DEPARTMENT OF HEALTH AND HUMAN SERVICES

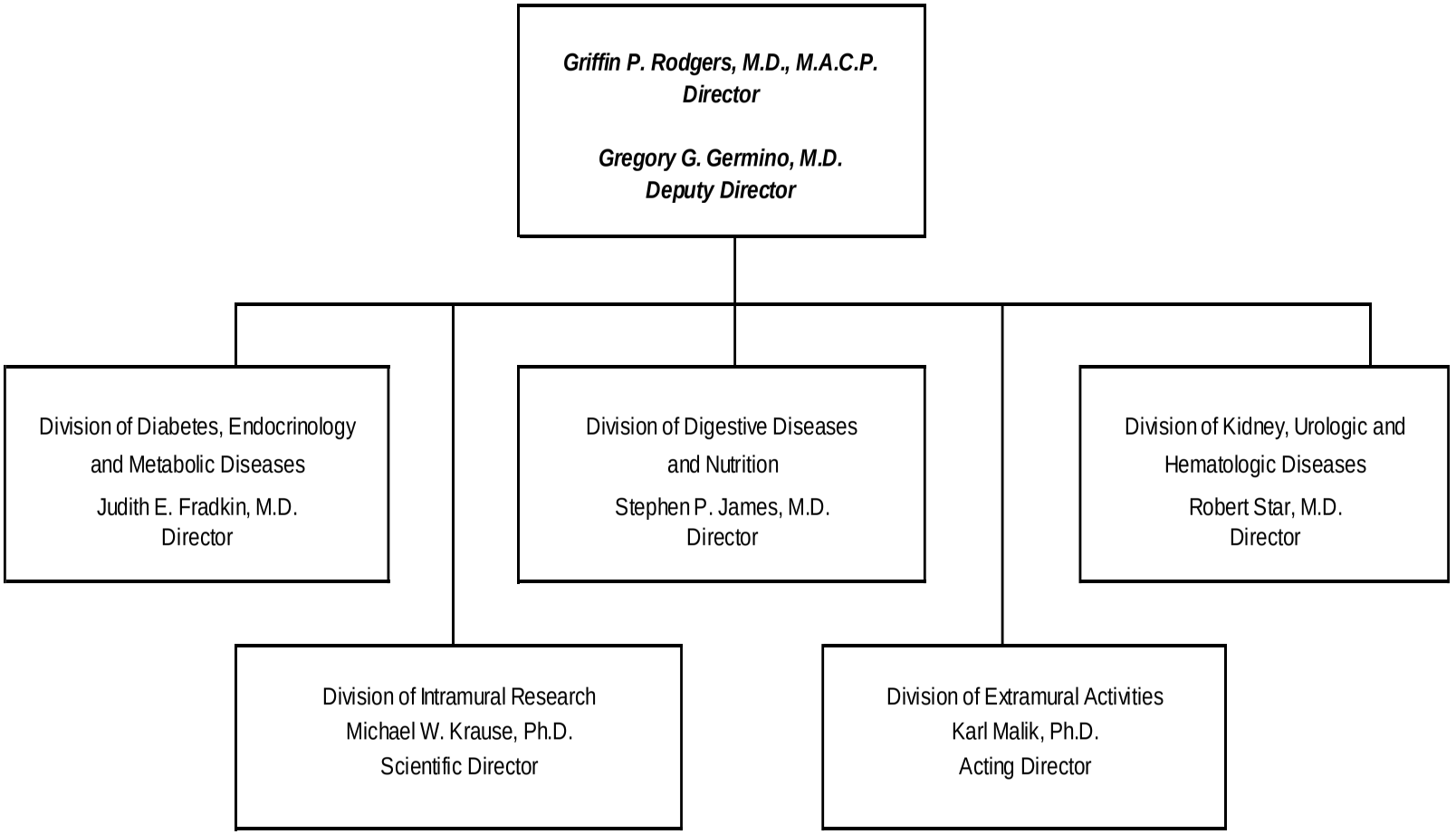
NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and Digestive and Kidney Diseases

Organization Structure



NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and Digestive and Kidney Diseases

For carrying out section 301, section 330B, and title IV of the PHS Act with respect to diabetes and digestive and kidney disease, 1,965,434,000, of which $150,000,000, to remain available until expended, shall be for making grants under such section 330B.

NATIONAL INSTITUTES OF HEALTH
National Institute of Diabetes and Digestive and Kidney Diseases

Amounts Available for Obligation[1]

(Dollars in Thousands)

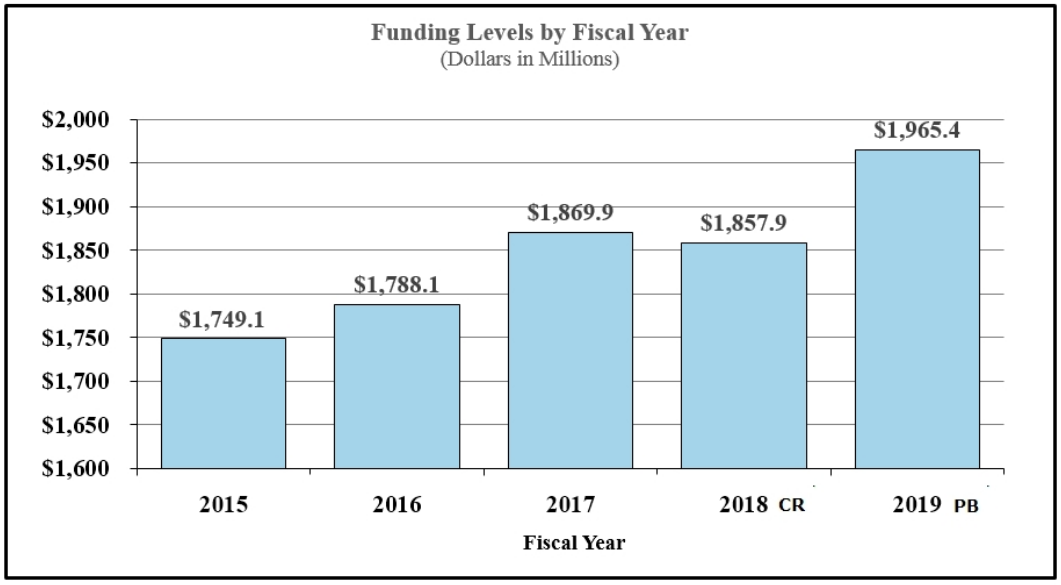
Source of Funding	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget[2]
Appropriation	$1,870,595	$1,870,595	$1,965,434
Mandatory Appropriation:			
Type 1 Diabetes	$139,650	$150,000	$0
Rescission	0	-12,703	0
Secretary's Transfer	-4,174		
Subtotal, adjusted appropriation	$2,006,071	$2,007,892	$1,965,434
OAR HIV/AIDS Transfers	3,433	0	0
Subtotal, adjusted budget authority	$2,009,504	$2,007,892	$1,965,434
Subtotal, adjusted budget authority	$2,009,504	$2,007,892	$1,965,434
Unobligated balance lapsing	-56	0	0
Total obligations	$2,009,448	$2,007,892	$1,965,434

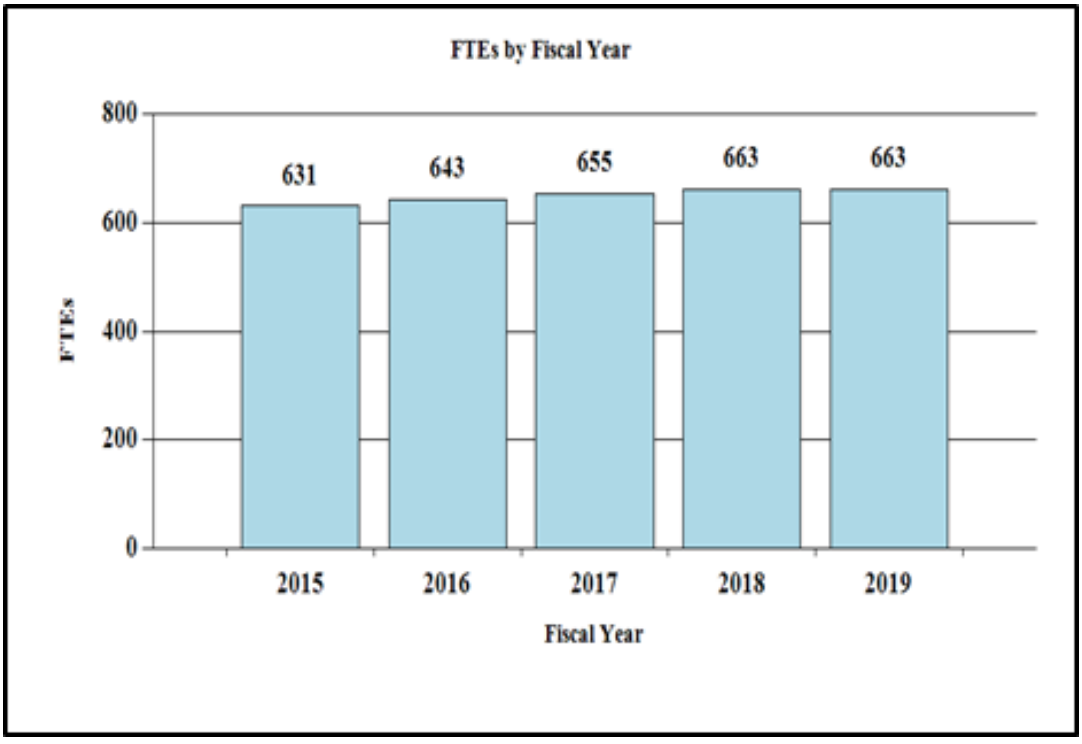
[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2017 - $3,762 FY 2018 - $6,000 FY 2019 - $6,000

[2] Includes $150M of discretionary funding for T1D.

Fiscal Year 2019 Budget Graphs

History of Budget Authority and FTEs:





NATIONAL INSTITUTES OF HEALTH
National Institute of Diabetes and Digestive and Kidney Diseases

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	$2,007,891,789	Indefinite	$1,965,434,000
National Institute of Diabetes and Digestive and Kidney Diseases	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$2,007,891,789		$1,965,434,000

NATIONAL INSTITUTES OF HEALTH
National Institute of Diabetes and Digestive and Kidney Diseases

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2009	$1,858,487,000	$1,767,071,000	$1,755,881,000	$1,911,338,000
Supplemental				$9,077,000
2010	$1,931,494,000	$1,974,251,000	$1,940,518,000	$1,958,100,000
2011	$2,007,589,000		$2,004,674,000	$1,958,100,000
Rescission				($15,876,196)
2012	$1,987,957,000	$1,987,957,000	$1,922,045,000	$1,950,447,000
Rescission				($3,402,845)
2013	$1,942,107,000		$1,947,539,000	$1,797,044,155
Rescission				($3,594,088)
Sequestration				($97,849,260)
2014	$1,961,786,000		$1,949,745,000	$1,894,274,000
Sequestration				($10,800,000)
2015	$1,893,336,000			$1,899,681,000
2016	$1,938,133,000	$1,921,388,000	$1,975,162,000	$1,968,357,000
2017[1]	$1,966,310,000	$1,962,093,000	$2,041,652,000	$2,020,595,000
Sequestration				($10,350,000)
2018	$1,599,534,000	$1,899,733,000	$1,935,597,000	$2,020,595,000
Rescission				($12,703,211)
2019	$1,965,434,000			

[1] Budget Estimate to Congress includes mandatory financing.

Justification of Budget Request

National Institute of Diabetes and Digestive and Kidney Diseases

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

Budget Authority (BA):

	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
BA*	$2,010,245,000	$2,007,892,000	$1,965,434,000	-$42,458,000
Type 1 Diabetes Mandatory	-$139,650,000	-$150,000,000	$0	-$150,000,000
Labor/HHS:	$1,870,595,000	$1,857,892,000	$1,965,434,000	-$42,458,000
FTEs	655	663	663	0

*CR amount rounded; includes T1D discretionary funding in FY 2019.

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

Director's Overview

The mission of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is to support and conduct research to combat diabetes and other endocrine and metabolic diseases, liver and other digestive diseases, nutritional disorders, obesity, and kidney, urologic, and hematologic diseases. These diseases are chronic, common, costly, and consequential for patients, their families, and the Nation. Diabetes afflicts an estimated 30.3 million people in the United States, greatly increasing the risk for many serious complications, such as heart disease and kidney failure.[1] Estimates of chronic kidney disease (CKD) show that more than 23 million Americans are affected, and over 590,000 have irreversible kidney failure.[2] Many urologic diseases, such as urinary incontinence, urinary tract infections, and benign prostatic hyperplasia, are also highly prevalent.[3] Digestive diseases account for an estimated 72 million ambulatory care visits to doctor's offices, outpatient hospital clinics, and emergency departments, as well as 13.5 million hospitalizations with a primary or secondary diagnosis.[4] Obesity affects nearly 40 percent of U.S. adults and over 18 percent of children and adolescents.[5] It is a strong risk factor

[1] Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2017.
[2] Levey AS, et al. Ann Intern Med 150: 604-612, 2009.; U.S. Renal Data System, USRDS 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2011.
[3] Urological Diseases in America. NIDDK/NIH Publication Number 12-7865, 2012.
[4] Everhart JE, et al. Gastroenterology 136: 376-386, 2009.
[5] Hales CM et al. 2017. CDC. National Center for Health Statistics Data Brief No. 288.

for type 2 diabetes, nonalcoholic steatohepatitis (NASH), and many other diseases. Cystic fibrosis and other genetic diseases within NIDDK's purview are less widespread, but still devastating in their impact. Building on emerging opportunities from past research investments, NIDDK will continue to pursue discovery, clinical, and translational research; research training and career development; efforts to support rigor and reproducibility in research; and health information dissemination, with continued focus on preserving a robust investigator-initiated research portfolio.

Theme 1: Tackling Complex Challenges by Leveraging Partnerships

In FY 2019, NIDDK will continue to make strides in addressing complex health problems through creating and leveraging partnerships within and beyond NIH. In addition to the feared health complications of vision loss, kidney failure, and amputation, diabetes increases the risk of other debilitating diseases. For example, diabetes doubles risk for heart disease, many forms of cancer, some forms of dementia, hearing loss, erectile dysfunction, urinary incontinence, and many other common diseases.[6] The Diabetes Prevention Program Outcomes Study (DPPOS) Phase 3, developed in partnership with the National Cancer Institute (NCI), the National Heart, Lung, and Blood Institute (NHLBI), and the National Institute on Aging (NIA), with additional support from the NIH Office of Research on Women's Health (ORWH), will study outcomes that are of increasing public health concern in the aging population with pre-diabetes and diabetes, including the potential benefits of metformin on development of cardiovascular disease and cancer.

The public-private Accelerating Medicines Partnership-Type 2 Diabetes (AMP-T2D) project, spearheaded by NIDDK, will continue augmenting content and access to genetic and clinical data on diabetes and related traits available through its Knowledge Portal. A 2017 assessment of the Knowledge Portal found that progress exceeded expectations, leading to approval of continued industry funding. There is also general agreement among partners on the value of sustaining the Knowledge Portal, and further discussions of directions and sustainability are planned.

NIDDK, NIA, the Department of Veterans Affairs (VA), and other organizations contributed to a successful Agency for Healthcare Research and Quality (AHRQ)-led effort to prevent catheter-associated urinary tract infection in people residing in nursing homes—a common, costly, and high risk problem in this population.[7] The NIDDK- and NCI-funded multi-center consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer will pursue clinical research on pancreatic diseases—including chronic pancreatitis, acute recurring pancreatitis, pancreatic cancer—and the type 3c diabetes (an underappreciated form of diabetes) that may result from these diseases. The consortium will also look for predictors for early diagnosis of pancreatic cancer in people diagnosed with diabetes. In 2017, NIDDK, NCI, and the Pancreatic Cancer Action Network held a workshop on pancreatic cancer and diabetes/obesity/inflammation to inform future efforts. The NIH Nutrition Research Task Force, chaired by the NIDDK Director and co-chaired by the Directors of NHLBI, NCI, and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), plans to complete and publish the

[6] Diabetes in America, 3rd ed. Cowie CC, et al, Eds. Bethesda, MD, National Institutes of Health, NIH Pub No. 17-1468, 2017.
[7] Mody L, et al. JAMA Intern Med 177: 1154-1162, 2017.

first NIH-wide strategic plan on nutrition with input from across NIH and from external stakeholders.

Theme 2: Supporting Basic Research

In FY 2019, NIDDK will continue its support of multidisciplinary projects studying the development of the genitourinary tract; the gut microbiome; autoimmune diseases such as type 1 diabetes, celiac disease, inflammatory bowel diseases (IBD), autoimmune liver diseases, and some forms of CKD; and metabolic conditions, including obesity, type 2 diabetes, and NASH. Using a cutting-edge technique called cryo-electron microscopy, NIDDK-supported scientists have determined a highly complex three-dimensional molecular structure that could lead to improved understanding of a class of hormone receptors that are the target of about 40 percent of all pharmaceutical drugs in use today.[8]

The Human Islet Research Network's Human Pancreas Procurement and Analysis Program has made robust progress in generating information that can help researchers better understand the cellular and molecular events that precede and lead to loss of the insulin-producing pancreatic beta cells in type 1 diabetes. The program will expand its scope to include studies of pancreatic tissue from ethnically diverse donors to look for factors that may influence development of—and differences in—type 2 diabetes.

Two recent research studies in mice have shed new light on the complex relationships between kidney physiology, salt intake, water balance, and hypertension.[9,10] These studies have the potential to pave the way for a more detailed understanding of how the human body maintains water balance in response to salt intake and the generation of novel therapeutic approaches for reducing the risk of hypertension. The (Re)Building a Kidney (RBK) Consortium will seek to use kidney cells to create an organ that replaces normal kidney function; in 2017, RBK reported a novel protocol for dissociating cells from mouse kidney biopsies that is being adapted to human samples.[11] RBK scientists also found that selecting the proper substrate for growth and structural support is critical to creating blood supply in a "kidney on a chip," a finding that may advance regenerative medicine by improving tissue engineering of all vascularized organs.[12] Similarly, investigators with the Intestinal Stem Cell Consortium have used human stem cells to develop cellular arrangements ("organoids") that model various aspects of the small intestine and its functioning, facilitating study of molecular pathways underlying problems such as motility disorders[13] and creating potential for tissue replacement therapy.[14]

Theme 3: Investing in Translational and Clinical Research

In FY 2019, NIDDK will continue to support research into the causes of and treatments and cures for human diseases and on ways to implement those findings. Outcomes from a workshop NIDDK and ORWH organized on early diagnosis and treatment of gestational diabetes mellitus (GDM) will help guide development of GDM-related initiatives and future GDM-related

[8] Zhang Y, et al. Nature 546: 248-253, 2017.
[9] Kitada K, et al. J Clin Invest 127: 1944-1959, 2017.
[10] Stegbauer J, et al. JCI Insight 2: e92720, 2017.
[11] Adam M, et al. Development 144: 3625-3632, 2017.
[12] Nagao RJ, et al. Tissue Eng Part A 22:1140-1150, 2016.
[13] Workman MJ, et al. Nat Med 23:49-59, 2017.
[14] Tsai YH, et al. Development 144: 1045-1055, 2017.

research. The Epidemiology of Diabetes Interventions and Complications (EDIC) study recently developed an evidence-based screening schedule for retinopathy in people with type 1 diabetes, with the frequency of screening tailored to an individual's current level of eye disease and risk.[15] NIDDK-supported scientists also developed a personalized treatment plan for a child suffering from a severe anemia after discovering that the cause was a rare mutation affecting erythropoietin, a protein that stimulates blood cell production and is already available in a therapeutic form.[16] NIDDK recently held a workshop bringing together clinical and translational experts in biliary atresia to discuss what is known and identify future research opportunities for this rare but severe pediatric liver disease.[17] Featured presenters included investigators from the Childhood Liver Disease Research Network (ChiLDReN), an effort funded by NIDDK with additional support from the Cystic Fibrosis Foundation and Alpha-1 Foundation. The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network reported numerous findings regarding urologic chronic pelvic pain syndromes, including the first report indicating that changes in pain symptoms over time may be predicted through noninvasive brain imaging.[18]

Theme 4: Fostering a Diverse and Talented Workforce

In FY 2019, NIDDK will continue to foster and grow a diverse biomedical research workforce that can meet, with innovation and creativity, the challenges posed by the multiple diseases and conditions within its mission. Special training opportunities to draw talented young adults into research include the NIDDK Summer Undergraduate Research Programs in Kidney, Urologic, and Hematologic Diseases. This effort supports summer programs at six academic institutions, including a program at Vanderbilt University in which recruitment is targeted to racial and ethnic groups underrepresented in the health-related sciences, and those from geographically- and economically-disadvantaged backgrounds as defined by the Federal Government. Another focused student program, the NIDDK Medical Student Research Program in Diabetes and Obesity, supports opportunities for medical students to conduct summer research studies at an NIDDK-funded Diabetes Research Center, with the goal of fostering the next generation of physician-researchers in diabetes, endocrinology, and obesity. Mentorship opportunities offered by the Network of Minority Health Research Investigators, which celebrated its 15th anniversary in 2017, focus on junior investigators and will continue to promote a diverse research pipeline. Recognition and support of outstanding mid-career and senior investigators, especially in rapidly growing areas such as research on the gut microbiome [19,20,21,22] (which has been advanced by the NIH Common Fund Human Microbiome Project), will also be important to sustaining discovery important to human health.

[15] Nathan DM, et al. N Engl J Med 376: 1507-1516, 2017.
[16] Kim AR, et al. Cell 168: 1053-1064, 2017.
[17] https://www.niddk.nih.gov/news/events-calendar/Pages/biliary-atresia-clinical-translational-workshop.aspx
[18] Kutch JJ, et al. Pain. 158: 1069-1082, 2017.
[19] Wagner VE, et al. Sci Transl Med 8: 366ra164, 2016.
[20] Griffin NW, et al. Cell Host Microbe 21: 84-96, 2017.
[21] Smits SA, et al. Science 357: 802-806, 2017.
[22] Guo CJ, et al. Cell 168: 517-526.e18, 2017.

Program Descriptions and Accomplishments

Diabetes, Endocrinology, and Metabolic Diseases

The objectives of this program are to enhance the understanding of diabetes and other endocrine and metabolic disorders, and to develop and test prevention and treatment strategies. The program supports basic, clinical, and translational research, as well as research training, in areas that include type 1, type 2, and gestational diabetes; cystic fibrosis; obesity; energy balance; and endocrinology. Knowledge from diabetes research is communicated to patients, health professionals, and the public through the National Diabetes Information Clearinghouse and the National Diabetes Education Program.

In FY 2019, NIDDK will continue to support research that makes important contributions to the treatment and prevention of diseases that are associated with the endocrine system and metabolism, such as diabetes and obesity. New findings about diabetes in youth—children and adolescents diagnosed before age 20 years—have emerged via a long-term study co-funded with the Centers for Disease Control and Prevention (CDC) that has been assessing trends in diabetes diagnosis, prevalence, and health care, and other impacts of the disease. One recent report showed that from 2002-2012, the adjusted annual increase in type 1 diabetes diagnosis among U.S. youth was 1.8 percent, and the annual increase in type 2 diabetes diagnosis was 4.8 percent. However, the increases varied across racial/ethnic groups, with the largest increases occurring in groups other than non-Hispanic White youth.[23] In another report, study investigators estimated that by about age 21, approximately 32 percent of the study participants with type 1 diabetes and 72 percent of participants with type 2 diabetes would have, or be at high risk for, at least one diabetes health complication.[24] These studies suggest a disparate burden of diabetes in youth from certain racial/ethnic groups, and that early monitoring of youth with diabetes could lead to earlier diagnosis and treatment of complications. Recent NIDDK-supported research efforts are also shedding new light on molecules and pathways affecting eating and metabolism. Researchers have identified a group of brain cells in mice that, upon activation, induces rapid binge eating and weight gain.[25] Another group of researchers has discovered, in a study in mice, that bones secrete a hormone called lipocalin 2 that both suppresses appetite and regulates blood glucose levels.[26] Findings such as these could open up new therapeutic avenues important to prevention of obesity and type 2 diabetes.

[23] Mayer-Davis EJ, et al. N Engl J Med 376:1419-1429, 2017.
[24] Dabelea D, et al. JAMA 317: 825-835, 2017.
[25] Zhang X, et al. Science 356: 853-859, 2017.
[26] Mosialou I, et al. Nature 543: 385-390, 2017.

Program Portrait: New Directions in Gestational Diabetes

An estimated 7 percent of pregnant women will develop gestational diabetes mellitus (GDM)—i.e., diabetes associated with pregnancy—a condition that heightens risk for problems such as high weight babies and miscarriage. However, the impact of GDM is not limited to pregnancy—about half of these women will develop type 2 diabetes 5 to 10 years post-partum,[27] and offspring of GDM-affected pregnancies are at increased risk for obesity and diabetes. How best to diagnose GDM is controversial, with alternative recommendations for both the test and the test values that should define the condition. The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study (co-funded by NIDDK and NICHD and completed in 2006), enrolled 23,316 pregnant women at 15 centers in nine countries. The HAPO study was designed to assess the risk of adverse perinatal outcomes associated with levels of hyperglycemia (high blood glucose levels) less severe than those defined as GDM by current diagnostic criteria. The central finding was a strong continuous association of maternal blood glucose levels with increased birth weight and complications involving both mother and child at the time of birth.[28,29] However, the question of long-term impact remained. Leveraging this important study, NIDDK, with co-support from NICHD, spearheaded the recently completed HAPO Follow Up Study (HAPO-FUS). HAPO-FUS was a long-term, multi-site observational study, conducted at 10 of the original HAPO sites, that sought to determine whether hyperglycemia during pregnancy less severe than GDM influences later levels of obesity in children and development of diabetes in mothers after giving birth. The HAPO-FUS cohort consisted of 4,810 mother-child pairs. Results of the primary study analyses were announced at the 2017 American Diabetes Association scientific conference. These indicate that, at 8 to 12 years after the pregnancy analyzed during the HAPO study, there is a strong relationship between glucose levels below the current GDM diagnostic threshold and subsequent type 2 diabetes in the mothers as well as obesity in the offspring. Other analyses of metabolic problems in offspring and measures of cardiovascular disease in mothers are under way and anticipated to be completed in the next year.

The important findings of HAPO and HAPO-FUS have helped spur new NIDDK activities in this area that will seek to determine the natural history of glucose elevation in pregnancy and, ultimately, whether there are interventions that might be beneficial to mothers and offspring earlier in pregnancy. NIDDK, together with ORWH, convened an international workshop on August 2-3, 2017, involving obstetricians, maternal-fetal medicine specialists, internists, and endocrinologists with expertise in GDM to address current research gaps. An area of particular focus at the workshop was lack of knowledge on when in pregnancy abnormal blood glucose levels first manifest. Testing for GDM currently takes place at 24 to 28 weeks gestation. Information on whether some women have hyperglycemia earlier during pregnancy has potential importance not only for early diagnosis of GDM, but also for different treatment strategies and therapeutic goals in the management of GDM. A definitive conclusion from the workshop was the need to better understand whether early diagnosis and treatment of maternal hyperglycemia would improve the health of the mother and her offspring. As a result, and if appropriations allow, planning is now under way for an FY 2019 research initiative that would center on collecting data about changes in maternal blood glucose levels earlier in pregnancy, leveraging new technologies such as continuous glucose monitors to obtain comprehensive data with less burden. It is anticipated that this planned initiative would pave the way for a subsequent clinical trial evaluating new approaches to GDM screening and intervention, with the ultimate goal of improving health of women and their children.

With FY 2019 resources, NIDDK will continue major diabetes clinical trials. FY 2019 funds will also support research capitalizing on new opportunities to identify diabetes risk genes in minority populations, to advance progress toward developing new therapeutic approaches, and to support comparative effectiveness research. NIDDK will also continue to fund translational research in FY 2019 and support health information dissemination activities to bring scientific discoveries in diabetes and obesity to real-world medical practice and other community settings. In FY 2019, NIDDK will continue an initiative encouraging collaborative, multidisciplinary research teams to work on complex biomedical problems in diabetes, endocrinology, and metabolic diseases. NIDDK will also continue funding for research centers to advance research

[27] Kim C, et al. Diabetes Care 25: 1862-1868, 2002.
[28] HAPO Study Cooperative Research Group. N Engl J Med 358: 1991-2002, 2008.
[29] HAPO Study Cooperative Research Group. Diabetes 58: 453-459, 2009.

relevant to diabetes and to cystic fibrosis and other genetic metabolic diseases. NIDDK plans for FY 2019 include capitalizing on new findings relevant to GDM and pursuing other efforts as part of an overall balanced research program.

Digestive Diseases and Nutrition

The objectives of this program are to enhance understanding of digestive diseases, nutrition, and obesity, and to develop and test strategies for disease prevention and treatment. This program supports discovery, clinical, and translational research, as well as research training, encompassing fundamental studies of the digestive system; disease-targeted research involving the esophagus, stomach, small intestine, large intestine and anorectum, liver and biliary system, and pancreas; studies relevant to nutrition; and research on obesity. Insights gleaned from scientific efforts are communicated to patients, health professionals, and the public through NIDDK's National Digestive Diseases Information Clearinghouse and Weight-control Information Network.

In FY 2019, NIDDK will continue to support programs aimed at improving the treatment and prevention of diseases associated with the digestive system. NIDDK held meetings in 2017 to identify digestive disease-, nutrition-, and obesity-related research opportunities, in collaboration with both Federal and non-Federal partners. These included workshops focusing on 1) the current state of clinical and translational science on biliary atresia; 2) the interface of pancreatic cancer with diabetes, obesity, and inflammation; 3) emerging roles for branched chain amino acids in human disease; 4) best practices in the study of diet and the intestinal microbiome, and developing precision medicine approaches for the treatment of severe obesity in adolescents; and 5) meetings led by the NIDDK Office of Nutrition Research and the NIH Nutrition Research Task Force to identify nutrition research opportunities. In 2017, NIDDK issued a solicitation to continue supporting research on liver injury caused by drugs or herbal/dietary supplements. Another solicitation issued in 2017 will support research investigating the role of the lymphatic system in digestive health and disease. The Institute also funded research through a new consortium established to study the relationships among chronic pancreatitis, diabetes, and pancreatic cancer. NIDDK will continue to support the Hepatitis B Research Network, which is testing treatments in at-risk populations of both children and adults, such as Asian Americans and Pacific Islanders, as well as conducting ancillary studies and assembling a large biospecimen repository and clinical database for future studies. NIDDK will also continue an observational follow up of Look AHEAD (Action For Health in Diabetes) study participants to examine whether the trial's lifestyle intervention, provided for 10 years during mid-life, has enduring health and other benefits that persist beyond the period of the intervention for older individuals with type 2 diabetes.

Program Portrait: Drug-Induced Liver Injury Network (DILIN)

Drug-induced liver injury, though relatively uncommon, represents the leading cause of acute liver failure in the Nation and is the top reason for regulatory actions by the U.S. Food and Drug Administration (FDA) against approved medications. However, knowledge has been limited concerning the scope of this problem in the U.S. population, mechanisms by which susceptible individuals develop drug-induced liver injury, and how to definitively diagnose these cases. NIDDK established the Drug-Induced Liver Injury Network (DILIN) in 2003 to collect and analyze cases of severe liver injury caused by prescription drugs, over-the-counter drugs, and alternative medicines, such as herbal and dietary supplements (HDS). Since that time, DILIN has collected data and specimens from more than 1,700 cases of liver toxicities due to these agents and made major contributions to characterizing potential mechanisms and disease processes; to defining the clinical spectrum, natural history, and outcomes of liver injury that results from these agents; and to aiding accurate diagnosis. For example, since DILIN's inception, the number of enrolled cases of HDS-induced liver injury has steadily increased, such that use of HDS products now accounts for more than 20 percent of cases reported in DILIN. Recent Network studies have provided new insights into outcomes from DILI, including the rate of fatal outcomes,[30] frequency of damage and loss of bile ducts in the liver,[31] and racial/ethnic disparities in disease severity.[32] An additional benefit of DILIN came in 2012 in the form of a website called "LiverTox," which was developed by NIDDK in conjunction with NIH's National Library of Medicine.[33] This website serves as a public resource to aid health care providers in diagnosing, and investigators in studying, liver injury due to drugs and HDS.

The major advances coming from the DILIN's extensive studies of how liver injury caused by drugs and HDS affects the U.S. population have not only expanded knowledge but also raised new and important questions. DILIN's research is also applicable to global health as noted at a 2015 workshop on HDS-related liver injury featuring reports from DILIN and other nationally based studies around the world that was co-sponsored by NIDDK and the American Association for the Study of Liver Diseases, together with the CDC, FDA, U.S. Government Accountability Office, the National Center for Complementary and Integrative Health, the National Institute of Environmental Health Sciences, and the NIH Office of Dietary Supplements.[34] In 2017, NIDDK announced an initiative to continue the current Network, comprised of six clinical centers and a data coordinating center, for an additional 5-year period. In its new phase, the Network will be asked to build upon its prior accomplishments and continue focus in three areas: 1) clinical, biochemical, histologic and biologic characterization of DILI, including acute and chronic disease, HDS-induced disease, ethnic and racial differences, genetic studies, and cytokines and immunological profiling; 2) pilot/feasibility studies that would lay the groundwork for future studies on treatment of severe DILI, in particular acute and symptomatic chronic cases; and 3) monitoring HDS and newly approved prescription medications (in collaboration with the FDA) for previously unreported adverse reactions and continuing to expand and maintain LiverTox. This renewal will enable progress on identification, understanding, diagnosis, and potential treatment of drug- and HDS-induced liver injury to be continued by DILIN's investigators and study participants.

In FY 2019, NIDDK will continue major clinical research networks to help understand and treat liver diseases, including hepatitis B and nonalcoholic steatohepatitis. Among its obesity-related efforts in FY 2019, NIDDK will continue to support major ongoing studies to assess the health risks and benefits of weight-loss surgery in extremely obese adolescents. NIDDK will also use FY 2019 funds to support Digestive Diseases Research Core Centers, and to sustain a consortium that is conducting cutting-edge genetic research on inflammatory bowel diseases. Research on intestinal stem cells that can benefit a variety of digestive diseases will continue in FY 2019, along with other efforts as part of an overall balanced research program.

[30] Hayashi PH, et al. Hepatology 66: 1275-1285, 2017.
[31] Bonkovsky HL, et al. Hepatology 65: 1267-1277, 2017.
[32] Chalasani N, et al. Am J Gastroenterol 112: 1382-1388, 2017.
[33] LiverTox: http://livertox.nih.gov/
[34] https://www.niddk.nih.gov/news/events-calendar/Pages/Liver-Injury-Herbal-Dietary-Supplements_5-15.aspx#tab-event-details

Kidney, Urologic, and Hematologic Diseases
The objectives of this program are to increase the understanding of diseases and disorders of the kidneys, urinary tract, and blood (hematologic), and to develop and test prevention and treatment strategies. Discovery, clinical, and translational research, as well as research training, are supported in the areas of chronic kidney disease (CKD), diabetic kidney disease, end-stage renal disease (ESRD or kidney failure), polycystic kidney disease, and many other kidney diseases; urinary incontinence, benign prostatic hyperplasia, interstitial cystitis/painful bladder syndrome, stones, impotence, congenital urologic disorders, and urinary tract infections; and disorders of the blood and blood-forming organs, including sickle cell disease, Cooley's anemia, hemochromatosis, and the anemia of inflammation and chronic disease.

In FY 2019, NIDDK will continue to support research aimed at improving the treatment and prevention of kidney, urologic, and hematologic diseases. Scientists recently developed the first method for calculating the average rate of blood filtration by individual nephrons in the human kidney.[35] This advance could lead to a greater understanding of the relationship between individual nephron function and overall kidney function and health. The NIDDK-supported Prevention of Urinary Stones with Hydration study (PUSH) clinical study[36] recently began recruiting participants to determine if a program of financial incentives, receiving advice from a health coach, and using a smart water bottle will result in reduced risk of kidney stone (also called urinary stone) recurrence over a two-year period. A clinical research consortium, the overarching goal of which is to build an evidence base for factors affecting bladder health in girls and women, successfully recruited focus groups that will inform the measurement of bladder health in longitudinal studies. Forms of the *APOL1* gene (genotypes) conferring high risk for non-diabetic kidney diseases are more commonly found in African Americans; in 2017, NIDDK established a multi-center clinical study to investigate the relationship of *APOL1* genotypes of kidneys donated by African Americans to both kidney recipient and donor outcomes. NIDDK will continue to support a pragmatic clinical trial that aims to determine whether guideline care facilitated by an enhanced electronic health record for people with diabetes, hypertension, and CKD improves rates of unplanned hospitalization, disease-specific hospitalization, 30-day readmission, or emergency room visits compared with usual care.

[35] Denic A, et al. N Eng J Med 376: 2349-2357, 2017.
[36] ClinicalTrials.gov: NCT03244189 (https://clinicaltrials.gov/ct2/show/NCT03244189)

Program Portrait: Kidney Precision Medicine Project (KPMP)

Acute kidney injury (AKI) and chronic kidney disease (CKD) impose a significant public health and financial burden; however, only a few drug therapies are available for CKD, and none currently exist for AKI. Development of pharmacologic agents for AKI and CKD has been hampered by non-predictive animal models, the inability to identify and prioritize human targets, and an underlying poor understanding of human AKI and CKD. A growing consensus suggests that CKD and AKI are not homogeneous diseases; rather, they are heterogeneous disorders that contain specific subgroups that are driven by different disease pathways. Thus, a better understanding of disease heterogeneity will likely inspire the development of more effective, individualized treatment options, but will require going directly to study of human tissue—a prospect that has been made feasible by recent advances in technologies for analyzing human tissue biopsies.

In 2017, NIDDK started the Kidney Precision Medicine Project (KPMP), with the goal of ethically and safely obtaining and evaluating human kidney biopsies from research participants with AKI or CKD; creating a kidney tissue atlas; defining disease subgroups; and identifying critical cells, extracellular components, and pathways that can be targeted for novel therapies. Human kidney biopsies will be analyzed to identify new markers that will characterize cells, cell states, and molecular disease pathways; these markers will then be linked to important patient clinical outcomes. Importantly, because the current kidney biopsy procedure carries risk, with well-defined complications, ethical and participant safety considerations will be a primary concern. Individuals who choose to participate in KPMP will be provided with clear information about the risks associated with undergoing a kidney biopsy. Specific, validated protocols for tissue handling and study will be developed and implemented to ensure that, when a participant donates his or her tissue to the KPMP, it yields the greatest possible benefit to that individual, the patient community, and society as a whole. NIDDK is also supporting research to develop safer biopsy methods and novel techniques to analyze human kidney tissue through its small business programs. To address any emerging technologic challenges and needs and help ensure that KPMP kidney biopsies yield useful research and clinical information, NIDDK intends to routinely solicit and fund pilot projects and ancillary studies to the KPMP. To achieve maximal success, the KPMP will foster partnerships among patients, academic researchers, private industry, advocacy organizations, and NIDDK. KPMP will also collaborate with other tissue mapping projects at NIH, including the GenitoUrinary Development Molecular Anatomy Project, the Human Biomolecular Molecular Atlas Platform, and Cancer Moonshot initiative. KPMP-developed resources will be shared openly and broadly. The kidney tissue atlas emerging from the KPMP effort will be used as a foundation to better understand kidney disease heterogeneity and can inform decision-making by pathologists, nephrologists, and patients with AKI and CKD. It is anticipated that KPMP will improve the scientific knowledge base of kidney diseases, the clinical utility of kidney biopsies, and improve the pipeline of new drugs for treatment. Furthermore, KPMP has the potential to increase the number of researchers and clinicians studying kidney diseases.

In FY 2019, NIDDK will continue support for ongoing major clinical studies of CKD in adults and children. NIDDK also plans to continue to sponsor planning grants to conduct translational research on the effectiveness of interventions shown in clinical trials to prevent, treat, and manage CKD, and will continue to sponsor studies to improve adherence to medical therapy in adolescents with CKD. In FY 2019, NIDDK will continue studies to improve measurements of outcomes in lower urinary tract disorders of the prostate and urinary bladder. Centers focused on kidney, urologic, and hematologic research will receive continued funding, as will research on acute kidney injury. NIDDK will also continue support for the Improving Chronic Disease Management with Pieces (ICD-Pieces) study, which implements a novel technology platform (Pieces) that enables the use of electronic health record data to improve CKD care within primary care practices or medical homes in the community.

Special Statutory Funding Program for Type 1 Diabetes Research

Complementing efforts of the Diabetes, Endocrinology, and Metabolic Disease program, the Special Program's goal is to foster improved treatment, prevention, and cure of type 1 diabetes and its complications through basic, clinical, and translational research. The program has six

scientific goals: 1) identifying genetic and environmental causes of type 1 diabetes ($33 million); 2) preventing or reversing the disease ($33 million); 3) developing cell replacement therapy ($40 million); 4) improving management and care ($25 million); 5) preventing or reducing diabetes complications ($10 million); and 6) attracting new talent and applying new technologies to research ($9 million) (FY 2019 estimate dollars). Although focused on type 1 diabetes, aspects of this research are relevant to other autoimmune disorders as well as type 2 diabetes. For example, shared characteristics of type 1 and type 2 diabetes include impaired function of the insulin-producing beta cells of the pancreas and the potential for serious health complications, such as heart disease, stroke, blindness, kidney failure, nerve damage, and lower limb amputations. In FY 2017, NIDDK supported new research in several areas, including: research into behavioral and psychosocial factors that affect diabetes management, including use of artificial pancreas devices; analysis of biosamples to identify predictors of autoimmunity and type 1 diabetes in high-risk infants enrolled in The Environmental Determinants of Diabetes in the Young (TEDDY) study; small business research to develop new type 1 diabetes therapeutics and diagnostic technologies; clinical trials networks to test agents to prevent or reverse type 1 diabetes; a clinical trial testing a safe and inexpensive medicine to reduce loss of kidney function in type 1 diabetes; and studies aimed at increasing understanding of how human insulin-producing beta cells are lost in type 1 diabetes and identifying strategies to protect or replace them.

Budget Policy: The FY 2019 President's Budget includes $150.000 million for Special Type 1 Diabetes discretionary funding.

Intramural Research

The objective of the Institute's Intramural Research Program (IRP) is to conduct basic, translational, and clinical biomedical research related to diabetes and other endocrine and metabolic diseases; digestive diseases, including liver diseases and nutritional disorders; obesity; kidney diseases; and hematologic diseases. Intramural research is conducted in the Institute's laboratories and clinical facilities in Bethesda, Maryland as well as in Phoenix, Arizona, where a long-standing research relationship with American Indian communities in the region has led to important scientific advances in diagnosing and treating type 2 diabetes and obesity. For example, NIDDK's IRP recently identified several biomarkers that predicted loss of kidney function in American Indians with type 2 diabetes, identifying early those individuals at increased risk of kidney failure.[37] IRP research using mouse models demonstrated new links between neuronal activity in specific brain regions and both physical activity and the drive to eat, further defining the critical roles of hormonal signaling in obesity-related animal behavior.[38,39] Other IRP research explored the relationship between appetite and weight loss in regulating food intake in humans,[40] uncovered a common signaling mechanism that stimulates pancreatic insulin secretion while suppressing glucose release from the liver,[41,42] and identified the causative gene mutation underlying certain tumors of the parathyroid gland.[43] Research training is also an

[37] Saulnier PJ, et al. Diabetes 65: 3744-3753, 2016.
[38] Burnett CJ, et al. Neuron 92: 187-201, 2016.
[39] Friend DM, et al. Cell Metabolism 25: 312-321, 2017
[40] Polidori D, et al. Obesity 24: 2289-2295, 2016
[41] Zhu L, et al. Nature Commun 8: 14295, 2017
[42] Zhu L, et al. J Clin Invest 127: 2941-2945, 2017
[43] Guan B, et al. Am J Hum Genet 99: 1034-1044, 2016.

integral component of the IRP. This training occurs in both clinical and basic laboratory research at the high school, post baccalaureate, masters, doctoral, postdoctoral, and clinical fellow level, including summer programs specifically targeting under-represented minorities.

Research Management and Support (RMS)
RMS activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. RMS functions also encompass strategic planning, coordination, and evaluation of the Institute's programs, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. Through RMS activities, NIDDK continues to administratively support meritorious discovery, clinical, and translational research and research training efforts, and also continues its health information dissemination and education/outreach activities.

NATIONAL INSTITUTES OF HEALTH
National Institute of Diabetes and Digestive and Kidney Diseases

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2017 Final			FY 2018 Annualized CR			FY 2019 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Diabetes, Endocrinology, and Metabolic Diseases									
Direct:	29	1	30	30	1	31	30	1	31
Reimbursable:	3	-	3	3	-	3	3	-	3
Total:	32	1	33	33	1	34	33	1	34
Division of Digestive Diseases and Nutrition									
Direct:	24	2	26	24	2	26	24	2	26
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	24	2	26	24	2	26	24	2	26
Division of Kidney, Urologic, and Hematologic Diseases									
Direct:	24	-	24	25	-	25	25	-	25
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	24	-	24	25	-	25	25	-	25
Division of Extramural Activities									
Direct:	66	-	66	67	-	67	67	-	67
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	66	-	66	67	-	67	67	-	67
Division of Intramural Research Programs									
Direct:	361	10	371	366	10	376	366	10	376
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	361	10	371	366	10	376	366	10	376
Office of the Director									
Direct:	135	-	135	135	-	135	135	-	135
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	135	-	135	135	-	135	135	-	135
Total	642	13	655	650	13	663	650	13	663
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									

FISCAL YEAR	Average GS Grade
2015	12.0
2016	12.0
2017	12.0
2018	12.0
2019	12.0

NATIONAL INSTITUTES OF HEALTH
National Institute of Diabetes and Digestive and Kidney Diseases

Detail of Positions[1]

GRADE	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	187,000	190,798	191,705
GM/GS-15	58	56	56
GM/GS-14	67	67	67
GM/GS-13	96	97	97
GS-12	64	67	67
GS-11	39	40	40
GS-10	0	0	0
GS-9	23	25	25
GS-8	16	16	16
GS-7	22	24	24
GS-6	0	0	0
GS-5	1	1	1
GS-4	1	0	0
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	387	393	393
Grades established by Act of July 1, 1944 (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	0	0	0
Senior Grade	7	7	7
Full Grade	1	1	1
Senior Assistant Grade	2	2	2
Assistant Grade	0	0	0
Subtotal	10	10	10
Ungraded	265	267	267
Total permanent positions	389	394	394
Total positions, end of year	663	671	671
Total full-time equivalent (FTE) employment, end of year	655	663	663
Average ES salary	187,000	190,798	191,705
Average GM/GS grade	12.0	12.0	12.0
Average GM/GS salary	106,730	108,898	109,415

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