budget request for Using Genomics to Improve the Effectiveness of Healthcare is $14.061 million, an increase of $3.107 million or 28.4 percent more than the FY 2015 Enacted level. NHGRI will expand its support of the CSER, eMERGE, and IGNITE networks in FY 2016 to include new projects related to pharmacogenomics and clinical implementation, 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: Common Disease Genomics

FY 2015 Level: $73.2 million
FY 2016 Level: $60.0 million
Change: -$13.2 million

The common diseases that are of great burden to our nation, such as diabetes and cardiovascular disease, often have a heritable component (i.e., they run in families). However, unlike the rarer Mendelian disorders that are typically caused by mutations in a single gene, the heritability of common diseases is much more complex – typically involving multiple mutations and genes - and often cannot be attributed to genetics alone. Rather, mutations (or combinations of mutations) interact with environmental factors in a fashion that results in the manifestation of disease.

NHGRI's investigation of common diseases is built on the success of its programs in innovative genome technology development and large-scale genome sequencing. The genomic study of common diseases requires very large numbers of samples, which is necessary to provide sufficient statistical power to make robust conclusions. Generating such large datasets is now feasible due to the ever-decreasing cost of DNA sequencing. Data generation is merely one component of these investigations though; the essential advances in data analysis – another accomplishment of NHGRI-supported genome sequencing and analysis groups and many other genomics investigators - has been critically important and is enabling robust genomic interrogation of common diseases.

NHGRI has been at the forefront of large-scale genomics studies, and these efforts will continue to accelerate efforts to elucidate the genomic bases of common diseases. These research projects, often pursued in collaboration with other NIH institutes, have been studying a range of conditions, including many forms of cancer, Alzheimer's disease, and diabetes. At a recent workshop to discuss future opportunities in large-scale genome sequencing, NHGRI concluded that while the institute cannot, by itself, study all common diseases, it could continue to provide leadership in this area through a focus on "exemplar" conditions that represent a spectrum of health- and disease-related phenotypes. In FY 2016, the institute's new Centers for Common Disease Genomics program will conduct investigations of a number of common diseases, and this will involve studying tens of thousands of people with each disease. Less funding will be needed in FY 2016 for these activities because we will focus on developing more efficient tools and approaches by studying several key examples of common diseases instead of studying those diseases broadly; the results of this research should not only yield important understanding of a few diseases but also make future studies of many common diseases more cost-effective.

Bioinformatics, Computational Biology, and Data Science: Given the precipitous decrease in the cost of genome sequencing, the major bottleneck in genomics has shifted from data generation to data management and analysis. The challenge of "Big Data" 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's strong interest in data science is evident by the Institute's commitment to the development of tools, resources, and infrastructure for dealing with genomic data. Similar to NHGRI's technology development program's stimulation of the development of faster and cheaper DNA sequencing platforms, the Institute is investing in the development of a collection of robust and easy-to-use computational tools in FY 2016 that should prove valuable to the wider biomedical research community beyond data science and bioinformatics specialists. Further, NHGRI maximizes the return on the nation's investment in programs such as 1000 Genomes, ENCODE, and The Cancer Genome Atlas through the support of publicly accessible data resources that enable biomedical researchers around the country and the globe to utilize the data in new and innovative ways.

Budget Policy:
The FY 2016 President's Budget request for Bioinformatics and Computational Biology is $122.980 million, an increase of $0.898 million or 0.7 percent more than the FY 2015 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 tool users with increasing efficiency and accessibility. The Institute also will continue to fund meritorious investigator-initiated applications that explore new concepts and develop innovative tools for gathering, analyzing and sharing genomic data.

Education and Training: The science of genomics is changing rapidly, and the next generation of scientists and clinicians must be equipped with the skills to lead their fields during the 21st Century in order to capitalize on the genomics research now being funded by NHGRI and other NIH institutes/centers. Three major NHGRI extramural research programs include training components 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. The goal of the Diversity Action Plan associated with these three programs was modified to ensure that participants are receiving the kinds of academic enhancements and research experiences that will prepare them to pursue a Ph.D. or MD/Ph.D. The Institute has also restructured the institutional training and career development awards in the following ways: 1) the Genomic Sciences Training Program will place more emphasis on quantitative sciences and computational biology and 2) the genomic sciences career development (K award) program – previously limited to those with degrees in math, physics, chemistry, computer science, or engineering science - will be expanded to include biomedical scientists. Companion programs recently initiated in the area of genomic medicine will continue to provide training in FY 2016, specifically: 1) a new postdoctoral institutional training grant program to train those with clinical degrees in quantitative sciences and computational biology, and 2) individual career awards in genomic medicine with a focus on quantitative sciences and computational biology.

Budget Policy:
The FY 2016 President's Budget request for Education and Training is $20.176 million, an increase of $0.273 million or 1.4 percent more than the FY 2015 Enacted level. In FY 2016, NHGRI will continue its support for training the next generation of genomics scientists, as well as programs aimed at increasing the diversity of the genomic workforce and 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: Clinical Sequencing Exploratory Research Program

FY 2015 Level: $14.9 million
FY 2016 Level: $17.4 million
Change: +$ 2.5 million

NHGRI's 2011 strategic plan identified the potential clinical benefits of comprehensive genomic data in light of the rapid deployment of new genome sequencing methods that were becoming available to clinicians. To meet this opportunity, the Institute developed the Clinical Sequencing Exploratory Research (CSER) program, a unique national consortium that involves clinicians, scientists, clinical laboratories, bioinformaticians, economists, legal scholars, and ethicists.

CSER grantees are addressing critical questions about the application of genome sequencing to clinical care, from the generation of genome sequence data to the interpretation of the data for the physician to the communication of that information to the patient. Importantly, each of the projects includes an examination of the ethical, legal, and psychosocial implications of bringing genomic information into the clinic. Many steps are necessary to integrate genomic knowledge into clinical care, including accurate annotation of the effect of genomic variants with respect to genome function, association of variants with disease diagnosis or prognosis, and determination of clinical utility of genomic information (a favorable balance of benefits to risks in terms of implications for health outcomes and personal impact to the patient). Within each project, the subset of genomic variants found to be useful for clinical decision-making are identified and presented to clinicians in an intuitive, user-friendly summary report. Taking advantage of infrastructure and expertise within the network, CSER is also identifying implementation challenges and opportunities inherent to the clinical workflow, such as return of genomic results in difficult clinical contexts and integration of relevant genomic data into the electronic medical record. The collaborative and cooperative nature of the CSER program and the variety of included clinical contexts are helping to explore the best uses of clinical genome sequencing and to facilitate the development of best practices for clinical implementation.

Also integrated within CSER are normative and empiric methods to investigate the experiences of patients and clinicians with respect to the return of individual genomic research results, as well as to examine the associated ethical and legal issues. CSER investigators seek to shed light on real-life applications of generating, interpreting, and returning genomic information, as well as to study some of the legal and ethical issues surrounding returning genomic research results.

Genomics and Society: Each year, approximately five percent of NHGRI's funding is dedicated to ELSI research studies and programs examining the increasing availability of genomic information and technologies within society. Led by NHGRI's Division of Genomics and Society, this research will continue to be a vital component of the Institute's strategic vision in FY 2016. NHGRI-funded ELSI researchers will continue to study issues related to informed consent for genomics research; privacy issues arising from the collection and sharing of individuals' genomic information in large 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.

Beyond providing opportunities for investigator-initiated research, several major NHGRI research programs also incorporate ELSI research, including CSER, the Electronic Medical Records and GEnomics (eMERGE) Network, and NSIGHT.

Within the Institute's Intramural Research Program, the Social and Behavioral Research Branch will continue to conduct leading-edge research in FY 2016. The Branch is testing the effectiveness of strategies for communicating information about genetic risks; developing and evaluating behavioral interventions relevant to genomics; analyzing how to use genomic discoveries in clinical practice; and exploring the social, ethical, and policy implications of genomics research.

Budget Policy:
The FY 2016 President's Budget request for Genomics and Society is $44.250 million, an increase of $0.353 million or 0.8 percent more than the FY 2015 Enacted level. In FY 2016, 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, economic 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. In FY 2016, flagship programs will include educational and outreach activities aimed at both the general public and healthcare professionals. In connection with the nationwide tour of the museum exhibition, *Genome: Unlocking Life's Code* (developed in partnership with the Smithsonian's National Museum of Natural History), NHGRI and local community leaders will partner to conduct community engagement programs to promote public genomic literacy in the cities visited during FY 2016.

NHGRI will also continue its work with health practitioner professional societies through the Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC) and other groups to facilitate and stimulate the exchange of practices and educational resources for clinical applications of genomics. Through this work, NHGRI will provide leadership in partnership with stakeholder organizations to guide the development of initiatives that will foster the maturation of genomic medicine.

Budget Policy:
The FY 2016 President's Budget estimate for the Research Management and Support Program is $28.926 million, an increase of $0.639 million or 2.3 percent above the FY 2015 Enacted level. In FY 2016, 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, novel models for engaging the public in research participation, and methods to facilitate broad and open genomic data sharing that is respectful of participants interests. 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 about research and other programmatic investments, guiding future directions and research portfolio management.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Budget Authority by Object Class[1]
(Dollars in Thousands)

		FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Total compensable workyears:				
	Full-time employment	332	332	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$182	$182	$0
	Average GM/GS grade	12.5	12.5	0
	Average GM/GS salary	$106	$107	$1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$108	$108	$0
	Average salary of ungraded positions	$134	$134	$0
	OBJECT CLASSES	**FY 2015 Enacted**	**FY 2016 President's Budget**	**FY 2016 +/- FY 2015**
	Personnel Compensation			
11.1	Full-Time Permanent	$15,848	$16,070	$223
11.3	Other Than Full-Time Permanent	16,668	16,902	234
11.5	Other Personnel Compensation	552	560	8
11.7	Military Personnel	828	840	12
11.8	Special Personnel Services Payments	4,192	4,251	59
11.9	**Subtotal Personnel Compensation**	**$38,088**	**$38,622**	**$535**
12.1	Civilian Personnel Benefits	$10,723	$11,061	$338
12.2	Military Personnel Benefits	617	629	12
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$49,428**	**$50,312**	**$885**
21.0	Travel & Transportation of Persons	$1,704	$1,755	$51
22.0	Transportation of Things	100	100	0
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	7	7	0
23.3	Communications, Utilities & Misc. Charges	515	523	8
24.0	Printing & Reproduction	2	2	0
25.1	Consulting Services	$410	$418	$9
25.2	Other Services	11,589	11,924	335
25.3	Purchase of goods and services from government accounts	62,257	66,330	4,073
25.4	Operation & Maintenance of Facilities	$640	$640	$0
25.5	R&D Contracts	4,371	3,903	-468
25.6	Medical Care	7,805	8,041	236
25.7	Operation & Maintenance of Equipment	2,110	2,174	64
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$89,183**	**$93,431**	**$4,249**
26.0	Supplies & Materials	$6,167	$6,355	$188
31.0	Equipment	5,236	5,394	158
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	346,335	357,610	11,275
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	**$449,249**	**$465,179**	**$15,929**
	Total Budget Authority by Object Class	**$498,677**	**$515,491**	**$16,814**

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

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National Human Genome Research Institute

Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Personnel Compensation			
Full-Time Permanent (11.1)	$15,848	$16,070	$223
Other Than Full-Time Permanent (11.3)	16,668	16,902	234
Other Personnel Compensation (11.5)	552	560	8
Military Personnel (11.7)	828	840	12
Special Personnel Services Payments (11.8)	4,192	4,251	59
Subtotal Personnel Compensation (11.9)	**$38,088**	**$38,622**	**$535**
Civilian Personnel Benefits (12.1)	$10,723	$11,061	$338
Military Personnel Benefits (12.2)	617	629	12
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$49,428**	**$50,312**	**$885**
Travel & Transportation of Persons (21.0)	$1,704	$1,755	$51
Transportation of Things (22.0)	100	100	0
Rental Payments to Others (23.2)	7	7	0
Communications, Utilities & Misc. Charges (23.3)	515	523	8
Printing & Reproduction (24.0)	2	2	0
Other Contractual Services:			
Consultant Services (25.1)	410	418	9
Other Services (25.2)	11,589	11,924	335
Purchases from government accounts (25.3)	49,398	50,553	1,155
Operation & Maintenance of Facilities (25.4)	640	640	0
Operation & Maintenance of Equipment (25.7)	2,110	2,174	64
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$64,147**	**$65,710**	**$1,563**
Supplies & Materials (26.0)	$6,167	$6,355	$188
Subtotal Non-Pay Costs	**$72,643**	**$74,453**	**$1,810**
Total Administrative Costs	**$122,070**	**$124,766**	**$2,695**

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2014 Actual			FY 2015 Est.			FY 2016 Est.		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Extramural Operations									
Direct:	15	-	15	15	-	15	15	-	15
Reimbursable:	1	-	1	1	-	1	1	-	1
Total:	16	-	16	16	-	16	16	-	16
Division of Genome Sciences									
Direct:	12	-	12	13	-	13	13	-	13
Reimbursable:	2	-	2	2	-	2	2	-	2
Total:	14	-	14	15	-	15	15	-	15
Division of Genomic Medicine									
Direct:	11	-	11	12	-	12	12	-	12
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	11	-	11	12	-	12	12	-	12
Division of Genomics and Society									
Direct:	4	-	4	4	-	4	4	-	4
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	4	-	4	4	-	4	4	-	4
Division of Intramural Research									
Direct:	195	8	203	195	8	203	195	8	203
Reimbursable:	21	2	23	21	2	23	21	2	23
Total:	216	10	226	216	10	226	216	10	226
Division of Management									
Direct:	39	-	39	39	-	39	39	-	39
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	39	-	39	39	-	39	39	-	39
Division of Policy, Communications and Education									
Direct:	12	-	12	12	-	12	12	-	12
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	12	-	12	12	-	12	12	-	12
Office of the Director									
Direct:	8	-	8	8	-	8	8	-	8
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	8	-	8	8	-	8	8	-	8
Total	320	10	330	322	10	332	322	10	332
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
2012	12.3
2013	12.3
2014	12.5
2015	12.5
2016	12.5

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National Human Genome Research Institute

Detail of Positions[1]

GRADE	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Total, ES Positions	1	2	2
Total, ES Salary	181,500	363,000	363,000
GM/GS-15	33	33	33
GM/GS-14	24	25	25
GM/GS-13	64	64	64
GS-12	40	40	40
GS-11	13	13	13
GS-10	1	1	1
GS-9	3	3	3
GS-8	15	15	15
GS-7	1	1	1
GS-6	0	0	0
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	197	197
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	6	6	6
Senior Grade	4	4	4
Full Grade	1	1	1
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	11	11	11
Ungraded	140	140	140
Total permanent positions	208	210	210
Total positions, end of year	348	350	350
Total full-time equivalent (FTE) employment, end of year	330	332	332
Average ES salary	181,500	181,500	181,500
Average GM/GS grade	12.5	12.5	12.5
Average GM/GS salary	104,914	105,963	107,023

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