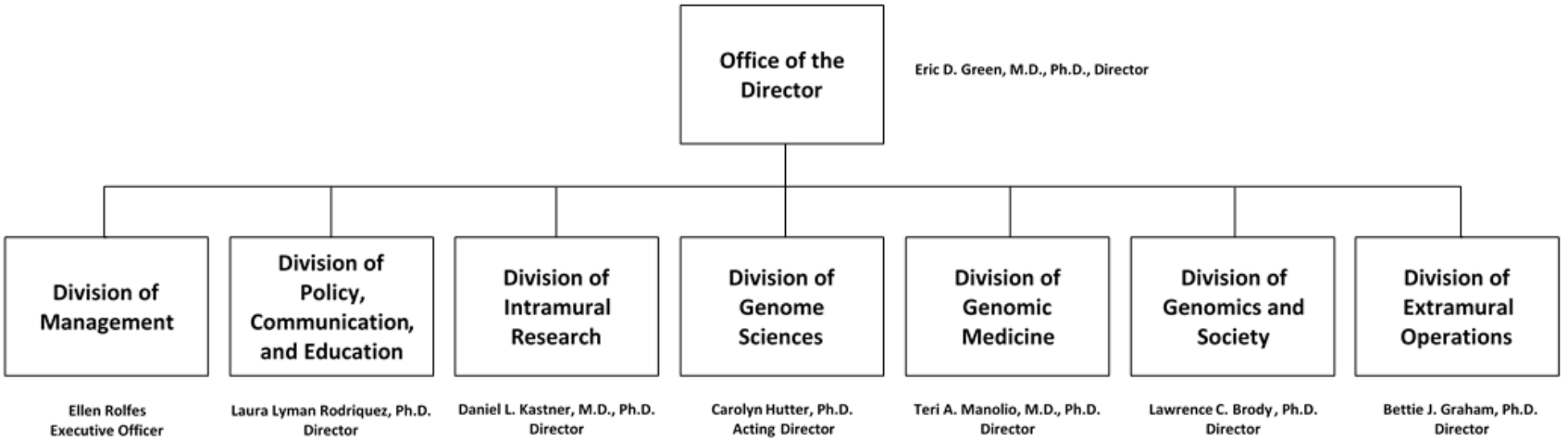
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Human Genome Research Institute (NHGRI)

FY 2019 Budget — Page No.

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, $368,785,000.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

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

Source of Funding	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Appropriation	$528,566	$528,566	$368,785
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*(0)*	*(0)*	*(0)*
Other Mandatory financing	*(0)*	*(0)*	*(0)*
Rescission	0	-3,589	0
Sequestration	0	0	0
Secretary's Transfer	-1,191		
Subtotal, adjusted appropriation	$527,375	$524,977	$368,785
OAR HIV/AIDS Transfers	971	0	0
Subtotal, adjusted budget authority	$528,346	$524,977	$368,785
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$528,346	$524,977	$368,785
Unobligated balance lapsing	-30	0	0
Total obligations	$528,316	$524,977	$368,785

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2017 - $27,175 FY 2018 - $27,175 FY 2019 - $18,917

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2017 Final		FY 2018 Annualized CR		FY 2019 President's Budget		FY 2019 +/- FY 2018	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	158	$160,148	182	$198,236	177	$155,001	-5	-$43,235
Administrative Supplements	*(34)*	9,447	*(28)*	8,499	*(0)*	0	*(-28)*	-8,499
Competing:								
Renewal	17	16,902	15	16,875	8	5,204	-7	-11,671
New	76	61,379	35	25,319	6	3,798	-29	-21,521
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	93	$78,281	50	$42,194	14	$9,002	-36	-$33,192
Subtotal, RPGs	251	$247,875	232	$248,929	191	$164,003	-41	-$84,926
SBIR/STTR	29	14,188	27	14,450	18	9,828	-9	-4,622
Research Project Grants	280	$262,064	259	$263,379	209	$173,831	-50	-$89,548
Research Centers:								
Specialized/Comprehensive	8	$16,506	5	$14,433	4	$7,391	-1	-$7,042
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	25	62,984	26	59,132	26	43,038	0	-16,094
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	33	$79,490	31	$73,565	30	$50,429	-1	-$23,136
Other Research:								
Research Careers	17	$2,416	26	$3,670	18	$2,628	-8	-$1,042
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	90	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	400	0	0	0	0	0	0
Other	33	17,737	29	18,986	24	12,075	-5	-6,911
Other Research	50	$20,643	55	$22,656	42	$14,703	-13	-$7,953
Total Research Grants	363	$362,196	345	$359,600	281	$238,963	-64	-$120,637
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	11	$466	14	$593	14	$580	0	-$13
Institutional Awards	159	8,114	164	8,530	164	8,542	0	12
Total Research Training	170	$8,579	178	$9,123	178	$9,122	0	-$1
Research & Develop. Contracts	13	$18,707	10	$17,421	5	$14,799	-5	-$2,622
(SBIR/STTR) (non-add)	*(0)*	*(155)*	*(0)*	*(0)*	*(0)*	*(30)*	*(0)*	*(30)*
Intramural Research	238	108,569	240	108,538	240	78,636	0	-29,902
Res. Management & Support	108	30,295	109	30,295	109	27,265	0	-3,030
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(5)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NHGRI	346	$528,346	349	$524,977	349	$368,785	0	-$156,192

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

Major Changes in Fiscal Year 2019 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 2019 President's Budget request for NHGRI, which is $368.785 million, a decrease of $156.192 million from the FY 2018 Annualized Continuing Resolution (CR) level. The FY 2019 President's Budget reflects the Administration's fiscal policy goals for the Federal Government. Within that framework, NHGRI will pursue its highest research priorities through strategic investments and careful stewardship of appropriated funds.

Research Project Grants (RPGs) (-$89.548 million; total $173.831 million):
NHGRI will reduce funding for non-competing RPGs by at least 20 percent which is a $43.235 million decrease from the FY 2018 funding level. Competing RPGs are expected to decrease by 72 percent or 36 grants compared to the FY 2018 Annualized CR level of 50 awards, and the amount to support competing awards will be reduced by $33.192 million from FY 2018. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Summary of Changes

(Dollars in Thousands)

FY 2018 Annualized CR	$524,977
FY 2019 President's Budget	$368,785
Net change	-$156,192

CHANGES	FY 2019 President's Budget		Change from FY 2018	
	FTEs	**Budget Authority**	**FTEs**	**Budget Authority**
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2018 pay increase & benefits		$41,560		$184
b. January FY 2019 pay increase & benefits		41,560		109
c. Paid days adjustment		41,560		157
d. Differences attributable to change in FTE		41,560		0
e. Payment for centrally furnished services		16,126		-120
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		20,949		-1,619
Subtotal				-$1,288
2. Research Management and Support:				
a. Annualization of January 2018 pay increase & benefits		$14,713		$64
b. January FY 2019 pay increase & benefits		14,713		32
c. Paid days adjustment		14,713		56
d. Differences attributable to change in FTE		14,713		0
e. Payment for centrally furnished services		779		-87
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		11,773		-360
Subtotal				-$295
Subtotal, Built-in				-$1,584

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

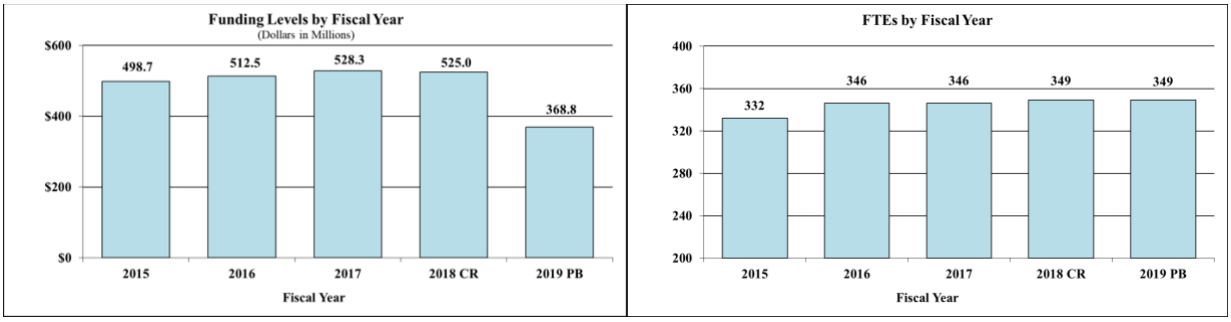
Summary of Changes - Continued

(Dollars in Thousands)

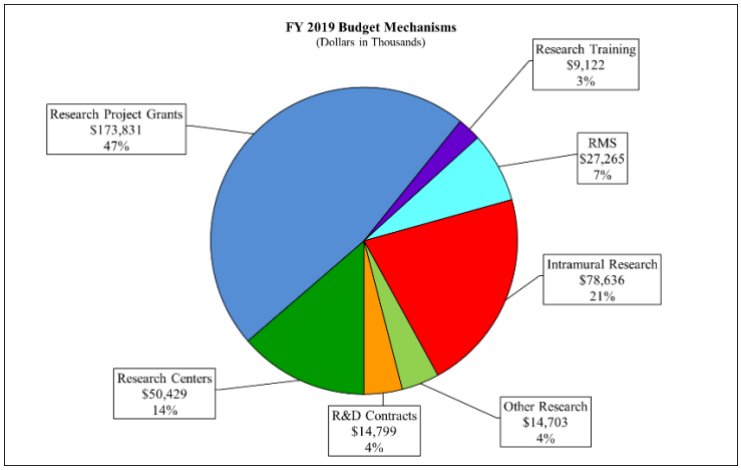
CHANGES	FY 2019 President's Budget		Change from FY 2018	
	No.	**Amount**	**No.**	**Amount**
B. Program:				
1. Research Project Grants:				
a. Noncompeting	177	$155,001	-5	-$51,734
b. Competing	14	9,002	-36	-33,192
c. SBIR/STTR	18	9,828	-9	-4,622
Subtotal, RPGs	209	$173,831	-50	-$89,548
2. Research Centers	30	$50,429	-1	-$23,136
3. Other Research	42	14,703	-13	-7,953
4. Research Training	178	9,122	0	-1
5. Research and development contracts	5	14,799	-5	-2,622
Subtotal, Extramural		$262,884		-$123,260
	FTEs		FTEs	
6. Intramural Research	240	$78,636	0	-$28,614
7. Research Management and Support	109	27,265	0	-2,735
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, Program	349	$368,785	0	-$154,608
Total changes				-$156,192

Fiscal Year 2019 Budget Graphs

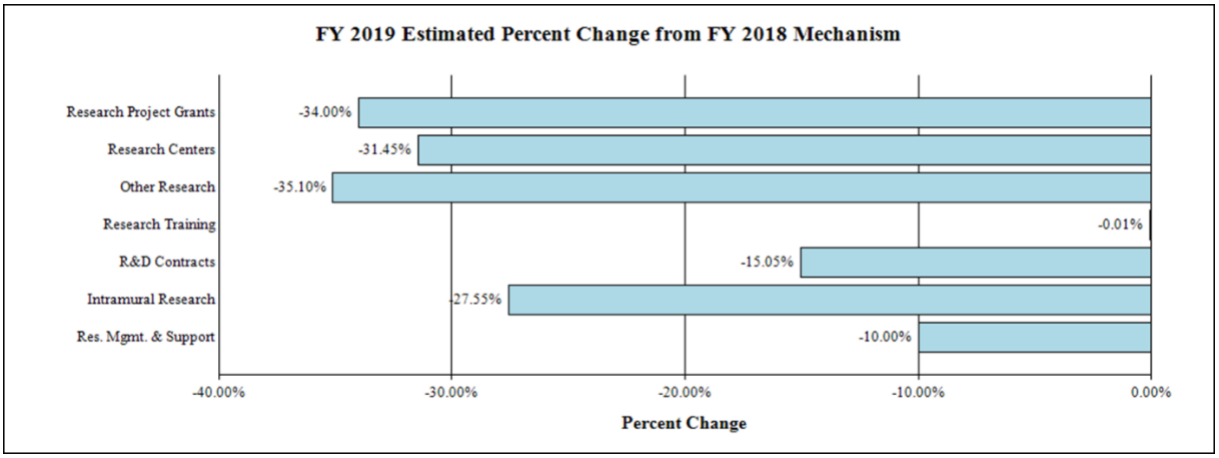
History of Budget Authority and FTEs:



Distribution by Mechanism:



Change by Selected Mechanisms:



NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

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

	FY 2017 Final		FY 2018 Annualized CR		FY 2019 President's Budget		FY 2019 +/- FY 2018	
Program Activity	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Understanding the Structure of Genomes		$26,354		$26,151		$17,922		-$8,229
Understanding the Biology of Genomes		91,228		90,568		62,298		-28,270
Using Genomics to Understand the Biology of Disease		124,784		124,034		86,126		-37,908
Using Genomics to Advance Medical Science		23,421		23,360		16,638		-6,721
Using Genomics to Improve the Effectiveness of Healthcare		14,746		14,674		10,275		-4,399
Bioinformatics, Computational Biology, and Data Science		144,653		143,521		98,278		-45,243
Education and Training		24,279		24,152		16,869		-7,282
Genomics and Society		48,585		48,223		33,114		-15,108
Subtotal, Program Activity*		**$498,051**		**$494,682**		**$341,520**		**-$153,162**
Extramural Research (non-add)		*(389,483)*		*(386,144)*		*(262,885)*		*(-123,259)*
Intramural Research (non-add)	**238**	*(108,569)*	**240**	*(108,538)*	**240**	*(78,636)*	**0**	*(-29,902)*
Research Management & Support	**108**	**$30,295**	**109**	**$30,295**	**109**	**$27,265**	**0**	**-$3,030**
TOTAL	**346**	**$528,346**	**349**	**$524,977**	**349**	**$368,785**	**0**	**-$156,192**

[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	2018 Amount Authorized	FY 2018 Annualized CR	2019 Amount Authorized	FY 2019 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$524,976,508	Indefinite	$368,785,000
National Human Genome Research Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$524,976,508		$368,785,000

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	$505,551,000	$526,166,000	$518,956,000
Rescission				$0
2017[1]	$513,227,000	$531,438,000	$534,516,000	$528,566,000
Rescission				$0
2018	$399,622,000	$536,774,000	$546,934,000	$528,566,000
Rescission				$3,589,492
2019	$368,785,000			

[1] Budget Estimate to Congress includes mandatory financing.

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 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
BA	$528,346,000	$524,976,508	$338,785,000	-$156,191,508
FTE	346	349	349	0

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

Director's Overview

The collaborative spirit of the Human Genome Project (HGP), continues to serve as a model for how the National Human Genome Research Institute (NHGRI) guides its research portfolio. NHGRI champions collaborative 'team science' and promotes widespread data sharing, elements that the Institute believes are fundamental for accelerating research and advancing medicine. The foundational work in technology development coupled with new strategic approaches for elucidating genome function fuels discoveries of how genomic variation relates to human health and disease; in turn, this knowledge is increasingly being applied to patient care through pilot projects that study the implementation of genomic medicine.

The amount of data being generated each year by genomics researchers is growing at an unprecedented rate. The greatest public benefit from these data is achieved when they are shared broadly for subsequent analyses. NHGRI's flagship Genome Sequencing Program (GSP), which works to discover the genomic bases of rare and common diseases, includes a set of Analysis Centers that are designed to analyze already-generated genome-sequence data. NHGRI also supports the Alliance for Genome Resources, a platform that integrates six independent data resources for model organisms (including yeast, zebrafish, and fruit fly) to facilitate cross-organism comparisons and analyses. Although these resources are widely used individually, integrating them into a unified platform allows for more robust and efficient bioinformatic studies aiming to gain insights about genome function. In FY 2019, NHGRI will continue to democratize access to data and data-science tools to enable more researchers to take a data-intensive approach in performing genomics research.

NHGRI aims to identify the differences (i.e., variants) among peoples' genomes and to establish the functional consequences of such genomic variation. As an example, the Zebrafish Core and Undiagnosed Diseases Program (UDP) within NHGRI's Intramural Research program collaborate to characterize how specific mutations cause rare human diseases; this involves the development and study of animal models that mimic specific diseases. The UDP relies on such work in zebrafish to understand better the rare diseases it encounters in patients. In FY 2019, researchers in both the UDP and the broader NIH Common Fund's Undiagnosed Diseases

Network will identify candidate disease genes in their patients and will use animal models to characterize the functions of these genes.

NHGRI strives to leverage its collective efforts to enable genomic medicine. One of the most promising areas for genomic medicine implementation is pharmacogenomics (PGx). PGx involves studying how genomic variation influences response to medications. Recognizing the importance of improving the selection of medications for individual patients, NHGRI funds projects that examine the barriers to implementing PGx approaches in medical care. NHGRI's Electronic Medical Records and Genomics (eMERGE) consortium is sequencing candidate PGx-relevant genes in over 9,000 participants, and then integrating these PGx data into electronic health records for clinical use. In FY 2019, through eMERGE-PGx and other programs, NHGRI will create and disseminate resources to guide PGx implementation, fund pilot studies that implement PGx in routine clinical care, support PGx-training programs for health professionals, and engage payers to promote reimbursement of clinically appropriate PGx tests.

Lastly, the full benefit of genomic medicine will not be realized unless all of the U.S.'s diverse populations benefit equitably from genomic advances. To make this possible, genomics projects must increase their attention to the recruitment, inclusion, and engagement of diverse and underrepresented populations in both basic and clinical genomics research. To this end, NHGRI's Clinical Sequencing Evidence-Generating Research Program (CSER2), aims to generate and analyze evidence for the use of genome sequencing in clinical care and to address barriers to genomic medicine implementation; this program has a targeted focus on recruiting ancestrally diverse and underserved populations. In tackling this complicated challenge, NHGRI has partnered with the National Institute on Minority Health and Health Disparities as well as the National Cancer Institute. Leveraging these partnerships will better position the Institute's research efforts to help bring more equitable access to genomic medicine in the future. In FY 2019, these projects and others will allow NHGRI to help create circumstances in which genomic medicine benefits diverse patient populations in a variety of clinical settings, to disseminate genomic advances in a culturally responsive manner, and to better understand and address health disparities related to genomics.

NHGRI's investments in basic, translational, and clinical research collectively aim to help improve the health of all Americans. From supporting collaborative science and the development and dissemination of basic science tools to the Institute's clinical research, NHGRI is uniquely poised to lead the field of genomics towards the realization of genomic medicine for all Americans.

Overall Budget Policy:
The FY 2019 President's Budget request is $368.785 million, a decrease of $156.195 million compared with the FY 2018 Annualized CR level. These reductions are distributed across all programmatic areas and basic, epidemiology, or clinical research.

Program Descriptions and Accomplishments

Understanding the Structure of Genomes

The successful dissemination of genomics into research and medicine requires the ability to decode accurately, affordably, and efficiently the order of the "letters" encoded in individual genomes. Since 2004, NHGRI's Advanced DNA Sequencing Technology Program has funded technology-development studies to drive down the cost of human-genome sequencing; these efforts have facilitated the reduction of this cost from more than $10 million in 2003 to close to $1,000 today, essentially removing a major barrier to genomics reaching its full potential. While generating a human genome sequence now costs the same as buying a laptop. The Institute continues to fund the development of innovative genomic technologies that aim to overcome the remaining scientific and technical barriers in genome sequencing and analysis. Already, the ease and low cost of new genome-sequencing technologies have allowed genomics research to flourish and to become a practical tool for precision medicine in oncology and for the care of acutely ill newborns (where a quick genomics-based diagnosis can often dramatically improve care and quality of life). Further refinements will make it increasingly viable for genome sequencing to be broadly adopted for use in medical care.

In FY 2019, NHGRI will continue funding high-risk, high-reward projects through the Novel Nucleic Acid Sequencing Technology Development and Novel Genomic Technology Development programs. The former program is funding projects to develop new methods to directly sequence DNA and RNA at high accuracy while maintaining low costs, while the latter program is funding the development of non-sequencing-based genomic technologies that will advance the field within five to seven years.

Budget Policy: The FY 2019 President's Budget request for Understanding the Structure of Genomes is $17.922 million, a decrease of $8.229 million or 31.5 percent from the FY 2018 Annualized CR level. Funds will support high-risk, high-reward projects that will propel innovative genomic technology development and further reduce the cost of genome sequencing, thereby enabling even more rapid advances in genomics research.

Understanding the Biology of Genomes

Establishing the order of the As, Ts, Gs, and Cs in our genomes is just the first step towards understanding how these letters guide biological processes. The Encyclopedia of DNA Elements (ENCODE) Project is creating a catalog of all the parts of the human genome that are functional (i.e., that play an active biological role). Now in its fourth phase, the ENCODE project will continue using Characterization Centers in FY 2019 to study the functions of identified regulatory elements (parts of the genome that choreograph when individual genes get turned on and off). One of the most fundamental tenets of ENCODE is that all generated data are freely available on the internet, providing every scientist access to this unique and valuable information for their research. In fact, ENCODE's value in biomedicine can be readily appreciated by the widespread use of these data: there are more than 2,000 scientific publications from groups that have used ENCODE data for their published work. In FY 2019, ENCODE will expand the understanding of functional genomic elements through two efforts: creating a more comprehensive catalog of candidate functional elements across the human genome and

developing a better understanding of those elements through characterization studies, computational analyses, and data integration.

The Knockout Mouse Phenotyping Project (KOMP2), an NHGRI-led Common Fund project that is now in its second phase, is creating a comprehensive public resource of mice strains that each contain a "null mutation" in a different gene in the mouse genome. Creating a mouse strain with a null mutation, in which a specific gene has been changed so that it no longer functions, allows researchers to study the biological role(s) of that gene. Because 99.0 percent of mouse genes have equivalent counterparts in the human genome, KOMP efforts are advancing our understanding of the role that gene mutations play in human health and disease. In FY 2019, the program will continue towards its goal of generating 3,000 new mice strains, and making them available to investigators studying particular genes of interest.

NHGRI's Intramural Research Program also investigates the functions of genes to enhance our understanding of the human genome. As discussed in the Director's Overview, the Institute's Zebrafish Core, the largest zebrafish research facility in the country, provides appropriate expertise and assistance that allows NHGRI investigators to model human diseases in zebrafish. Analogous to KOMP2, eliminating, modifying, or adding genes to zebrafish can help in understanding how similar changes in the human genome could affect biological and disease processes in humans. In FY 2019, the Zebrafish Core will continue to support NHGRI researchers' efforts to use this powerful strategy for elucidating the molecular bases of human disease.

Budget Policy: The FY 2019 President's Budget request for Understanding the Biology of Genomes is $62.298 million, a decrease of $28.270 million or 31.2 percent from the FY 2018 Annualized CR level. Funds will go towards improving our understanding of genome function through ENCODE's establishment of a more comprehensive catalog of functional elements in the human genome. FY 2019 funds will also support studies that provide a more robust understanding of all genes that contribute to human health and disease.

Using Genomics to Understand the Biology of Disease

NHGRI's longstanding Genome Sequencing Program (GSP) continues its foundational work to identify genomic variants associated with disease and to provide resources for the research and clinical communities to discover the genomic underpinnings of disease. By carrying out this basic research, GSP scientists are revealing insights about human disease that would not come about by clinical research alone. The largest component of the GSP is the Centers for Common Disease Genomics (CCDGs) program. Over the course of the current grant period, the CCDGs program will conduct an in-depth genomics study of roughly 10 common diseases to identify genomic variants that either increase or decrease risk associated with those diseases. This change in risk for a disease is usually quite subtle in a given person, so truly understanding the role that genomic variants play in influencing the risk for diseases necessitates the study of tens of thousands of individuals (to get sufficient statistical power for drawing reliable conclusions). In FY 2019, the CCDGs program will focus on four disease areas: cardiovascular disease, neuropsychiatric and developmental disorders, inflammatory and autoimmune disorders, and osteoporosis and other bone diseases.

The Electronic Medical Records and Genomics (eMERGE) Network, now in its third phase, is another key element for gaining a deeper understanding of how genomic variation relates to human disease. The eMERGE Network is studying both the genomic data and the electronic medical records (EMRs) of thousands of individuals, with the integrative analysis of such information offering a powerful way to identify the genomic bases of disease risk as well as to gain insights about genomic medicine implementation. The network also seeks to incorporate genomic data and state-of-the-art electronic phenotyping into medical records, while developing methods and best practices for the protection of patient privacy. In FY 2019, the eMERGE Network will complete genome sequencing and deposit the relevant data into the EMRs of about 25,000 participants, helping to advance the understanding of how genomic variation affects human traits and disease risks.

Program Portrait: Unraveling the Genomic Bases of Rare Diseases
FY 2018 Level: $66.7 million
FY 2019 Level: $47.0 million
Change: -$19.7 million

In the United States, a rare disease is defined as a condition that affects less than 200,000 Americans. However, with nearly 30 million Americans facing the challenges of living with a rare disease, this category of disorders collectively represents a large burden on our national health. Approximately 7,000 different rare diseases have been identified to date. These rare disorders pose a challenge to our traditional models of clinical care and research because most doctors rarely, if ever, encounter patients affected with them. This situation often makes diagnosis a slow and arduous process for both families and providers, with disease management often relying upon trial and error to address symptoms without fully understanding the underlying condition. Even when recognized properly, there is often no treatment beyond managing individual symptoms. Recruitment for rare-disease studies is also often challenged by the relative paucity of affected patients available for recruitment. Genome sequencing offers patients and their healthcare providers a powerful tool to help unravel the causes of rare and undiagnosed diseases, particularly by providing the ability to identify genomic variants that directly cause the underlying disease – which often gives key clues about potential treatment options and appropriate clinical management.

Within NHGRI's Intramural Research Program, investigators are collectively conducting research on over 45 rare diseases. FY 2019 funds will continue to support these intramural studies of known rare diseases as well as the work of the NIH Undiagnosed Diseases Program (UDP), which combines genome-sequence analysis with the extraordinary expertise of a network of medical specialists at the NIH Clinical Research Center to study the most vexing undiagnosed conditions. In FY 2013, the trans-NIH UDP was extended to become part of the NIH Common Fund's Undiagnosed Diseases Network (UDN); work at the UDN centers around the country is now leading to a diagnosis for approximately 25 percent of the enrolled participants. Many other participants in the UDN program, while not receiving a diagnosis, do receive important information that can lead to improved clinical management and an enhanced quality of life. Further, UDN brings together both basic and clinical researchers so that in addition to the potential for determining the cause of undiagnosed disease and the end of a long diagnostic odyssey for a patient, investigators are poised to immediately examine the underlying mechanisms associated with disease manifestation. The latter is an important way that NHGRI's investment in rare-disease research complements the Institute's common-disease research portfolio – since knowledge about the biological pathways disrupted in rare diseases are often informative to understanding the biology of common disorders.

Most rare diseases are caused by disruptions in a single gene. Often these so-called "Mendelian" disorders (which resemble the inheritance pattern first described by Gregor Mendel) are due to a single

point of genomic variation passed from parent to child. While 7,000 rare diseases have been identified to date, the genomic cause has been established for only 60 percent of them. To address this knowledge gap, NHGRI, the National Heart, Lung, and Blood Institute, and the National Eye Institute will continue to co-fund the Centers for Mendelian Genomics (CMGs) in FY 2019, with the goal of identifying the genomic cause of every known rare disease. In contrast to (and complementing) the UDN strategy that studies one affected patient at a time, the CMG program relies on a larger-scale approach that involves analyzing the genomes from as many affected individuals as are available for study. However, there are multiple means for sharing information across these different rare-disease research efforts, which has turned out to be incredibly valuable.

Finally, in FY 2019, NHGRI will continue to support the Genetic and Rare Disease Information Center (GARD) in collaboration with the National Center for Advancing Translational Sciences. This resource helps to meet the critical needs of rare-disease patients and their families seeking relevant information about clinical care and disease management. GARD's online information and call-based center helps patients and their families find the most up-to-date information about rare diseases (in English and Spanish), and is staffed by trained information specialists and genetic counselors. In FY 2017, GARD responded to over 7,100 inquiries. When appropriate, GARD directs patients and medical professionals to the UDN or CMG program for further information and evaluation.

Budget Policy: The FY 2019 President's Budget request for Using Genomics to Understand the Biology of Disease is $86.126 million, a decrease of $37.908 million or 30.6 percent from the FY 2018 Annualized CR level. The GSP and the eMERGE Network will continue to advance our understanding of how genomic differences influence our susceptibility to disease.

Using Genomics to Advance Medical Science

Genomics has the potential to revolutionize medicine in a variety of areas, including newborn screening; identification and treatment of rare disorders; cancer prevention, diagnosis, and treatment; and identifying susceptibility to common disorders to improve prevention. However, clinical researchers and healthcare providers are inundated with information about genomic advances, making it difficult to keep track of the most up-to-date and clinically-relevant information. For this reason, NHGRI, through the Clinical Genome Resource (ClinGen), seeks to ensure that the clinical genomics community (both researchers and healthcare providers) have accessible and authoritative information about the clinical relevance of genomic variants.

To create a high-quality resource, ClinGen investigators are developing methods to standardize the interpretation and annotation of genomic variants. They then curate the enormous amount of information being generated about genomic variants in specific clinical domains (e.g., cardiovascular disease) to produce evidence-based summaries of clinical utility that can be used to determine medical actionability. In FY 2019, ClinGen will continue its partnerships with the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the American Society of Hematology, and the Food and Drug Administration to expand into new disease areas (e.g., platelet disorders), accelerate curation efforts, and identify opportunities for streamlining the review and approval of genome-sequencing-based diagnostics. ClinGen will also leverage working groups that focus on complex disease curation, integrate computational predictors into curation frameworks, and ensure that ancestrally diverse populations are represented in the resource.

Program Portrait: Clinical Sequencing Evidence-Generating Research (CSER2) Program
FY2018 Level: $15.8 million
FY2019 Level: $11.6 million
Change: -$4.2 million

One of the many places that the promise of the Human Genome Project is being realized is in medicine, where genome sequencing is taking root in the routine clinical practice of oncology and prenatal testing. At the same time, the large-scale deployment of genome sequencing in healthcare is inevitably encountering numerous challenges and raising many questions. To address these issues, NHGRI, the National Cancer Institute, and the National Institute on Minority Health and Health Disparities came together to fund the Clinical Sequencing Evidence-Generating Research (CSER2) Program. CSER2 focuses on diverse and medically underserved populations, with the aim of generating cutting-edge approaches and best practices to promote the implementation of genomic medicine in a fashion that benefits all Americans. This consortium builds upon the highly successful Clinical Sequencing Exploratory Research (CSER) Program, which established many of the initial first approaches for understanding how to incorporate genome sequencing into clinical care while simultaneously examining the associated ethical, legal, and psychosocial implications. In FY 2019, CSER2 will capitalize on the advances made by CSER in addressing barriers to utilizing genome-sequence information in medical practice – but with particular attention being paid to overcoming the barriers encountered in underserved and underrepresented populations.

CSER2 projects are bringing a holistic approach to examining the challenges of incorporating genome-sequence information into healthcare through multi-disciplinary research teams that include sociologists, anthropologists, economists, and ethicists – in addition to bench and clinical genomics researchers. The utilization of such a broad range of expertise uniquely positions CSER2 to recruit successfully underserved and underrepresented populations to genomic medicine implementation programs. In addition, FY 2019 funds will support work at the University of Washington's CSER2 Coordinating Center to refine frameworks for harmonizing the broad datasets being generated at the different consortium study sites, which will be important as the breadth of diversity in the CSER2 study populations and research settings will be more significant than previous studies of this kind.

To date, the vast majority of research studies recruit from large academic hospitals. CSER2 will be unique in that it will recruit more than 70 percent of its participants from ancestrally diverse populations and from historically underserved populations in community-based healthcare settings. This will include low health-literacy areas in the Pacific Northwest, where cancer assessments will be conducted and the utility of genome sequencing for patient care will be measured. Other care settings include underprivileged neighborhoods in Harlem and the Bronx, where genome-sequence generation for sick pediatric patients will be conducted and its clinical utility measured. Other study sites in Texas, North Carolina, California, and the Southeastern United States will use genome sequencing as part of the clinical care of pediatric cancer patients, infants, and children with serious developmental disorders, and newborns. Research in all of these settings will increase understanding about how patients receive and use genomic information; improve communication mechanisms among patients, laboratories, and physicians; examine the ethical, social, and economic influences associated with returning complicated genomic test results to underrepresented minorities and medically underserved populations; and establish how best to return genomic information in communities that may lack a breadth of specialized clinicians. The findings generated by these various projects will be highly complementary and will enhance the implementation of genomic medicine across all American healthcare systems.

Budget Policy: The FY 2019 President's Budget request for Using Genomics to Advance Medical Science is $16.638 million, a decrease of $6.721 million or 28.8 percent from the FY

2018 Annualized CR level. ClinGen will continue to enhance its reputation as an authoritative resource for the compilation of genomic variants that have relevance in medical care and will work to diversify the ancestral populations that are represented in the resource.

Using Genomics to Improve the Effectiveness of Healthcare

We are quickly approaching a reality in which genomic testing is a routine part of healthcare in America. NHGRI is investing in translational and clinical research to ensure the smooth integration of genomics into healthcare in a manner that is effective and equitable. The Program Portrait for the CSER2 Program specifically highlights how ancestrally diverse and underrepresented populations will be recruited to participate in genomic medicine research to establish how genomics can be used most effectively in the clinic. CSER2 projects include studies to explore how genomics can improve care for children with rare diseases and cancers, and how to detect cancer predisposition to improve preventive care and screening.

The IGNITE Network, now in its second phase, is continuing its work to enhance the implementation of genomic medicine. IGNITE II will conduct research to inform the adoption of genetic tests and genome sequencing in a variety of healthcare settings across the country. Importantly, IGNITE II projects will take place in diverse communities and involve underserved populations, helping to ensure that genomic medicine will be disseminated and implemented equitably.

In FY 2019, IGNITE II will conduct pragmatic clinical trials (i.e., trials designed to test real-world effectiveness) of genomic medicine implementation. The benefit of pragmatic clinical trials is that they mirror the clinical experience closely, and thus the results can be generalized to routine practice settings. In the spirit of sharing resources to help others implement genomic medicine, IGNITE II will also continue to develop its interactive SPARK (Supporting Practice through Applications, Research and Knowledge) toolbox, an online information resource for helping clinicians incorporate genomics into their practices and researchers study the implementation of genomics in healthcare.

Additionally, NHGRI is accelerating its work to bring pharmacogenomics into routine medical practice. Pharmacogenomics (PGx), which studies how genomic variants influence the response to medications, is a promising area for integration into healthcare. The eMERGE-PGx project, described in the Director's Overview, aims to sequence candidate PGx-relevant genes in over 9,000 participants, integrate these data into their EMRs, and study how this information influences clinical care. ClinGen has a PGx working group that evaluates and annotates PGx-relevant genes with information about how variants in these genes might affect drug response. In FY 2019, NHGRI's PGx portfolio will fund pilot studies and support the training of healthcare professionals.

Budget Policy: The FY 2019 President's Budget request for Using Genomics to Improve the Effectiveness of Healthcare is $10.275 million, a decrease of $4.399 million or 30 percent from the FY 2018 Annualized CR level. NHGRI will continue to support CSER2 and IGNITE II and the efforts of these programs to realize the equitable implementation of genomic medicine. NHGRI programs will also create and disseminate resources to guide implementation of PGx and support PGx-focused training opportunities for healthcare professionals.

Bioinformatics, Computational Biology, and Data Science
Genomics research generates large datasets, the study of which requires substantial data aggregation and complex analytic methods. NHGRI is committed to democratizing access to data resources and data-science tools that enable the scientific community to study large genomic datasets effectively and efficiently. NHGRI-funded efforts in this area include the development and dissemination of tools for storing, managing, and analyzing genomic data. In FY 2019, NHGRI will support the Analysis, Visualization, and Informatics Lab-space (AnVIL), which serves as a cloud-based resource for the storage and analysis of large genomic datasets. This resource will interact closely with the recently established NIH Data Commons.

In addition, as described in the Director's Overview, NHGRI's GSP has multiple Analysis Centers that are creating analytic tools for performing genomic analyses that will be freely available for researchers. Moreover, NHGRI supports the Alliance for Genome Resources that is integrating six independent data resources into one platform, thereby enhancing the value of all the assimilated data. By investing in such open-access tools and databases, NHGRI fuels genomic advances at a more rapid pace by enabling scientists and clinicians from both small and large institutions to participate in genomics research without high-cost barriers to entry.

Budget Policy: The FY 2019 President's Budget request for Bioinformatics, Computational Biology and Data Science is $98.278 million, a decrease of $45.243 million or 31.5 percent from the FY 2018 Annualized CR level. Funds will go towards creating and disseminating data-science tools for analyzing genomics data to the broader research community, including generating a cloud-based resource for storage and analysis of genomic data.

Genomics Education and Training
Continued progress in biomedical research depends on fostering the development of the next generation of scientists and clinical researchers. NHGRI seeks to do this through institutional training grants, individual fellowships, solicitation of supplements to recruit underrepresented minorities, and career development awards. The Institute also has a Diversity Action Plan (DAP) that funds research experiences for underrepresented minorities at all stages of training (including undergraduate, post-baccalaureate, graduate, postdoctoral, and faculty), which demonstrates our commitment to increasing the number of underrepresented minorities pursuing careers in genomics and biomedical research.

Budget Policy: The FY 2019 President's Budget request for Genomics Education and Training is $16.869 million, a decrease of $7.282 million or 30.1 percent from the FY 2018 Annualized CR level. Funds will support the work of a diverse set of trainees at different stages in their careers.

Genomics and Society
A unique feature of NHGRI's portfolio is the explicit commitment to fund research investigating the ethical, legal, and social implications (ELSI) of genomics and the advances emanating from this continually expanding field. This ELSI research is especially important given the rapid evolution and deployment of new technologies that are finding their way into routine healthcare. The Institute's ELSI Research Program is devoted to funding studies and training opportunities

that foster basic and applied research, that explore questions about the return of genomic research results to participants, that improve informed-consent processes associated with genomics research, and that examine the complex concerns about data privacy inherent to genomic studies.

One component of NHGRI's ELSI research portfolio, the Centers of Excellence in ELSI Research (CEER) Program, supports centers that conduct trans-disciplinary research on timely genomics-oriented ethics and societal topics in a way that can rapidly respond to new developments. These Centers are also charged with preparing junior researchers for conducting ELSI research. Complementing these topic-focused Centers, NHGRI also supports ELSI research projects that are embedded within other NHGRI research programs, such as CSER2 and eMERGE. Embedding ELSI projects into these networks allows for the real-time study of how genomics shapes the actions of research participants and investigators. It also allows for the development of research questions that capitalize on the experience of the program.

Program Portrait: Community Engagement in Genomics
FY2018 Level: $7.7 million
FY2019 Level: $4.9 million
Change: -$2.8 million

The successful integration of genomics into medicine will depend on the broad acceptance of genomic medicine by healthcare professionals, patients, and the public at large. For this to occur, and in light of the complexity of genomic science and the ethical and societal issues related to the use of genomic information, it is imperative that the genomics research community actively engage all stakeholders and the diverse communities within them. Recognizing the importance of such a dialogue, NHGRI is devoting an increasing amount of attention and its programmatic priorities to community engagement in genomics.

NHGRI's translational and clinical research consortia [e.g., the Electronic Medical Records and Genomics (eMERGE) and the Clinical Sequencing Evidence-Generating Research (CSER2) networks], are emphasizing community engagement as a fundamental aspect of the research enterprise. In FY 2019, eMERGE investigators at Columbia University will work with their large, multi-ethnic cohort to create an electronic portal for patients and healthcare providers to receive genomic information and to provide feedback on how it is being used. By analyzing the feedback from these communities, researchers will determine the most effective methods for returning genomic test results to patients and their providers, evaluate patient understanding of such results, and determine how best to prepare patients to make medical decisions based on genomic information. A key aim of CSER2 (see Program Portrait for more information) is to engage traditionally underrepresented patient populations in genomics research. For example, investigators at the Icahn School of Medicine will use FY 2019 funds to work with primary care providers, local communities, and the parents of participating pediatric patients from project sites in Harlem and the Bronx to study misunderstandings related to the "language" of genome sequencing and to explore how and why such misunderstandings generate barriers to genomic medicine implementation.

Beyond the research itself, NHGRI staff will continue to engage and partner with diverse communities to increase awareness about public perspectives and priorities regarding the use of genomic information in healthcare. In FY 2019, the Institute will continue to foster the recently established Tribal Colleges Consortium on Genomics Training, which is an informal network of tribal colleges and universities dedicated to expanding genomics training for faculty as well as to preparing students for careers in genomics. This work and other community-engagement activities will be informed by discussions with

the Community Engagement in Genomics Working Group of the National Advisory Council for Human Genome Research. This new working group, comprised of community liaisons and health advocates representing diverse populations, will assist in building community-oriented relationships, in providing diverse perspectives and feedback for the development of NHGRI educational tools and programs, and identifying areas for collaboration among NHGRI, NIH, and diverse communities and organizations.

Finally, in FY 2019, NHGRI will also leverage its relationships to promote genomic literacy among healthcare providers, students, and the general public. The Institute will facilitate partnerships between museums and their local communities associated with the travelling NHGRI-Smithsonian exhibition *Genome: Unlocking Life's Code*. At a national level, NHGRI will collaborate to produce community events and educational resources with partners such as the Smithsonian National Museum of African American History and Culture, the Public Broadcasting Service, national educational organizations, and private sector partners who share our interests in increasing genomic literacy. These collective efforts aim to make genomic medicine more approachable and accessible to all Americans, irrespective of their community or cultural background.

Budget Policy: The FY 2019 President's Budget request for Genomics and Society is $33.114 million, a decrease of $15.108 million or 31.3 percent from the FY 2018 Annualized CR level. NHGRI will continue to fund ELSI research related to advances in genomics and the implementation of genomic medicine, through investigator-initiated projects and embedded ELSI projects.

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National Human Genome Research Institute

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

		FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Total compensable workyears:				
	Full-time employment	349	349	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$185	$185	$0
	Average GM/GS grade	12.5	12.5	0.0
	Average GM/GS salary	$112	$112	$0
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$114	$117	$3
	Average salary of ungraded positions	$150	$150	$0
OBJECT CLASSES		**FY 2018 Annualized CR**	**FY 2019 President's Budget**	**FY 2019 +/- FY 2018**
	Personnel Compensation			
11.1	Full-Time Permanent	$20,333	$20,508	$175
11.3	Other Than Full-Time Permanent	16,616	16,759	143
11.5	Other Personnel Compensation	612	154	-457
11.7	Military Personnel	792	816	23
11.8	Special Personnel Services Payments	4,841	4,883	42
11.9	**Subtotal Personnel Compensation**	**$43,195**	**$43,120**	**-$75**
12.1	Civilian Personnel Benefits	$12,333	$12,531	$199
12.2	Military Personnel Benefits	604	622	18
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$56,132**	**$56,273**	**$141**
21.0	Travel & Transportation of Persons	$1,925	$558	-$1,366
22.0	Transportation of Things	271	35	-237
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	0	0	0
23.3	Communications, Utilities & Misc. Charges	500	234	-266
24.0	Printing & Reproduction	12	1	-11
25.1	Consulting Services	$423	$117	-$306
25.2	Other Services	15,352	4,221	-11,131
25.3	Purchase of goods and services from government accounts	67,446	56,076	-11,370
25.4	Operation & Maintenance of Facilities	$255	$142	-$113
25.5	R&D Contracts	1,185	353	-832
25.6	Medical Care	1,170	178	-992
25.7	Operation & Maintenance of Equipment	2,176	757	-1,420
25.8	Subsistence & Support of Persons	49	8	-41
25.0	**Subtotal Other Contractual Services**	**$88,057**	**$61,852**	**-$26,205**
26.0	Supplies & Materials	$6,299	$835	-$5,463
31.0	Equipment	3,059	911	-2,147
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	368,722	248,085	-120,637
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	**$468,845**	**$312,512**	**-$156,333**
	Total Budget Authority by Object Class	**$524,977**	**$368,785**	**-$156,192**

[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 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Personnel Compensation			
Full-Time Permanent (11.1)	$20,333	$20,508	$175
Other Than Full-Time Permanent (11.3)	16,616	16,759	143
Other Personnel Compensation (11.5)	612	154	-457
Military Personnel (11.7)	792	816	23
Special Personnel Services Payments (11.8)	4,841	4,883	42
Subtotal Personnel Compensation (11.9)	**$43,195**	**$43,120**	**-$75**
Civilian Personnel Benefits (12.1)	$12,333	$12,531	$199
Military Personnel Benefits (12.2)	604	622	18
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$56,132**	**$56,273**	**$141**
Travel & Transportation of Persons (21.0)	$1,925	$558	-$1,366
Transportation of Things (22.0)	271	35	-237
Rental Payments to Others (23.2)	0	0	0
Communications, Utilities & Misc. Charges (23.3)	500	234	-266
Printing & Reproduction (24.0)	12	1	-11
Other Contractual Services:			
Consultant Services (25.1)	423	117	-306
Other Services (25.2)	15,352	4,221	-11,131
Purchases from government accounts (25.3)	54,138	44,880	-9,257
Operation & Maintenance of Facilities (25.4)	255	142	-113
Operation & Maintenance of Equipment (25.7)	2,176	757	-1,420
Subsistence & Support of Persons (25.8)	49	8	-41
Subtotal Other Contractual Services	**$72,393**	**$50,125**	**-$22,268**
Supplies & Materials (26.0)	$6,299	$835	-$5,463
Subtotal Non-Pay Costs	**$81,400**	**$51,789**	**-$29,611**
Total Administrative Costs	**$137,531**	**$108,061**	**-$29,470**

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Detail of Full-Time Equivalent Employment (FTE)

	FY 2017 Final			FY 2018 Annualized CR			FY 2019 President's Budget		
OFFICE/DIVISION	**Civilian**	**Military**	**Total**	**Civilian**	**Military**	**Total**	**Civilian**	**Military**	**Total**
Division of Extramural Operations									
Direct:	14	-	14	14	-	14	14	-	14
Reimbursable:	1	-	1	1	-	1	1	-	1
Total:	15	-	15	15	-	15	15	-	15
Division of Genome Sciences									
Direct:	11	-	11	12	-	12	12	-	12
Reimbursable:	4	-	4	4	-	4	4	-	4
Total:	15	-	15	16	-	16	16	-	16
Division of Genomic Medicine									
Direct:	10	-	10	10	-	10	10	-	10
Reimbursable:	2	-	2	2	-	2	2	-	2
Total:	12	-	12	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:	200	6	206	202	6	208	202	6	208
Reimbursable:	29	3	32	29	3	32	29	3	32
Total:	229	9	238	231	9	240	231	9	240
Division of Management									
Direct:	44	-	44	44	-	44	44	-	44
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	44	-	44	44	-	44	44	-	44
Division of Policy, Communications and Education									
Direct:	13	-	13	13	-	13	13	-	13
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	13	-	13	13	-	13	13	-	13
Office of the Director									
Direct:	5	-	5	5	-	5	5	-	5
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	5	-	5	5	-	5	5	-	5
Total	337	9	346	340	9	349	340	9	349
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**
2015	12.5
2016	12.6
2017	12.5
2018	12.5
2019	12.5

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Detail of Positions[1]

GRADE	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	363,744	370,656	370,656
GM/GS-15	35	36	36
GM/GS-14	29	29	29
GM/GS-13	65	65	65
GS-12	43	44	44
GS-11	17	18	18
GS-10	1	1	1
GS-9	3	3	3
GS-8	14	14	14
GS-7	0	0	0
GS-6	0	0	0
GS-5	1	1	1
GS-4	0	0	0
GS-3	1	1	1
GS-2	2	2	2
GS-1	0	0	0
Subtotal	211	214	214
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	0	0	0
Senior Assistant Grade	1	1	1
Assistant Grade	0	0	0
Subtotal	9	9	9
Ungraded	119	125	125
Total permanent positions	222	225	225
Total positions, end of year	341	350	350
Total full-time equivalent (FTE) employment, end of year	346	349	349
Average ES salary	181,872	185,328	185,328
Average GM/GS grade	12.5	12.5	12.5
Average GM/GS salary	109,599	111,717	111,717

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