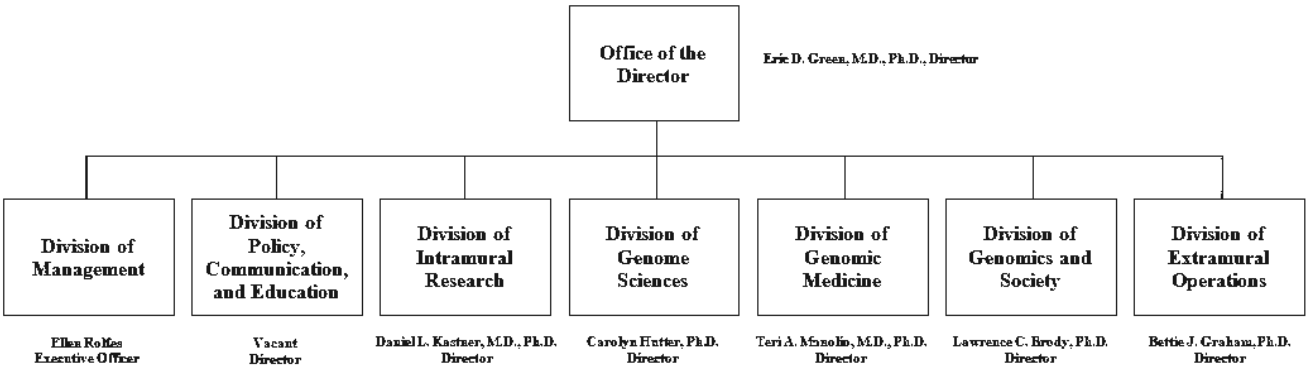
DEPARTMENT OF HEALTH AND HUMAN SERVICES

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, [$606,349,000]*$550,116,000*.

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Amounts Available for Obligation[1]

(Dollars in Thousands)

Source of Funding	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Appropriation	$575,579	$606,349	$550,116
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*(0)*	*(0)*	*(0)*
Other Mandatory financing	*(0)*	*(0)*	*(0)*
Rescission	0	0	0
Sequestration	0	0	0
Secretary's Transfer	-1,977	0	0
Subtotal, adjusted appropriation	$573,602	$606,349	$550,116
OAR HIV/AIDS Transfers	1,785	-2,231	0
HEAL Transfer from NINDS	0	0	0
Subtotal, adjusted budget authority	$575,387	$604,118	$550,116
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$575,387	$604,118	$550,116
Unobligated balance lapsing	-26	0	0
Total obligations	$575,361	$604,118	$550,116

[1] Excludes the following amounts (in thousands) for reimbursable activities carried out by this account:
FY 2019 - $24,803 FY 2020 - $25,554 FY 2021 - $23,304

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National Human Genome Research Institute

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 +/- FY 2020 Enacted	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	204	$214,089	215	$161,100	203	$129,101	-12	-$31,999
Administrative Supplements	*(47)*	26,561	*(43)*	64,000	*(58)*	41,561	*(15)*	-22,439
Competing:								
Renewal	5	4,585	22	21,011	25	18,024	3	-2,987
New	65	36,643	66	43,215	95	71,421	29	28,206
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	70	$41,228	88	$64,226	120	$89,445	32	$25,219
Subtotal, RPGs	274	$281,878	303	$289,326	323	$260,107	20	-$29,219
SBIR/STTR	30	15,319	32	16,573	28	14,657	-4	-1,916
Research Project Grants	304	$297,197	335	$305,899	351	$274,764	16	-$31,135
Research Centers:								
Specialized/Comprehensive	2	$4,335	2	$4,136	3	$3,763	1	-$373
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	22	49,845	24	54,385	24	49,498	0	-4,887
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	24	$54,179	26	$58,521	27	$53,261	1	-$5,260
Other Research:								
Research Careers	28	$4,043	30	$4,353	26	$3,961	-4	-$392
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	0	0	0	0	0	0	0
Other	49	40,685	48	47,680	48	43,400	0	-4,280
Other Research	77	$44,728	78	$52,033	74	$47,361	-4	-$4,672
Total Research Grants	405	$396,104	439	$416,453	452	$375,386	13	-$41,067
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	13	$545	14	$643	13	$584	-1	-$59
Institutional Awards	168	8,509	181	9,750	165	8,873	-16	-877
Total Research Training	181	$9,054	195	$10,393	178	$9,457	-17	-$936
Research & Develop. Contracts	12	$18,639	12	$19,789	7	$19,472	-5	-$317
(SBIR/STTR) (non-add)	*(0)*	*(165)*	*(0)*	*(176)*	*(0)*	*(150)*	*(0)*	*(-26)*
Intramural Research	223	117,665	240	122,132	240	112,218	0	-9,914
Res. Management & Support	98	33,926	109	35,351	109	33,583	0	-1,768
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(6)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NHGRI	321	$575,387	349	$604,118	349	$550,116	0	-$54,002

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

Major Changes in Fiscal Year 2021 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 2021 President's Budget request for NHGRI, which is $550.1 million, a decrease of $54.0 million from the FY 2020 Enacted level. The FY 2021 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) (-$31.1 million; total $274.8 million):
NHGRI will reduce funding for non-competing RPGs by 7.0 percent which is a $9.7 million decrease from FY 2021 committed levels. These reductions are distributed across all programmatic areas and basic, epidemiology, or clinical research. Competing RPGs are expected to increase by 36 percent, or 32 grants compared to the FY 2020 Enacted level of 88 awards, and the amount to support competing awards will increase by $25.2 million from FY 2020. The FY 2021 planned competing cohort includes the potential renewal of programs supported by large grant awards while also supporting additional investigator-initiated applications.

Research Centers (-$5.3 million; total $53.3 million):
NHGRI will reduce funding for Research Centers grants by 9.0 percent compared to the FY 2020 Enacted level. These reductions are distributed across all the programmatic areas including resource grants for community resource projects.

Other Research (-$4.7 million; total $47.4 million):
NHGRI will reduce funding for Other Research grants by 9.0 percent compared to the FY 2020 Enacted level. These reductions are distributed across all the programmatic areas and basic, epidemiology, or clinical research.

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National Human Genome Research Institute

Summary of Changes

(Dollars in Thousands)

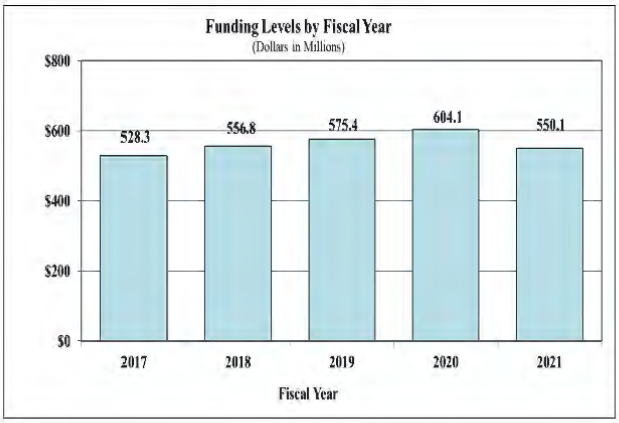
FY 2020 Enacted	$604,118
FY 2021 President's Budget	$550,116
Net change	-$54,002

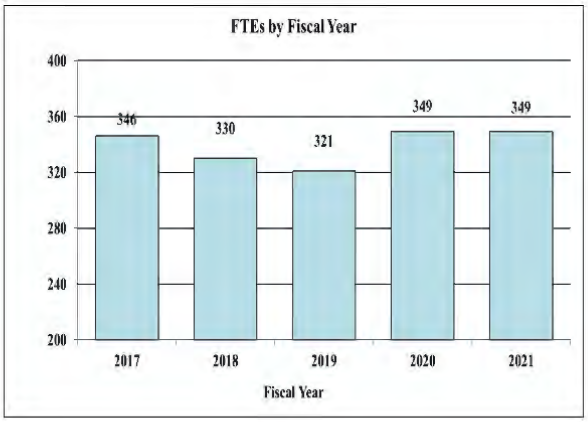
CHANGES	FY 2021 President's Budget FTEs	FY 2021 President's Budget Budget Authority	Change from FY 2020 Enacted FTEs	Change from FY 2020 Enacted Budget Authority
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2020 pay increase & benefits		$45,110		$292
b. January FY 2021 pay increase & benefits		45,110		679
c. Paid days adjustment		45,110		-168
d. Differences attributable to change in FTE		45,110		0
e. Payment for centrally furnished services		18,618		-980
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		48,489		-229
Subtotal				-$407
2. Research Management and Support:				
a. Annualization of January 2020 pay increase & benefits		$15,584		$100
b. January FY 2021 pay increase & benefits		15,584		235
c. Paid days adjustment		15,584		-58
d. Differences attributable to change in FTE		15,584		0
e. Payment for centrally furnished services		1,103		-58
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		16,897		82
Subtotal				$301
Subtotal, Built-in				-$106

CHANGES	FY 2021 President's Budget No.	FY 2021 President's Budget Amount	Change from FY 2020 Enacted No.	Change from FY 2020 Enacted Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	203	$170,662	-12	-$54,438
b. Competing	120	89,445	32	25,219
c. SBIR/STTR	28	14,657	-4	-1,916
Subtotal, RPGs	351	$274,764	16	-$31,135
2. Research Centers	27	$53,261	1	-$5,260
3. Other Research	74	47,361	-4	-4,672
4. Research Training	178	9,457	-17	-936
5. Research and development contracts	7	19,472	-5	-317
Subtotal, Extramural		$404,315		-$42,320
	FTEs		FTEs	
6. Intramural Research	240	$112,218	0	-$9,507
7. Research Management and Support	109	33,583	0	-2,069
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, Program	349	$550,116	0	-$53,896
Total changes				-$54,002

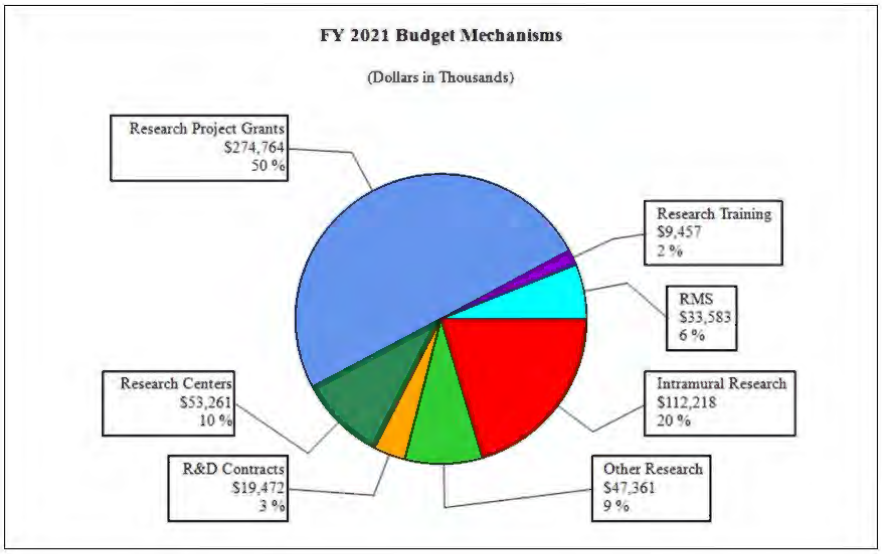
Fiscal Year 2021 Budget Graphs

History of Budget Authority and FTEs:

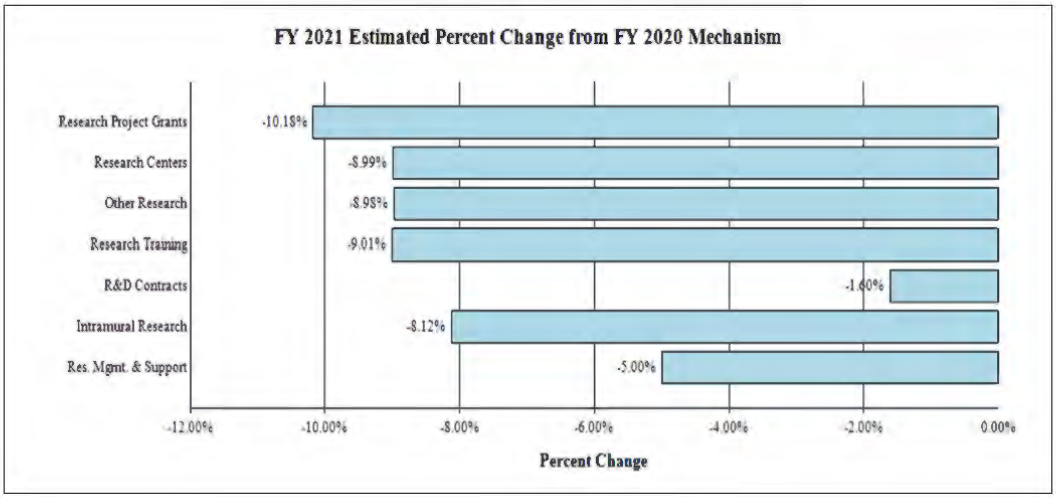




Distribution by Mechanism:



Change by Selected Mechanism:



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National Human Genome Research Institute

Budget Authority by Activity[1]

(Dollars in Thousands)

Program Activity	FY 2019 Final FTE	FY 2019 Final Amount	FY 2020 Enacted FTE	FY 2020 Enacted Amount	FY 2021 President's Budget FTE	FY 2021 President's Budget Amount	FY 2021 +/- FY2020 FTE	FY 2021 +/- FY2020 Amount
Detail								
Understanding the Structure of Genomes		$35,251		$37,104		$33,630		-$3,474
Understanding the Biology of Genomes		89,011		93,555		84,914		-8,641
Using Genomics to Understand the Biology of Disease		139,697		146,560		133,262		-13,299
Using Genomics to Advance Medical Science		29,704		31,014		28,332		-2,682
Using Genomics to Improve the Effectiveness of Healthcare		18,131		18,995		17,295		-1,700
Bioinformatics, Computational Biology, and Data Science		147,399		155,118		140,619		-14,499
Education and Training		25,971		27,202		24,774		-2,428
Genomics and Society		56,297		59,219		53,707		-5,512
Subtotal, Program Activity*		**$541,461**		**$568,767**		**$516,533**		**-$52,234**
Extramural Research (non-add)	*(0)*	*(423,796)*	*(0)*	*(446,635)*	*(0)*	*(404,315)*	*(0)*	*(-42,320)*
Intramural Research (non-add)	**223**	*(117,665)*	**240**	*(122,132)*	**240**	*(112,218)*	**0**	*(-9,914)*
Research Management & Support	**98**	**$33,926**	**109**	**$35,351**	**109**	**$33,583**	**0**	**-$1,768**
TOTAL	**321**	**$575,387**	**349**	**$604,118**	**349**	**$550,116**	**0**	**-$54,002**

[1]Includes FTEs whose payroll obligations are supported by the

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2020 Amount Authorized	FY 2020 Enacted	2021 Amount Authorized	FY 2021 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$604,118,000	Indefinite	$550,116,000
National Human Genome Research Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$604,118,000		$550,116,000

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	$556,881,000
Rescission				$0
2019	$512,979,000	$563,531,000	$575,882,000	$575,579,000
Rescission				$0
2020	$495,448,000	$603,710,000	$607,999,000	$606,349,000
Rescission				$0
2021	$550,116,000			

[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 2019 Final	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
BA	$575,387,000	$604,118,000	$550,116,000	-$54,002,000
FTE	321	349	349	0

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

Director's Overview

The National Human Genome Research Institute (NHGRI) has always been – and will continue to be – at *The Forefront of Genomics*. Starting with the Institute's pivotal leadership of the Human Genome Project (HGP) and guided by a new strategic plan that will be unveiled in late 2020, NHGRI consistently accelerates scientific and medical breakthroughs by supporting cutting-edge research, developing new technologies, and studying the impact of genomic advances on society.

By embracing its role at *The Forefront of Genomics*, NHGRI has developed a rich history of pushing the field of genomics forward, resulting in breathtaking advances on a regular basis. In 2001, the first draft sequence of the human genome was published[1] and made available to the scientific community, with a more refined sequence completed two years later to end the HGP. Since then, NHGRI-funded technology advances have lowered the costs of DNA sequencing a million-fold, such that a human genome can now be sequenced for roughly $1,000 (down significantly from the $1 billion required during the HGP).[2] As these new genome-sequencing technologies became widely available, genomics spread throughout the biomedical research ecosystem, with NHGRI facilitating a greater investment in genomics by NIH. For example, in the early 2000s, NHGRI was responsible for funding over 90 percent of human genomics research funded by NIH; today, that figure is 10-15 percent because of the significant increase in funding of genomics by other NIH institutes and centers. This overall growth of NIH-supported genomics research has allowed NHGRI to focus on the most cutting-edge ideas and challenges, catalyzing new innovations and eliminating common barriers.

[1] International Human Genome Sequencing Consortium. *Nature*. 409: 860-921, 2001.
[2] www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost

One foundational responsibility that NHGRI continues to embrace is the ongoing generation, enhancement, and refinement of 'reference' information about the human genome sequence. Through the provision of a consensus coordinate system and associated data about genomic variation, such a resource is essential for all researchers who compare and analyze experimental or patient genome sequences. NHGRI recently reaffirmed its commitment to maintaining fundamental reference information about the human genome by launching the Human Genome Reference Program (HGRP). This new program will provide a more robust infrastructure for capturing and synthesizing data about genomic variation, which will be critical for the next phases of genomics research and genomic medicine implementation. In FY 2021, researchers in NHGRI's HGRP will focus on acquiring more ancestrally diverse, high-quality human genome sequences, advancing methods for assimilating and representing these diverse sequence data, and developing new bioinformatics tools for analyzing the available sequences.

In addition to creating computational tools to further genomics research, NHGRI enables and enhances the use of genomics to improve patient care. Two highly successful NHGRI efforts, the Electronic Medical Records and Genomics (eMERGE) and Clinical Sequencing Evidence-Generating Research (CSER) programs, seek to explore the real-world integration of genomic data with existing medical infrastructure and the effective implementation of genomics into various clinical settings. In their most recent iterations, these programs are enhancing clinicians' abilities to use genomic information as part of routine medical care and discovering the most effective ways to communicate such genomic information to patients and their families. In FY 2021, eMERGE and CSER will continue their efforts to facilitate the use of genomics in medicine.

NHGRI also recognizes the need to be good stewards of genomic data by balancing the tension between broadly sharing data across the research community and needing to protect research participants' interests (such as those related to privacy and autonomy). Since its inception, NHGRI has supported a robust research portfolio of studies that examine the ethical, legal, and social implications (ELSI) of genomic advances. For example, one of the NHGRI-funded Centers of Excellence in ELSI Research (CEER) studies the privacy risks associated with genomic information, the effectiveness of legal and policy efforts to reduce privacy risks, and the likelihood that lapses in protecting genomic information will allow people to be identified. In FY 2021, this center and other components of NHGRI's ELSI Research Program will broaden our understanding of complex issues such as genomic privacy and identity.

NHGRI recently designed and launched a new program, the Genomic Innovator Awards. The inaugural round of this program (see Program Portrait for additional details) funded six highly creative, early-stage investigators to pursue research in diverse areas of genomics. In FY 2021, NHGRI will continue to identify and support emerging junior investigators with paradigm-shifting ideas for pursuing genomics research.

Since 2011, NHGRI has been guided by a published strategic plan, entitled "Charting a Course for Genomic Medicine from Base Pairs to Bedside."[3] As the title implies, this plan has focused on using basic advances in genomics to understand human disease and implement genomic medicine. Now, as we enter a new decade, NHGRI is in the final stages of a two-year strategic planning process that has extensively engaged myriad scientific, clinical, and public communities to identify the most compelling research opportunities at *The Forefront of Genomics*. In FY 2021, the Institute will finalize this "Genomics2020" strategic plan, which will be published at the time of the 30th anniversary of the launch of the HGP.

Overall Budget Policy: The FY 2021 President's Budget request is $550.1 million, a decrease of $54.0 million compared with the FY 2020 Enacted level. These reductions are distributed across all programmatic areas and basic, epidemiology, or clinical research.

Program Descriptions and Accomplishments

Understanding the Structure of Genomes: A central aspect of understanding the structure of genomes is the ability to decipher DNA's "code" of As, Ts, Cs, and Gs quickly, accurately, and cost-effectively. Since 2004, NHGRI's Advanced Sequencing Technology Program has been funding research to improve these three metrics. It took an international collaboration involving hundreds of scientists 13 years to generate the first complete human genome sequence. Today, a human genome can be sequenced by one person in a day and, as highlighted in the Director's Overview, at a fraction of the cost. The ability to sequence DNA and decipher human genomes continually improves, catalyzed by NHGRI's ongoing Genome Technology Program (GTP). The GTP funds the development of both novel nucleic acid sequencing technologies and other related technologies needed for characterizing the functional complexities of the human genome. Together, awards from these programs support advancements that will improve the current state of nucleic acid sequencing with respect to data quality, throughput, and comprehensiveness, which in turn will push the field of genomics forward. For example, in 2019, GTP-funded research yielded an entirely new type of microscopy, DNA microscopy, that allows for the simultaneous visualization of the sequence and location of nucleic acids within a cell, which will be useful for studying diverse cells (e.g., immune cells). In FY 2021, the GTP will continue its remarkable track record of advancing capabilities in genome sequencing and analysis, enabling the continued growth of genomic applications in biomedicine.

Comparing genomes from different animal species is a useful approach for gaining clues about the functional components of the human genome and, in turn, the unique features of human biology. The advances in genome-sequencing technologies have allowed the genomes of an increasing variety of animal species to be sequenced and studied. NHGRI's Comparative Genomics Research Program (CGRP), co-funded by the United States Department of Agriculture, is supporting the development of methods and resources to increase the ability to use genomic information from multiple species to answer questions relevant to human health and

[3] Green, E.D., et. al. *Nature*. 470: 204-213, 2011.

disease. In FY 2021, CGRP will continue to expand and build the capacity to use comparative-genomic approaches for making discoveries about the structure and function of the human genome.

Budget Policy: The FY 2021 President's Budget request for Understanding the Structure of Genomes is $33.6 million, a decrease of $3.5 million or 9.4 percent from the FY 2020 Enacted level. With these funds, the GTP will continue to produce novel genomic sequencing and analysis technologies to increase the field's capabilities. The CGRP will provide insight into how the genome's sequence and structure affect its function in relation to human disease. NHGRI will also continue to fund the efforts of the HGRP to produce a "pan-genome" that is representative of greater human variation.

Understanding the Biology of Genomes: The completion of the HGP unlocked opportunities to more systematically detect and study the functional components of the human genome. To lead such an effort, NHGRI launched the Encyclopedia of DNA Elements (ENCODE) project in 2003. ENCODE's initial pilot phase focused its work on a targeted one percent of the human genome. Since the completion of that pilot phase, the ENCODE project has expanded its sights and completed whole-genome analyses of the human genome and three additional model organisms' genomes (the latter pursued by a sibling project, called modENCODE). Today, ENCODE provides an invaluable catalog containing information about many thousands of functional elements in the human genome, which is now routinely used by researchers from all areas of biomedical sciences. In fact, over 3,100 scientific publications have reported the use of ENCODE data in their studies.[4] In FY 2021, ENCODE will continue its pioneering efforts in characterizing the functional landscape of the human genome and disseminating the resulting information in a highly accessible fashion.

To enable access to state-of-the-art genome-sequencing technologies, NHGRI supports the Center for Inherited Disease Research (CIDR). Established by NHGRI in 1996 and currently funded by multiple NIH Institutes, CIDR represents a valuable resource for the genomics community. By allowing individual investigators to utilize genomic analyses that could not be carried out in their own laboratories, CIDR-supported efforts resulted in 16 publications in 2018.[5] In FY 2021, NHGRI will continue to enable individual investigators to use genomics in their research through CIDR.

Budget Policy: The FY 2021 President's Budget request for Understanding the Biology of Genomes is $84.9 million, a decrease of $8.6 million or 9.2 percent from the FY 2020 Enacted level. NHGRI will continue to fund programs that seek to understand the biology of genomes and their relation to human health. CIDR will continue to support investigators in pursuing their genomic research objectives.

[4] www.encodeproject.org/publications/
[5] phoenixweb.cidr.jhmi.edu/publications/sponsor

Using Genomics to Understand the Biology of Disease: Increased DNA-sequencing capabilities have led to the discovery of many sites across the human genome at which people tend to vary; in fact, over 100 million such variable sites have now been identified. However, the great majority of the known genomic variants do not have any consequence with respect to human traits or health; reliably identifying those that are consequential remains a major challenge in genomics. In FY 2018, NHGRI began supporting a Variant, Function, and Disease (VFD) Program. The VFD Program now funds investigators to develop transformative approaches for studying the effects of genomic variation on biological function and to establish which genomic variants lead to changes in disease risk or health outcomes. In FY 2021, the VFD Program will expand its efforts in supporting investigators that are making the important links between genomic variation and human disease.

NHGRI fosters interdisciplinary efforts to accelerate innovations in genomics through its Centers of Excellence in Genomic Sciences (CEGS) program. The CEGS program has increased the total number of funded centers. For example, one of the new CEGS is developing new technologies to improve the precision and effectiveness of disease diagnosis by establishing approaches to elucidate the regulation of a person's genome throughout the progression and treatment of disease. In FY 2021, the CEGS program will continue to support high-risk, high-reward research making genomic advances that will accelerate our ability to understand the genomic basis of disease.

NHGRI has always recognized the importance of broad, open sharing of data. This core value is, in part, based on the recognition that the widespread availability of data will help the field of genomics grow and disseminate into all areas of biomedical research. As such, the Institute has a long-standing history of supporting data resources – from the model organism databases to newer clinically oriented genomic repositories, such as the Clinical Genome Resource (ClinGen). The continued support of these vital resources serves to maximize the utilization of data that have already been generated and curated; equally important is expanding the capacity of such resources to support the rapid growth of genomic data generation. In FY 2021, NHGRI will support expanding the capacity of its funded genomic resources to meet the growing needs of the research community.

Budget Policy: The FY 2021 President's Budget request for Using Genomics to Understand the Biology of Disease is $133.3 million, a decrease of $13.3 million or 9.1 percent from the FY 2020 Enacted level. These funds will allow the VFD program to increase the ability to discern which genomic variants play a role in human health and CEGS to expand the understanding of the human genome. NHGRI will also use these funds to continue to support the maintenance and expanded capacity of critical genomic data- and knowledge-bases.

Using Genomics to Advance Medical Science: Following a highly successful first phase that yielded over 340 publications, the Clinical Sequencing Evidence-Generating Research (CSER) program began its second phase in 2017. CSER is focusing on the generation and analysis of evidence for the clinical utility of genome sequencing, as well as on identifying real-world

barriers to integrating genome sequencing into clinical care. CSER also strives to foster equity in the adoption and accessibility of genomics in clinical care by engaging healthcare stakeholders and recruiting at least 60 percent of participants from racial or ethnic minority populations, underserved populations, or populations who experience poorer medical outcomes. In FY 2021, CSER's work will come to fruition as the program enters the final year of its second phase.

Program Portrait: Clinical Genome (ClinGen) Resource

Implementing genomics in medicine will require that researchers and clinicians have access to accurate, clinically validated information about the relationship between genomic variants and human disease. NHGRI's Clinical Genome (ClinGen) Resource is working to develop standardized criteria for assessing whether potential variant-disease connections have sufficient evidence and sufficient health effects to be clinically important and medically actionable. Expert panels then use those criteria to curate the evidence about specific genes and genomic variants, classify them accordingly, and provide informative reports through the program's website (www.clinicalgenome.org). ClinGen also has a close partnership with the National Library of Medicine's ClinVar database, a freely available archive of genomic variants connected to health; expert panels include unpublished or uncurated genomic variants from ClinVar in their analyses, then submit curated information back into ClinVar for easy public access.

ClinGen's initial phase began in FY 2013 with nine principal investigators overseeing 30 researchers and staff members supported by three NHGRI grants. With additional funding from the National Institute of Child Health and Human Development for curation efforts, the program has since grown into a consortium of nearly 1,000 clinicians and researchers spread across the country. These professionals participate in 23 working groups to develop the program and curation processes and 46 expert panels to determine whether variants in specific genes contribute to diseases. Additional panels are being added regularly as researchers and working groups suggest new areas of focus.

The number of diseases that ClinGen can tackle depends on the availability of experts; therefore, a community curation program is working to create new experts. Interactive training modules teach trainees and other volunteers about the curation process, providing opportunities for them to apply the standards established by the working groups to assess the relevance of new genomic variants. As of the end of FY 2019, 248 people have volunteered – of those, 116 have completed the training and are ready to be assigned to expert panels.

In FY 2019, ClinGen's catalog of expert-curated variants became the first public database to be recognized by the Food and Drug Administration as a source of information about genomic variants that have a high likelihood of resulting in disease. The recognition includes a number of variants currently in the curation pipeline as well as future variants curated by ClinGen's expert panels. Importantly, FDA recognition will make it easier to develop and use clinical tests that detect curated variants. ClinGen's working groups will continue establishing standards for the curation of other types of genomic variants through at least FY 2020. NHGRI plans to maintain ClinGen's expert-curation process through FY 2021 and likely beyond because it provides a critical resource for accurate, clinically actionable information about genomic variants. ClinGen is a foundational resource for the genomics community and is now bringing to fruition the goal of taking NHGRI's research efforts from bench to bedside.

Budget Policy: The FY 2021 President's Budget request for Using Genomics to Advance Medical Science is $28.3 million, a decrease of $2.7 million or 8.6 percent from the FY 2020

Enacted level. In FY 2021, CSER and ClinGen will utilize these funds to continue to advance the field of medicine by supporting the successful integration of genomics into clinical decision making and care.

Using Genomics to Improve the Effectiveness of Healthcare: NHGRI's eMERGE Network is entering its fourth phase, during which it will study the impact of integrating one type of genomic risk assessments, called polygenic risk scores (PRSs), into clinical care. Methods for calculating PRSs are being developed to determine an individual's risk for common diseases (caused by many genomic variants); in general, much excitement is building about the possible use of PRSs as part of genomic medicine. However, a major barrier to the large-scale adoption of PRSs is the ability to seamlessly integrate genomic information into electronic medical records and into tools that provide clinical decision support. In FY 2021, the eMERGE Network will work to validate methods for deriving PRSs and develop a protocol for risk estimation and management for 15 conditions. Simultaneously, it will study the impact of integrating PRSs and risk-management recommendations into clinical workflows. This new phase of the eMERGE Network will also include enhanced diversity clinical sites, which will recruit at least 75 percent of participants from racial or ethnic minority populations, underserved populations, or populations who experience poorer medical outcomes. This latter component of the eMERGE Network will be valuable for assessing the applicability of PRSs to different populations since, to date, most studies have focused exclusively on individuals of European ancestry.

As an emerging discipline, genomic medicine is still in its infancy. As such, more information is needed about the utility and cost-effectiveness of genomic-based interventions compared to the current standards of care. Now in its second phase, NHGRI's Implementing Genomics in Practice (IGNITE) Program will generate clinical evidence through two network-wide pragmatic clinical trials. One trial will study the use of pharmacogenomics in treating post-surgical pain, chronic pain, and depression. The second trial will study the effects of returning genomic risk information to hypertensive patients of African ancestry and their primary care providers to better understand renal disease disparities across the United States. NHGRI has expanded the IGNITE Program, which will lead to the generation of more evidence and, as a result, a greater understanding of factors influencing the successful implementation of genomic medicine. In FY 2021, the IGNITE Program will generate clinical evidence and generalizable knowledge about implementing genomic medicine interventions to inform healthcare providers, patients, and policy makers.

Budget Policy: The FY 2021 President's Budget request for Using Genomics to Improve the Effectiveness of Healthcare is $17.3 million, a decrease of $1.7 million or 9.0 percent from the FY 2020 Enacted level. Using FY 2021 funds, eMERGE and IGNITE will continue to pioneer and study real-world applications of genomics in healthcare to improve patient outcomes.

Bioinformatics, Computational Biology, and Data Science: The field of genomics has progressed at a breathtaking pace since the end of the HGP. Genome-sequencing technologies have evolved considerably, with each new technical iteration requiring new computational methods to capture and refine the data. For example, nanopore-based DNA sequencing allows for the analysis of single molecules of DNA in a fashion that generates long stretches of sequence. However, the nuances of this method require the development of sophisticated

computational tools that can appropriately analyze the primary data. Helping this ongoing effort is NHGRI's intramural Genome Informatics Section (GIS), a group of researchers that are developing standard-setting computational methods for nanopore-based genome sequencing. In 2018, a study involving GIS members was published reporting the first human genome sequenced using the nanopore technology.[6] In FY 2021, the GIS will advance the computational capabilities for genome sequencing and contribute to the goal of routinely generating complete human genome sequences.

With genome sequencing becoming cheaper and faster, a new bottleneck emerges – the ability to process, store, access, analyze, and understand genomic data. One of the ways that NHGRI supports the development of innovative computational methods to keep pace with the generation of larger datasets is through investigator-initiated research grants supported by the Computational Genomics and Data Science (CGDS) Program. One such investigator-initiated project in FY 2019 supports the development of new computational models for improving CRISPR genome-editing methods to identify functional elements in the human genome. In FY 2021, the CGDA program will fund innovative projects to help overcome the computational and data-science bottleneck facing genomics research.

Program Portrait: Genomic Data Science Analysis, Visualization, and Informatics Lab-space (AnVIL) Resource

Progress in genomics research and genomic medicine requires that investigators share large datasets and complex analysis methods. The sharing of genomic data, in particular, can be logistically difficult given the ever-increasing size of the datasets and the need to respect the privacy and consent parameters of the research participants. To overcome these challenges, NHGRI created and supports the Genomic Data Science Analysis, Visualization, and Informatics Lab-space (AnVIL) Resource, which provides researchers with a modern, cloud-based environment for storing, sharing, accessing, and analyzing genomic data. In line with the NIH Strategic Plan for Data Science, AnVIL is working with other institutes and centers to make its platform interoperable with other cloud-based NIH data resources, so that researchers can access and combine datasets and implement analysis workflows from other data resources (e.g., the National Cancer Institute's Genomic Data Commons and the National Heart, Lung, and Blood Institute's DataSTAGE) through AnVIL.

NHGRI awarded two AnVIL grants in FY 2018 – one to build the data-sharing infrastructure and one to develop analysis tools and training packages. Working together, the two funded teams have made significant progress; for example, AnVIL was approved as an NIH-designated data repository consistent with the NIH Genomic Data Sharing policy and officially opened to the public in FY 2020. AnVIL already hosts a variety of controlled-access and publicly available datasets and is currently the only repository providing access to raw next-generation DNA-sequencing data from the latest release of the Genotype-Tissue Expression (GTEx) Project. Other datasets from existing NHGRI-funded clinical research programs [such as the Electronic Medical Records and Genomics (eMERGE) Network and the Clinical Sequencing Evidence-Generating Research (CSER) Consortium] will soon be made available on AnVIL. eMERGE and CSER will then be able to use AnVIL to study how genomic resources can be integrated into a healthcare environment to support clinical decision-making. Datasets from other NHGRI-funded programs will also be hosted on AnVIL, with the platform providing tools for users and

[6] Jain, M., et. al. *Nature Biotechnology*. 36: 338-345, 2018.

consortia to share and control access to their datasets. Two new systems being piloted on AnVIL will streamline researchers' ability to find and access relevant datasets while maintaining security.

In addition to a cloud-based infrastructure for data sharing, AnVIL aims to provide pipelines for analyzing genomic data tailored for both experienced and new users. Incorporating simple tools and training modules within a cloud-based infrastructure will make it possible for AnVIL to engage research communities that have not previously been well-represented in genomics, such as community college and high school students. In addition, widely used software packages, such as the NHGRI-supported bioinformatics tools Galaxy and Bioconductor, are being integrated into the AnVIL platform this year to allow more complex analyses to be performed by experienced users. AnVIL will also allow third parties to build novel applications and tools using its platform; guidelines are being developed to ensure that these applications and tools are in accordance with AnVIL's data-security standards.

Beyond providing access to high-value genomic datasets, analysis pipelines, and visualization tools in the cloud, AnVIL will enable collaborations among investigators by helping them securely share data and analysis methods. The future implementation of trans-NIH authentication and authorization protocols in conjunction with AnVIL's interoperable design will allow researchers to access the data they need in one location, regardless of the origin(s) of that data. As the program matures, AnVIL is poised to play an integral role in the emerging federated data ecosystem.

Budget Policy: The FY 2021 President's Budget request for Bioinformatics, Computational Biology, and Data Science is $140.6 million, a decrease of $14.5 million or 9.3 percent from the FY 2020 Enacted level. With FY 2021 funds, NHGRI will continue to push the boundaries of genomic sequencing and processing technologies through its intramural GIS and its extramural CGDS program. AnVIL will provide a cutting-edge resource for the storage, analysis, and sharing of such data.

Education and Training: Looking towards the future, NHGRI is cognizant of the need to engage and recruit trainees from diverse backgrounds to build a strong and effective genomics workforce. Two initiatives working towards this goal are the Initiative to Maximize Research Education in Genomics: Diversity Action Plan (DAP) and the Human Genetics Scholars Initiative. The DAP effort involves individuals at the undergraduate, post-baccalaureate, and graduate levels of their training; it has now expanded to 14 sites around the country and focuses both on research experiences in genomics and skills development to help prepare students for graduate school. The Human Genetics Scholars Initiative is a new public-private partnership with the American Society of Human Genetics, Color Genomics, and Biogen that involves late-stage graduate students, postdoctoral fellows, and early-career researchers. This two-year program accepted eight individuals in 2019 and aims to help launch their careers by providing dedicated mentoring, support for attending scientific conferences, and opportunities for professional development. In FY 2021, NHGRI will strive to enhance the diversity of the genomics workforce by supporting additional individuals from underserved populations through programs such as the DAP and the Human Genetics Scholars Initiative.

Program Portrait: Genomic Innovator Award

From the Human Genome Project to current programs like the Encyclopedia of DNA Elements (ENCODE) and the Clinical Genome (ClinGen) Resource, NHGRI has championed the use of team science in genomics research. One limitation of such large, collaborative undertakings is the shortage of opportunities they provide for early-career researchers to assume the traditional role of 'principal investigator' in projects. Such a limitation can jeopardize researchers' accrual of the individual accolades needed for career advancement through grant funding and academic promotion. To help reconcile the value of having talented young scientists participate in team-science genomics projects with the need for individual recognition, NHGRI established the Genomic Innovator Award in FY 2018. This award strives to reward early-career investigators who have made significant contributions to research consortia and other team-science efforts via the provision of funds to support the establishment of their independent research careers.

Like the NIH Director's New Innovator Award, the Genomic Innovator Award focuses on identifying early-career researchers with generalized potential for contributing to genomics research through innovative strategies, as opposed to funding specific projects. Awardees receive five years of funding with the option to either continue working on team-based projects or begin their own independent projects. Awardees are not tied to a single project; rather, they are provided the flexibility to follow new leads that arise from their work.

Due to the number of high-quality applications received upon launching the program, NHGRI was able to fund an initial set of six awards in late FY 2019. The awardees' research spans the genomics landscape – from basic science to clinical applications. One awardee, for example, is developing technologies to simplify the process of designing and breeding laboratory mice that have genomic modifications in specific tissue or under specific conditions. Another awardee is building computational methods to bridge the gap between molecular understandings of gene function and clinical observations that give hints about how genes influence health outcomes. A third awardee is working to improve how genomic information is integrated into the healthcare system, with the aim of improving communications between doctors and patients regarding genomic tests.

The Genomic Innovator Award will allow promising, inventive scientists to establish their own genomics research programs as independent investigators. Their experience in team-science projects will facilitate the dissemination of the methods and tools that they develop, benefiting the biomedical research enterprise more broadly. NHGRI will continue to solicit new applications for the Genomic Innovator Award in FY 2021.

Budget Policy: The FY 2021 President's Budget request for Education and Training is $24.8 million, a decrease of $2.4 million or 8.9 percent from the FY 2020 Enacted level. These funds will be used by NHGRI to continue to support diverse trainees in genomics at all stages of their careers.

Genomics and Society: Since its inception, NHGRI has recognized that understanding the implications of genomic advances for society is critical to maintaining a strong ethical foundation for the field. This commitment is exemplified by the Institute's well-respected Ethical, Legal, and Social Implications (ELSI) Research Program, which accounts for roughly

five percent of its research funding. NHGRI supports ELSI research projects within many of its large clinical research programs (such as eMERGE, CSER, and IGNITE), understanding that systematically studying the integration of genomics into clinical care is essential for the successful implementation of genomic medicine.

In 2018, NHGRI introduced a new ELSI Research Program initiative, the Center for ELSI Resources and Analysis (CERA). Similar to other NHGRI-supported genomic resources that assimilate and disseminate the results of genomics research, the CERA will serve to curate and make available ELSI research results, tools, and products to the broader scientific community. In FY 2021, the now-established multi-institutional CERA will enhance ELSI and bioethics research more broadly, well beyond the set of investigators funded directly by NHGRI.

Budget Policy: The FY 2021 President's Budget request for Genomics and Society is $53.7 million, a decrease of $5.5 million or 9.3 percent from the FY 2020 Enacted level. In FY 2021, NHGRI will continue to fund ELSI research that is critical for ethical and successful advances in genomics research.

Research Management and Support (RMS): NHGRI's Division of Policy, Communications, and Education uses RMS funds to support outreach, education, and stakeholder engagement through initiatives that align with the Institute's vision to improve the health of all humans through advances in genomics research. For example, the Inter-Society Coordinating Committee (ISCC) for Practitioner Education in Genomics aims to improve genomic literacy of healthcare providers and enhance the effective practice of genomics in clinical care. Since its formation in 2013, the ISCC membership has steadily increased, as have the number of project groups working towards their targeted goals. In FY 2021, NHGRI will convene and facilitate interactions among key stakeholders in genomics education through initiatives such as the ISCC.

In FY 2021, the traveling NHGRI-Smithsonian exhibition, *Genome: Unlocking Life's Code,*[7] will be wrapping-up its multi-year North American tour, which engages and informs the public about genomics. To expand the reach of this exhibition to additional audiences, NHGRI is partnering with the Smithsonian's National Museum of Natural History to create and distribute a do-it-yourself (DIY) version of the *Genome: Unlocking Life's Code* exhibition, which will consist of printable graphic panels containing core content that can be brought into the classroom or the home.

Budget Policy: The FY 2021 President's Budget request for Research Management and Support is $33.6 million, a decrease of $1.8 million or 5.0 percent from the FY 2020 Enacted level. These funds will be used to support a number of outreach, education, and stakeholder engagement initiatives in FY 2021.

[7] unlockinglifescode.org/

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Budget Authority by Object Class[1]

(Dollars in Thousands)

	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Total compensable workyears:			
Full-time equivalent	349	349	0
Full-time equivalent of overtime and holiday hours	0	0	0
Average ES salary	$198	$200	$2
Average GM/GS grade	12.6	12.6	0.0
Average GM/GS salary	$120	$122	$1
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$122	$126	$4
Average salary of ungraded positions	$161	$163	$2

OBJECT CLASSES		FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
	Personnel Compensation			
11.1	Full-Time Permanent	20,571	20,808	237
11.3	Other Than Full-Time Permanent	18,418	18,629	212
11.5	Other Personnel Compensation	842	852	10
11.7	Military Personnel	547	561	14
11.8	Special Personnel Services Payments	5,030	5,088	58
11.9	**Subtotal Personnel Compensation**	**$45,407**	**$45,938**	**$530**
12.1	Civilian Personnel Benefits	13,814	14,353	539
12.2	Military Personnel Benefits	394	404	10
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$59,615**	**$60,694**	**$1,080**
21.0	Travel & Transportation of Persons	2,232	1,981	-251
22.0	Transportation of Things	163	148	-15
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	0	0	0
23.3	Communications, Utilities & Misc. Charges	243	236	-7
24.0	Printing & Reproduction	31	28	-3
25.1	Consulting Services	291	265	-26
25.2	Other Services	27,610	23,191	-4,419
25.3	Purchase of goods and services from government accounts	74,294	69,791	-4,503
25.4	Operation & Maintenance of Facilities	217	197	-20
25.5	R&D Contracts	841	592	-249
25.6	Medical Care	731	665	-66
25.7	Operation & Maintenance of Equipment	2,789	2,038	-751
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$106,774**	**$96,741**	**-$10,034**
26.0	Supplies & Materials	6,158	4,104	-2,054
31.0	Equipment	2,056	1,341	-715
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	426,846	384,843	-42,003
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	1	1	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$544,503**	**$489,422**	**-$55,082**
	Total Budget Authority by Object Class	**$604,118**	**$550,116**	**-$54,002**

[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 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Personnel Compensation			
Full-Time Permanent (11.1)	$20,571	$20,808	$237
Other Than Full-Time Permanent (11.3)	18,418	18,629	212
Other Personnel Compensation (11.5)	842	852	10
Military Personnel (11.7)	547	561	14
Special Personnel Services Payments (11.8)	5,030	5,088	58
Subtotal Personnel Compensation (11.9)	**$45,407**	**$45,938**	**$530**
Civilian Personnel Benefits (12.1)	$13,814	$14,353	$539
Military Personnel Benefits (12.2)	394	404	10
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$59,615**	**$60,694**	**$1,080**
Travel & Transportation of Persons (21.0)	$2,232	$1,981	-$251
Transportation of Things (22.0)	163	148	-15
Rental Payments to Others (23.2)	0	0	0
Communications, Utilities & Misc. Charges (23.3)	243	236	-7
Printing & Reproduction (24.0)	31	28	-3
Other Contractual Services:			
Consultant Services (25.1)	291	265	-26
Other Services (25.2)	27,610	23,191	-4,419
Purchases from government accounts (25.3)	58,419	53,179	-5,240
Operation & Maintenance of Facilities (25.4)	217	197	-20
Operation & Maintenance of Equipment (25.7)	2,789	2,038	-751
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$89,326**	**$78,871**	**-$10,455**
Supplies & Materials (26.0)	$6,158	$4,104	-$2,054
Subtotal Non-Pay Costs	**$98,153**	**$85,368**	**-$12,785**
Total Administrative Costs	**$157,767**	**$146,062**	**-$11,706**

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2019 Final			FY 2020 Enacted			FY 2021 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Extramural Operations									
Direct:	13	-	13	14	-	14	14	-	14
Reimbursable:	1	-	1	1	-	1	1	-	1
Total:	14	-	14	15	-	15	15	-	15
Division of Genome Sciences									
Direct:	11	-	11	13	-	13	13	-	13
Reimbursable:	3	-	3	3	-	3	3	-	3
Total:	14	-	14	16	-	16	16	-	16
Division of Genomic Medicine									
Direct:	11	-	11	12	-	12	12	-	12
Reimbursable:	3	-	3	3	-	3	3	-	3
Total:	14	-	14	15	-	15	15	-	15
Division of Genomics and Society									
Direct:	3	-	3	4	-	4	4	-	4
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	3	-	3	4	-	4	4	-	4
Division of Intramural Research									
Direct:	190	5	195	206	5	211	206	5	211
Reimbursable:	26	2	28	27	2	29	27	2	29
Total:	216	7	223	233	7	240	233	7	240
Division of Management									
Direct:	39	-	39	43	-	43	43	-	43
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	39	-	39	43	-	43	43	-	43
Division of Policy, Communications and Education									
Direct:	9	-	9	11	-	11	11	-	11
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	9	-	9	11	-	11	11	-	11
Office of the Director									
Direct:	5	-	5	5	-	5	5	-	5
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	5	-	5	5	-	5	5	-	5
Total	314	7	321	342	7	349	342	7	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
2017	12.5
2018	12.6
2019	12.7
2020	12.6
2021	12.6

NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Detail of Positions[1]

GRADE	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	384,508	396,428	400,393
GM/GS-15	31	33	33
GM/GS-14	30	33	33
GM/GS-13	66	70	70
GS-12	37	43	43
GS-11	13	16	16
GS-10	1	1	1
GS-9	5	6	6
GS-8	11	11	11
GS-7	0	1	1
GS-6	0	0	0
GS-5	0	0	0
GS-4	0	0	0
GS-3	2	2	2
GS-2	0	0	0
GS-1	0	0	0
Subtotal	196	216	216
Grades established by Act of July 1, 1944 (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	3	3	3
Senior Grade	2	2	2
Full Grade	1	1	1
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	6	6	6
Ungraded	133	142	142
Total permanent positions	204	224	224
Total positions, end of year	337	366	366
Total full-time equivalent (FTE) employment, end of year	321	349	349
Average ES salary	192,254	198,214	200,196
Average GM/GS grade	12.7	12.6	12.6
Average GM/GS salary	117,088	120,347	121,550

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