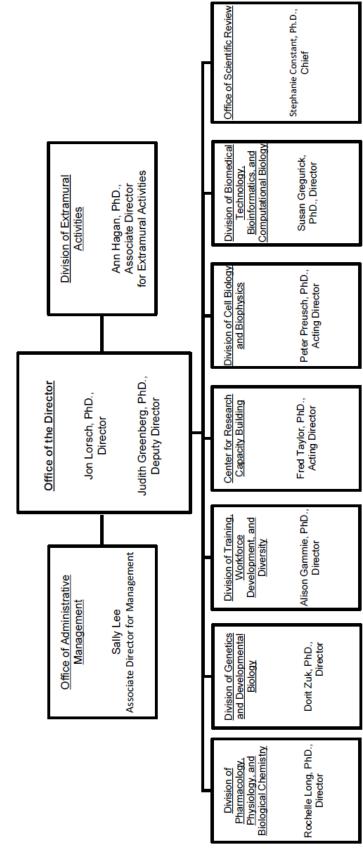
# DEPARTMENT OF HEALTH AND HUMAN SERVICES

# NATIONAL INSTITUTES OF HEALTH

# National Institute of General Medical Sciences (NIGMS)

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**Organization Structure** 

# NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

For carrying out section 301 and title IV of the PHS Act with respect to general medical sciences, \$2,185,509,000 of which \$780,000,000 shall be from funds available under section 241 of the PHS Act.

#### Amounts Available for Obligation<sup>1</sup>

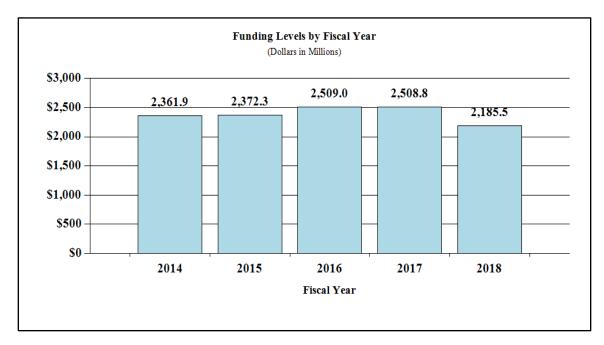
(Dollars in Thousands)

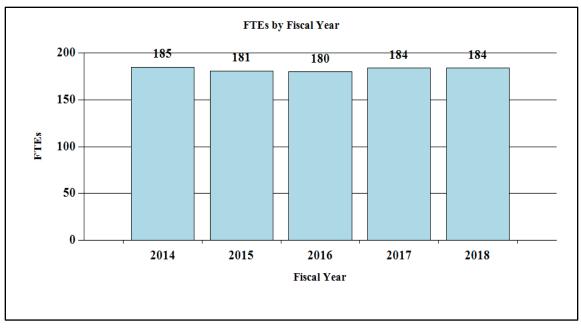
Course of Funding	FY 2016 Final	FY 2017 Annualized	FY 2018 President's
Source of Funding	F F 2016 Fillal	CR	Budget
Appropriation	\$2,512,073	\$2,512,073	\$2,185,509
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	(0)	(0)	(0)
Other Mandatory financing	(0)	(0)	(0)
Rescission	0	-3,293	0
Sequestration	0	0	0
Zika Intra-NIH Transfer	-3,477	0	0
Subtotal, adjusted appropriation	\$2,508,596	\$2,508,780	\$2,185,509
OAR HIV/AIDS Transfers	364	0	0
Subtotal, adjusted budget authority	\$2,508,960	\$2,508,780	\$2,185,509
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	\$2,508,960	\$2,508,780	\$2,185,509
Unobligated balance lapsing	-92	0	0
Total obligations	\$2,508,868	\$2,508,780	\$2,185,509

<sup>1</sup> Excludes the following amounts for reimbursable activities carried out by this account: FY 2016 - \$781,412 FY 2017 - \$781,412 FY 2018 - \$781,433

# Fiscal Year 2018 Budget Graphs







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	PHS Act/	U.S. Code	2017 Amount	FY 2017 Annualized CR	2018 Amount	2017 Amount FY 2017 Amualized CR 2018 Amount FY 2018 President's Budget
	Other Citation	Citation	Authorized		Authorized	
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
National Institute of General Medical				\$1,728,780,000		★ \$1,405,509,000
Sciences	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				\$1,728,780,000		\$1,405,509,000

# **Appropriations History**

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2008	\$1,941,462,000	\$1,966,019,000	\$1,978,601,000	\$1,970,228,000
Rescission				\$34,420,000
Supplemental				\$10,296,000
2009	\$1,937,690,000	\$2,004,295,000	\$1,991,609,000	\$1,997,801,000
Rescission				\$0
2010	\$2,023,677,000	\$2,069,156,000	\$2,031,886,000	\$2,051,798,000
Rescission				\$0
2011	\$2,125,090,000		\$2,121,783,000	\$2,051,798,000
Rescission				\$18,016,009
2012	\$2,102,300,000	\$2,102,300,000	\$2,347,309,000	\$2,434,637,000
Rescission				\$4,601,464
2013	\$2,378,835,000		\$2,387,112,000	\$2,430,035,536
Rescission				\$4,860,071
Sequestration				(\$121,971,075)
2014	\$2,401,011,000		\$2,435,570,000	\$2,364,147,000
Rescission				\$0
2015	\$2,368,877,000			\$2,371,476,000
Rescission				\$0
2016	\$2,433,780,000	\$2,439,437,000	\$2,511,431,000	\$2,512,073,000
Rescission				\$0
2017 <sup>1</sup>	\$2,512,437,000	\$2,538,851,000	\$2,633,755,000	\$2,512,073,000
Rescission				\$3,293,000
2018	\$2,185,509,000			

<sup>1</sup> Budget Estimate to Congress includes mandatory financing.

# Justification of Budget Request National Institute of General Medical Sciences

Authorizing Legislation: Section 301 and Title IV of the Public Health Service Act, as amended. Budget Authority (BA):

	FY 2016	FY 2017	FY 2018	FY 2018 + / -
	Actual	Annualized CR	PB	FY 2017
BA	\$ 2,508,960,173	\$2,508,780,000	\$2,185,509,000	-\$323,271,000
FTE	180	184	184	0

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

## **Director's Overview**

# Strategic Investments for Future Discovery

The National Institute of General Medical Sciences (NIGMS) supports fundamental research that expands knowledge about living systems -- which in turn underpins medical breakthroughs. As responsible stewards of taxpayer funds, NIGMS employs a data-driven process to maximize scientific return on investment and ensure fiscal accountability. To enhance its ability to make data-driven decisions, the Institute is in the process of launching a sophisticated analytics "dashboard" system enabling NIGMS leadership and staff to view, in real time, various metrics on investments, and their outcomes. This system will enable NIGMS to improve iteratively the efficiency and impact of its programs, helping to get taxpayers more high-quality biomedical research for their money. One example of this approach is a current effort to harmonize the various programs used to support "team science." Although most NIGMS funding goes to individual researchers at universities and other research institutions across the country, in some cases complex modern biomedical problems require problem-solving teams. Using data-driven evaluations of the Institute's current approaches to supporting such teams, combined with input from stakeholders, NIGMS is developing a single, coherent team-science funding mechanism. This new method of supporting scientific teams will be tested to determine if it increases their efficiency and productivity.

# Maximizing the Value of Research Support Across States

Some key concepts of commerce and industry are also relevant to scientific research, including economies of scale and consolidation of processes and products. Research institutions in states that have historically received low levels of NIH funding have proven to be crucibles for innovation in conducting research more efficiently. The lessons learned from these states can be shared across the country to create a more efficient national biomedical research enterprise. This past year, NIGMS funded a program to allow grantees in Institutional Development Award (IDeA) states an opportunity to optimize operations with state-of-the-art technology resources. Through this program, the Institute hopes to increase access to cutting-edge technology facilities -- which is essential for advances in biomedical research but is often a limiting factor for scientists, especially those in IDeA states – and to develop more efficient models that can be used nationally. An example of efficiencies and economies of scale being enabled by this

program is a new collaboration between Arkansas and Oklahoma to create a single, regional high-tech facility for measuring the identities and levels of proteins involved in a variety of disease processes in complex samples such as blood. This IDeA program will train researchers across the region to use these powerful new "proteomics" technologies and will give more scientists access to them than was possible when each state was working on its own.

## From Exploration to Application: Enabling the Development of New Technologies

As noted above, biomedical research is often advanced by the development of new technologies. New imaging technologies such as cryo-electron microscopy, are having a huge impact today (see Program Portrait, p. 11). NIGMS deems it essential to support actively the creation of new tools to address previously unanswerable questions. This past year, the Institute conducted an analysis of its technology development investment portfolio and determined that more funding for early-stage technology development – including high-risk, high-reward ideas – is needed. To address this need, the Institute created a three-stage pipeline for supporting technology development. The first stage funds high-risk proof-of-concept grants for innovative new ideas, such as new micro-devices to measure subtle changes in DNA structure inside a living cell. The second stage aims to take a prototype technology – such as a nuclear magnetic resonance (NMR) machine -- and make it more usable by the scientific community to answer important biomedical questions. Finally, in the third stage, cutting-edge new technologies will be refined and turned into national resources for large communities of scientists. For example, scientists attempting to determine the three-dimensional structures of biological molecules often use beamlines that carry X-ray radiation created as a byproduct of physics research at synchrotron facilities in the National Labs. These types of technologies are too expensive and require too much space for individual institutions to obtain and maintain; thus, a national strategy is required to connect these key technological resources with the researchers that use them.

# **Supporting and Protecting Creative Minds**

The intensified competition for grant funding in recent years has taxed scientists' productivity, as they spend increasing time writing applications rather than making discoveries. NIGMS is testing a new approach to research funding to alleviate these pressures. The Maximizing Investigators' Research Award (MIRA) program funds NIGMS-relevant research in an investigator's laboratory via a single, five-year grant. It aims to provide more stability and flexibility for investigators, allowing them to be more ambitious and creative in their work and to follow new ideas and opportunities as they arise. By reducing the number of applications they have to write and the administrative burden associated with running multiple grants, it also aims to open up more time for doing science. With positive results from the first MIRA pilot for experienced researchers, the Institute extended MIRA eligibility to early-stage investigators: junior scientists just starting their labs. One unexpected – and promising – outcome of this pilot was a decrease in the age at which these early-stage investigators recieved their first grant. Early-stage MIRA awardees were two years younger, on average, than traditional research project ("R01") grantees. Ensuring new scientists get to work as early as possible in their independent careers – when they are often at their most creative and energetic -- is a win-win strategy for researchers and for the public.

### Sustaining a Diverse Workforce for the Future

As stated in the new NIH Strategic Plan, diversity in the biomedical research workforce is critical for producing scientific discoveries. NIGMS has a strong track record of supporting the training of individuals from diverse backgrounds through programs targeting all stages of the career-development pathway. The Institute has identified a pressing need to focus on career inflection points, notably the transition from trainee to scientific independence. The Institutional Research and Academic Career Development Award (IRACDA) program addresses this need by combining a traditional postdoctoral research experience with an opportunity to develop academic skills, including teaching, through workshops and mentored teaching assignments at a partner (typically underserved) undergraduate institution. A recent evaluation demonstrated that this program is achieving its goals. IRACDA has sponsored about 400 scholars who have completed training since the program's 1999 inception. A majority of these alumni (70 percent) now hold faculty positions at a range of educational institutions. One interesting finding from this analysis is that IRACDA scholars are considerably more diverse than both a comparable pool of NIH-funded postdoctoral fellows and the overall NIH-funded research workforce.

<u>Overall Budget Policy</u>: The FY 2018 President's Budget request is \$2.1 billion, a decrease of \$323 million compared with the FY 2017 Annualized CR level. These reductions are distributed across all programmatic areas and basic, epidemiology or clinical research.

#### **Program Descriptions and Accomplishments**

**Cell Biology and Biophysics (CBB):** The CBB program fosters the study of cells and their components through physics- and chemistry-based technological approaches. Critical basic research supported by the program promotes the development of precise, targeted therapies as well as diagnostics for a range of diseases. In FY 2017, CBB continued support of the Regional Consortia for High-Resolution Cryoelectron Microscopy (cryo-EM see program portrait, below) and plans are underway to re-announce this initiative in FY 2018. This program will provide access to state-of-the-art cryo-EM technology to a broad range of investigators. In addition, CBB has invested in supplements to foster collaborations in cryo-EM to give more investigators expertise in this important technology. CBB also continues to support research that makes use of advanced techniques in cell biology, biophysics, cellular imaging, and structural biology to provide fundamental insights into biological processes.

#### Viewing Health with Extreme Precision

In addition to the creativity of the human mind, cutting-edge technologies are essential for advances in biomedical research. However, technology resources are often not accessible to researchers because of limited supply, location, or high cost. NIGMS is using a range of approaches to improve the nation's research infrastructure, providing investigators better access to shared research resources and technologies. For the past half-century, scientists in the field of structural biology have determined the three-dimensional structures of biological molecules, revealing important information about how those molecules work normally, misfire in disease states, and how their functions can be altered by drugs. For some time, X-ray crystallography has been the method of choice to allow researchers to see the three-dimensional shapes of proteins and other biological molecules. Because of recent technology advances, a new method, cryo-electron microscopy, or cryoEM, is now beginning to overtake X-ray crystallography as a potentially more powerful way to image the structures of these cellular molecules, including those that cannot be visualized using X-ray crystallography. Thus, cryo-EM has the potential to open up significant new horizons for biomedical research. By bombarding a flash-frozen specimen with electrons, cryo-electron microscopy allows scientists to obtain a "freeze-frame" image of protein molecules. The images are combined using a computer and the result is a super-crisp, high-resolution picture of the protein. Cryo-EM can be used to learn how molecules fit together to make the biological machines that run our bodies or to understand how dangerous bacteria and viruses infect us. Because of its very high cost, state-of-the-art cryo-EM equipment is out of reach for most of the country's researchers, and yet demand for access to this technology has far-outstripped supply. The United States is in danger of falling behind Europe and Asia in providing access to cryo-EM technology for our researchers. In response, NIGMS created a program to support the purchase and maintenance of cryo-EM technology used by groups of scientists in regional consortia, thus producing significant economies of scale and expanding the number of scientists with access to these powerful machines. This investment is paying off with exciting new discoveries underpinning health and disease. Examples of important health-related molecules captured by this freeze-frame method include brain receptors implicated in Alzheimer's disease and protein "studs" on the surface of HIV, the discovery of which was a key step in developing a new anti-HIV antibody. Less deadly, but scientifically important, is a recently obtained freeze-frame image of the "Wasabi receptor." This protein creates the satisfying burn in our mouths from the familiar sushi condiment, and its link to pain sensation could help researchers figure out how to block pain in novel, non-addictive ways. In FY 2016, NIGMS also co-led, with the National Eye Institute, the development of an NIH Director's Common Fund initiative to support the establishment of shared, national cryo-EM facilities that will give broader access to this technology to researchers throughout the country.

**Genetics and Developmental Biology (GDB):** The GDB program promotes studies directed toward understanding the cellular and molecular mechanisms that underlie inheritance, gene expression, and development. This fundamental research provides a strong foundation for more disease-targeted projects that are supported by other NIH Institutes and Centers. To complement GDB's large investment in research that is performed in a wide variety of research organisms, GDB will also employ FY 2018 funds to bolster human research studies aimed at revealing the underpinnings of genetic components of human biology and human disease. Finally, GDB continues to support research that elucidates fundamental insights about the basic biology of stem cells and research on the interactions and dynamics of microbial communities associated with the human body or with other organisms.

**Pharmacology, Physiology, and Biological Chemistry (PPBC):** The PPBC program supports fundamental research in chemistry, biochemistry, pharmacology, and physiology that contributes to understanding human biology in health and disease and generates knowledge for new ways to diagnose and treat disease. In addition, PPBC funds research that explores clinical issues involving whole-body responses, including traumatic injury, burns, wound healing, sepsis, anesthesia, and clinical pharmacology. In FY 2018, PPBC will implement new NIH policies for clinical trials oversight to ensure that supported studies will be safe for patients and effective toward making new research discoveries. Additionally, projects at the interface of chemistry and

biology are expected to yield new understanding of life processes; for example, how metals activate enzymes that control cellular physiological responses.

#### Program Portrait: Demystifying General Anesthesia

More than 20 million Americans undergo general anesthesia every year.<sup>1</sup> The procedure is necessary for surgeons to do their work and keep a patient still and free of pain caused by incisions and other invasive procedures. Doctors use different drugs to "put a person under," a colloquial term for anesthesia, depending on the length of time needed for a given procedure and other factors. General anesthetics have been called a "modern medical mystery" because, even though they are safely administered to millions of Americans, we still don't know exactly how the drugs work. Sustained NIGMS support in this area has led to meaningful progress toward solving the mystery. Research supported by the Institute has revealed that anesthetics affect many different molecules and communication pathways in the body and in the brain. These studies have caused a major shift in the field over the past several years focusing researchers to look more broadly at many simultaneous effects throughout the body. One new finding has emerged from studies on the research organism C. elegans (a roundworm). Scientists can systematically tease apart various anesthetic effects in this organism because its entire genome has been decoded and a great deal is known about the functions of its proteins. By shutting down certain genes one-by-one, and in various combinations, these researchers could narrow down which genes contribute to anesthetic responses. The work revealed an unexpected target: mitochondria, the power plants of our cells. Follow-up work in humans confirmed that children who are overly sensitive to anesthetics have decreased mitochondrial function. Other research using a system-wide approach employed custom-designed molecules that resemble the size and shape of anesthetic drugs as "bait," enabling them to fish for the proteins inside of cells that anesthetics attach to. That work revealed new targets through which anesthetic drugs likely do their work in the brain, heart, and spinal cord and has led to the discovery of the first new class of experimental anesthetics since the 1970s. Still other research is recording brain activity using electroencephalograms, to understand better consciousness and how anesthetics affect it. Researchers have discovered that anesthetic-induced brain waves are highly organized and larger than the brain's natural waves. This research has also shed light on how a person's age affects the dose of anesthetics needed for loss of consciousness because the size of anesthetic-induced brain waves is smaller in older adults than in younger ones. These researchers are now working to understand the exact mechanisms through which anesthetics affect brain waves, which should lead to insights into how these drugs alter consciousness and other body functions. NIGMS support of anesthesia is part of the Institute's focus on clinical issues involving whole-body responses. Knowing more about how anesthetics work is critical to coming up with new versions with fewer side effects (for example, cardiac and respiratory suppression), faster recovery times, and for tailoring medications to specific surgical procedures and patient profiles.

Division of Biomedical Technology, Bioinformatics, and Computational Biology (BBCB):

The BBCB program promotes the development, use, and dissemination of novel computational methods, sophisticated mathematical and statistical approaches, and unique biomedical technologies that advance biomedical research. Examples include mechanistic and informatics studies of cellular processes, computational analyses of the relationships between therapeutic drugs and humans, and quantitative modeling of the spread of infectious diseases. A major effort in BBCB is the Biomedical Technology Research Resources initiative that creates pioneering technologies and applies them to a broad range of basic, translational, and clinical research areas. These resources are used by thousands of NIH-supported scientists each year.

**Division of Training, Workforce Development, and Diversity (TWD):** The TWD program is responsible for supporting the training of an outstanding and diverse biomedical research workforce for the future. TWD supports training of Ph.D. and M.D.-Ph.D. students, as well as postdoctoral fellows in basic, translational, and clinical research. TWD also supports student-

<sup>&</sup>lt;sup>1</sup> Sebel PS, Bowdle TA, Ghoneim MM, Rampil IJ, et al. The Incidence of Awareness During Anesthesia: A Multicenter United States Study. *Anesthesia & Analgesia* 2004:99(3):833-39.

development programs focused on enhancing diversity in undergraduate STEM training leading to research careers. TWD will continue its support for specialized programs in the biomedical sciences that recruit and train students from diverse backgrounds.

**Center for Research Capacity Building (CRCB):** CRCB supports research, research training, faculty development, and research infrastructure improvement in states and institutions that have been historically underrepresented in NIH funding. CRCB administers three major programs. The Institutional Development Award (IDeA) program broadens the geographic distribution of NIH funding for biomedical research in 23 states and Puerto Rico through four initiatives: development of thematic, multidisciplinary centers (COBRE); establishment of statewide networks for expanding research access and capabilities (INBRE); advancement of clinical and translational research that addresses regional health concerns (IDeA-CTR); and increasing the pool of NIH funded investigators (co-funding). The Support of Competitive Research (SCORE) program seeks to increase the research competitiveness of faculty at institutions that have an explicitly stated historical mission focused on serving students from underrepresented groups. The Native American Research Centers for Health (NARCH) program supports partnerships between American Indian/Alaska Native tribes or tribally-based organizations and institutions that conduct intensive biomedical research.

**Intramural**: NIGMS has a small but unique intramural research training program, the NIGMS Postdoctoral Research Associate (PRAT) Program. PRAT postdoctoral research fellows (currently 21) are supported for up to three years. They pursue independent research in intramural NIH laboratories under the guidance of tenured/tenure-track investigators, and they receive specialized training and career mentoring from NIGMS staff. Fellows in this highly-regarded program have received numerous honors and awards for their innovative research in areas ranging from cell and molecular biology to pharmacology and genetics.

**Research Management and Support (RMS)**: RMS provides administrative, budgetary, logistical, and scientific support toward the review, award, and monitoring of research grants, training awards, and research and development contracts. The program also encompasses strategic planning, coordination, and evaluation of NIGMS programs; regulatory compliance; and coordination and liaison with other Federal agencies, Congress, and the public. RMS funds improvements in information technology tools to facilitate the paylist process where grant applications are discussed and prioritized for possible funding. In FY 2018, NIGMS will use RMS funds to migrate NIGMS systems and services to the "cloud." Such activities will result in significant cost savings, enhance information technology Acquisition Reform Act (FITARA). RMS funds will also be used to update critical infrastructure platform components and support technologies. Extending beyond technological improvements, NIGMS plans to enhance its public outreach and transparency through a redesigned website and public web blogs.

#### Detail of Full-Time Equivalent Employment (FTE)

	I	Y 2016 Fin:	al	FY 20	17 Annualiz	ed CR	FY 2018	President's	Budget
OFFICE/DIVISION	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Research Capacity Building Total:	9	-	9	10	-	10	10	-	10
Division of Biomedical Technology, Bioinformatics and Computational Biology Total:	11	-	11	11	-	11	11	-	11
Division of Cell Biology and Biophysics Total:	14	-	14	14	-	14	14	-	14
Division of Genetic and Developmental Biology Total:	12	-	12	12	-	12	12	-	12
Division of Pharmacology, Physiology and Biological Chemistry Total:	13	-	13	13	-	13	13	-	13
Division of Training, Workforce Development and Diversity Total:	10	-	10	12	-	12	12	-	12
Office of Administrative Management Total:	25	-	25	25	-	25	25	-	25
Office of Extramural Activities Total:	52	-	52	52	-	52	52	-	52
Office of Scientific Review Total:	15	-	15	15	-	15	15	-	15
Office of the Director Total: Direct: Reimbursable:	19 19 -	-	19 19 -	20 20 -	-	20 20 -	20 20 -	-	20 20
Office of Scientific Review Direct: Reimbursable:	15	-	15	15	-	15	15	-	15
Office of Administrative Management Direct: Reimbursable:	25	-	25	25	-	25	25	-	25
Office of Extramural Activities Direct: Reimbursable:	52	-	52	52	-	52	52	-	52
Division of Genetic and Developmental Biology Direct: Reimbursable:	12	-	12	12	-	12	12	-	12
Division of Pharmacology, Physiology and Biological Chemistry Direct: Reimbursable:	13	-	13	13	-	13	13	-	13
Division of Training, Workforce Development and Diversity Reimbursable:	-	-	-	-	-	-	-	-	-
Division of Biomedical Technology, Bioinformatics and Computational Biology Reimbursable:	-	-	-	-	-	-	-	-	-
Division of Cell Biology and Biophysics Direct: Reimbursable:	14 -	-	14	14	-	14	14	-	14
Division of Biomedical Technology, Bioinformatics and Computational Biology Direct:	11	-	11	11	-	11	11	-	11
Division of Training, Workforce Development and Diversity Direct:	10	-	10	12	-	12	12	-	12
Center for Research Capacity Building Direct: Reimbursable:	9	-	9	10	-	10	10	-	10
Total Includes FTEs whose payroll obligations are supported by the	180 NIH Comm		180	184	-	184	184	-	184
FIEs supported by funds from Cooperative Research and Development Agreements. FISCAL YEAR	0		0		0 rage GS Gi	0 rade	0	0	0
2014 2015 2016 2017				Ave	12.5 12.7 12.7 12.7 12.7	ute			
2018			10 14		12.7				

#### **Detail of Positions**<sup>1</sup>

GRADE	FY 2016 Final	FY 2017 Annualized CR	FY 2018 President's Budget
Total, ES Positions	0	1	1
Total, ES Salary	0	171,614	174,960
GM/GS-15	19	18	18
GM/GS-14	62	63	63
GM/GS-13	49	51	51
GS-12	8	9	9
GS-11	5	5	5
GS-10	0	0	0
GS-9	2	2	2
GS-8	5	5	5
GS-7	14	14	14
GS-6	1	1	1
GS-5	0	0	0
GS-4	1	1	1
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	166	169	169
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	0	0	0
Senior Grade	0	0	0
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	0	0	0
Ungraded	24	24	24
Total permanent positions	166	170	170
Total positions, end of year	190	194	195
Total full-time equivalent (FTE) employment, end of year	180	184	184
Average ES salary	0	171,614	174,960
Average GM/GS grade	12.7	12.7	12.7
Average GM/GS salary	114,289	116,517	118,790

<sup>1</sup> Includes FTEs whose payroll obligations are supported by the NIH Common Fund.