#### DEPARTMENT OF HEALTH AND HUMAN SERVICES

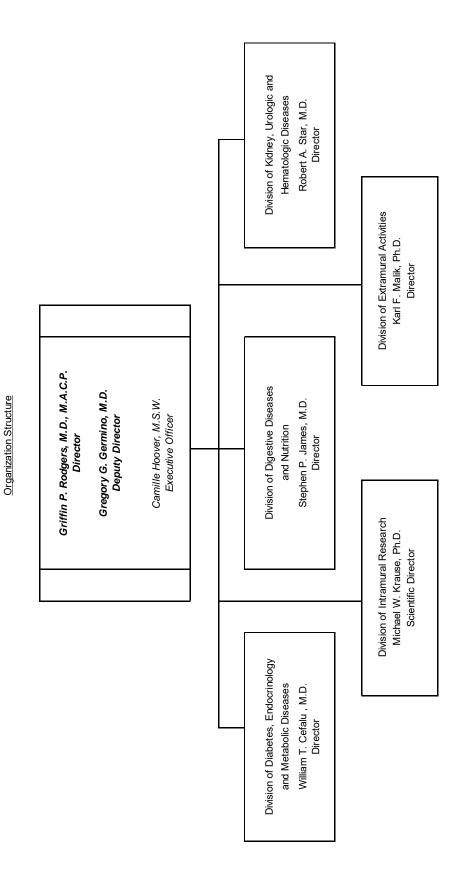
#### NATIONAL INSTITUTES OF HEALTH

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

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NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and Digestive and Kidney Diseases



#### NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and Digestive and Kidney Diseases

For carrying out section 301 and title IV of the PHS Act with respect to diabetes and digestive and kidney diseases, [\$2,114,314,000]\$1,924,211,000.

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

(Dollars in Thousands)

Source of Funding	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Appropriation	\$2,029,823	\$2,114,314	\$1,924,211
Mandatory Appropriation: (non-add)			
Type 1 Diabetes: Current Law	(150,000)	(96,575)	(0)
Type 1 Diabetes: Proposed Extension	(0)	(53,425)	(150,000)
Secretary's Transfer	-6,972	0	0
Subtotal, adjusted appropriation	\$2,022,851	\$2,114,314	\$1,924,211
OAR HIV/AIDS Transfers	2,660	832	0
Subtotal, adjusted budget authority	\$2,025,511	\$2,115,146	\$1,924,211
Unobligated balance lapsing	-169	0	0
Total obligations	\$2,025,342	\$2,115,146	\$1,924,211

 $<sup>^{\</sup>rm 1}$  Excludes the following amounts (in thousands) for reimbursable activities carried out by this account:

FY 2019 - \$3,281 FY 2020 - \$6,000 FY 2021 - \$6,000

#### Budget Mechanism - Total<sup>1</sup>

(Dollars in Thousands)

MECHANISM	FY 2019 Final		FY 2020 Enacted		FY 2021 Pr	resident's Budget	FY 2021 +/- FY 2020 Enacted	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,938	\$925,965	1,949	\$962,296	1,965	\$913,064	16	-\$49,232
Administrative Supplements	(103)	13,096	(102)	13,000	(80)	10,000	(-22)	-3,000
Competing:								
Renewal	163	90,299	177	97,889	143	74,000	-34	-23,889
New	492	225,364	532	244,000	427	182,000	-105	-62,000
Supplements	2	248	2	250	2	200	0	-50
Subtotal, Competing	657	\$315,910	711	\$342,139	572	\$256,200	-139	-\$85,939
Subtotal, RPGs	2,595	\$1,254,972	2,660	\$1,317,435	2,537	\$1,179,264	-123	-\$138,17
SBIR/STTR	115	62,464	120	64,929	118	59,000	-2	-5,929
Research Project Grants	2,710	\$1,317,436	2,780	\$1,382,364	2,655	\$1,238,264	-125	-\$144,100
Research Centers:								
Specialized/Comprehensive	97	\$116,886	104	\$126,000	96	\$115,000	-8	-\$11,000
Clinical Research	0	0	0	0	0	0	0	(11,000
Biotechnology	0	0	0	0	0	0	0	
Comparative Medicine	Ĭ	50	0	50	0	47	0	
Research Centers in Minority Institutions	Ĭ	0	0	0	0	0	0	
Research Centers	97	\$116,936	104	\$126,050	96	\$115,047	-8	-\$11,003
Other Research:								
Research Careers	453	\$78,971	463	\$80,700	460	\$75,500	-3	-\$5,200
Cancer Education	0	0	0	0	0	0	0	(
Cooperative Clinical Research	0	0	0	0	0	0	0	(
Biomedical Research Support	0	0	0	0	0	0	0	(
Minority Biomedical Research Support	0	531	0	532	0	500	0	-32
Other	122	72,960	122	73,000	120	68,000	-2	-5,000
Other Research	575	\$152,463	585	\$154,232	580	\$144,000	-5	-\$10,232
Total Research Grants	3,382	\$1,586,835	3,469	\$1,662,646	3,331	\$1,497,311	-138	-\$165,335
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	297	\$13,894	300	\$14,400	308	\$13,800	8	-\$600
Institutional Awards	783	50,060	765	50,100	784	48,100	19	-2,000
Total Research Training	1,080	\$63,954	1,065	\$64,500	1,092	\$61,900	27	-\$2,600
Research & Develop. Contracts	124	\$91,173	126	\$93,000	122	\$89,000	4	-\$4,000
(SBIR/STTR) (non-add)	(3)	(732)	(3)	(740)	(3)	(720)	(0)	-54,000 (-20)
(DDITED TTY (NON-MAN)	(3)	(732)	(5)	(740)	(3)	(720)	(0)	(-20)
Intramural Research	345	206,830	360	215,000	360	200,000	0	-15,000
Res. Management & Support	276	76,719	300	80,000	300	76,000	0	-4,000
Res. Management & Support (SBIR Admin) (non-add)	(0)	(14)	(0)	(15)	(0)	(10)	(0)	(-5)
Total, NIDDK	621	\$2,025,511	660	\$2,115,146	660	\$1,924,211	0	-\$190,935

<sup>&</sup>lt;sup>1</sup> All items in italics and brackets are non-add entries.

#### NATIONAL INSTITUTES OF HEALTH Type 1 Diabetes

#### Budget Mechanism - Total<sup>1,2</sup>

(Dollars in Thousands)

MECHANISM	FY	FY 2019 Final <sup>3</sup>		FY 2020 Enacted <sup>4</sup>		resident's Budget	FY 2021 +/- FY 2020 Enacted	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
D 10 10								
Research Projects: Noncompeting	(0)	674 522	50	\$48,072	75	\$72,367	25	624.205
	(9)	\$74,532 15,014	50 (16)	22,200	75 (14)	20,000	25	\$24,295
Administrative Supplements	(9)	15,014	(10)	22,200	(14)	20,000	(-2)	-2,200
Competing: Renewal		24.115	2	7.500	2	10.000		2.500
	4	24,115	2	7,500	3	10,000	1	2,500
New	32	21,946	93	61,580	58	35,733	-35	-25,847
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	36		95	\$69,080	61	\$45,733	-34	-\$23,347
Subtotal, RPGs	105	,	145	\$139,352	136	\$138,100		-\$1,252
SBIR/STTR	14	- 7	12	5,475	12	5,475	0	0
Research Project Grants	119	\$141,649	157	\$144,827	148	\$143,575	-9	-\$1,252
Research Centers:								
Specialized/Comprehensive	0	\$0	0	\$0	0	\$0	0	so
Clinical Research	0	30	0	30	0	30	0	30
Biotechnology	0	0	0	0	0	0	0	ů,
Comparative Medicine	0		0	0	0	0	0	Ö
Research Centers in Minority Institutions	0	0	0	0	0	0	0	ů,
Research Centers	0	\$0	0	\$0	0	\$0	0	\$0
Research Cemers	0	50	0	30	U	\$0	U	30
Other Research:								
Research Careers	9	\$4,851	5	\$2,173	6	\$2,425	1	\$252
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	2,000	0	2,000	0	2,000	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	1	1,500	1	1,000	2	2,000	1	1,000
Other Research	10	,	6	\$5,173	8	\$6,425	2	\$1,252
Total Research Grants, T1D	129	,	163	\$150,000	156	\$150,000	-7	\$0

<sup>1</sup> All items in italics and brackets are non-add entries.
2 Figures reflect budget authority provided in each year. A portion of this budget authority will be carried over and obligated in later years. The Type 1 Diabetes program also carried over \$124.1 million in budget authority provided in FY 2018, with \$0.4 million in obligations made in FY 2019 and \$123.7 million in obligations estimated to be made in FY 2020 and later years.
3 Includes Type 1 Diabetes (million pot obligated in FY 2019 and 57 Y2020.
4 Includes \$96.6 million in funded enacted through May 22, 2020 and \$53.4 million in requested funding to reach full-year level of \$150.0 million.

#### Major Changes in the 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 mechanisms and activity detail and these highlights will not sum to the total change for the FY 2021 President's Budget. The FY 2021 President's Budget request for NIDDK, excluding the proposed \$150.0 million of mandatory funding for Type 1 Diabetes, is \$1,924.2 million, a decrease of \$190.9 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, NIDDK will pursue its highest research priorities through strategic investments and careful stewardship of appropriated funds.

Research Project Grants (RPGs) (-\$144.1 million; total \$1,238.3 million): NIDDK will reduce funding for non-competing RPGs by \$49.2 million, including reducing individual non-competing awards by 7.0 percent from their full commitment level. Competing RPGs are expected to decrease by 19.5 percent or 139 grants compared to the FY 2020 Enacted level of 711 awards, and the amount to support competing awards will be reduced by \$85.9 million from the FY 2020 Enacted level. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

Research Centers (-\$11.0 million; total \$115.0 million): NIDDK will reduce funding for Research Centers by 8.7 percent compared to the FY 2020 Enacted level. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

Other Research (-\$10.2 million; total \$144.0 million): NIDDK will reduce funding for Other Research by 6.6 percent compared to the FY 2020 Enacted level. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

<u>R&D Contracts (-\$4.0 million; total \$89.0 million)</u>: NIDDK will reduce funding for R&D Contracts by 4.3 percent compared to the FY 2020 Enacted level. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

<u>Intramural Research (-\$15.0 million; total \$200.0 million):</u> NIDDK will reduce funding for Intramural Research by 7.0 percent compared to the FY 2020 Enacted level. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

Research Management and Support (-\$4.0 million; total \$76.0 million): NIDDK will reduce funding for Research, Management, and Support by 5.0 percent compared to the FY 2020 Enacted level. These reductions are distributed across all administrative support areas of basic, translational or clinical research.

#### **Summary of Changes**

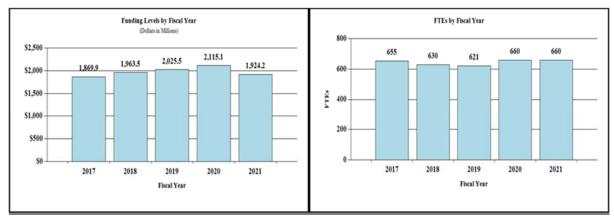
(Dollars in Thousands)

FY 2020 Enacted FY 2021 President's Budget		\$2,115,146 \$1,924,211
Net change		-\$190,935
	FY 2021 President's Budget	Change from FY 2020 Enacted
CHANGES	FTEs Budget Authority	FTEs Budget Authority
A. Built-in:		
1. Intramural Research:		
<ul> <li>a. Annualization of January 2020 pay increase &amp; benefits</li> </ul>	\$84,573	\$486
b. January FY 2021 pay increase & benefits	84,573	1,456
c. Paid days adjustment	84,573	-277
d. Payment for centrally furnished services	35,000	0
e. Cost of laboratory supplies, materials, other expenses, and non-recurring costs	80,427	-16,665
Subtotal		-\$15,000
2. Research Management and Support:		
<ul> <li>a. Annualization of January 2020 pay increase &amp; benefits</li> </ul>	\$51,342	\$327
b. January FY 2021 pay increase & benefits	51,342	981
c. Paid days adjustment	51,342	-196
d. Payment for centrally furnished services	970	-57
e. Cost of laboratory supplies, materials, other expenses, and non-recurring costs	23,689	-5,055
Subtotal		-\$4,000
Subtotal, Built-in		-\$19,000

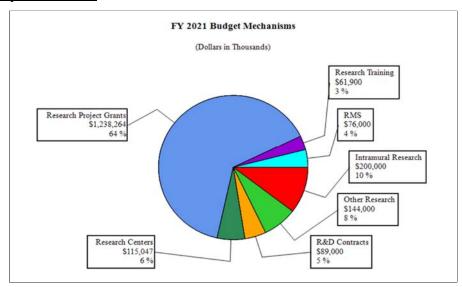
	FY 2021 President's Budget		Change from FY	2020 Enacted
CHANGES	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	1,965	\$923,064	16	-\$52,232
b. Competing	572	256,200	-139	-85,939
c. SBIR/STTR	118	59,000	-2	-5,929
Subtotal, RPGs	2,655	\$1,238,264	-125	-\$144,100
2. Research Centers	96	\$115,047	-8	-\$11,003
3. Other Research	580	144,000	-5	-10,232
4. Research Training	1,092	61,900	27	-2,600
5. Research and development contracts	122	89,000	-4	-4,000
Subtotal, Extramural		\$1,648,211		-\$171,935
	FTEs		FTEs	
6. Intramural Research	360	\$200,000	0	\$0
7. Research Management and Support	300	76,000	0	0
Subtotal, Program	660	\$1,924,211	0	-\$171,935
Total changes				-\$190,935

#### Fiscal Year 2021 Budget Graphs

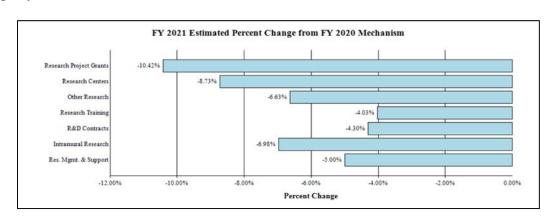
#### History of Budget Authority and FTEs:



#### **Distribution by Mechanism:**



#### Change by Selected Mechanism:



# Budget Authority by Activity<sup>1</sup> (Dollars in Thousands)

	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 +/- FY2020	
Extramural Research	FTE	<u>Amount</u>	FTE	<u>Amount</u>	FTE	<u>Amount</u>	FTE	Amount
<u>Detail</u>								
Diabetes, Endocrinology, and Metabolic Diseases		\$700,209		\$731,636		\$662,524		-\$69,112
Digestive Diseases and Nutrition		586,963		613,308		555,373		-57,935
Kidney, Urologic, and Hematologic Diseases		454,790		475,202		430,314		-44,888
Type 1 Diabetes (mandatory): Current Law		(150,000)		(96,575)		(0)		(-96,575)
Type 1 Diabetes (mandatory): Proposed Extension		(0)		(53,425)		(150,000)		(96,575)
Subtotal, Extramural		\$1,741,962		\$1,820,146		\$1,648,211		-\$171,935
Intramural Research	345	\$206,830	360	\$215,000	360	\$200,000	0	-\$15,000
Research Management & Support	276	\$76,719	300	\$80,000	300	\$76,000	0	-\$4,000
TOTAL	621	\$2,025,511	660	\$2,115,146	660	\$1,924,211	0	-\$190,935

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

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

# Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2020 Amount Authorized	FY 2020 Enacted	2021 Amount Authorized	2021 Amount FY 2021 President's Budget Authorized
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
National Institute of Diabetes and Digestive and Kidney Diseases	Section 401(a)	42§281	Indefinite	\$2,115,146,000	Indefinite	\$1,924,211,000
Total, Budget Authority				\$2,115,146,000		\$1,924,211,000

## Appropriations History<sup>1</sup>

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	\$1,966,310,000	\$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	\$2,120,797,000
2019	\$1,965,434,000	\$2,144,333,000	\$2,180,892,000	\$2,179,823,000
2020	\$1,896,493,000	\$2,129,027,000	\$2,155,327,000	\$2,210,889,000
2021	\$2,074,211,000			

<sup>&</sup>lt;sup>1</sup> Includes mandatory financing. Enacted amount for FY 2020 reflects \$96,575,000 enacted appropriation for Type 1 Diabetes.

#### **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 2019 Final	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
ВА	\$2,175,511,000	\$2,265,146,000	\$2,074,211,000	-\$190,935,000
Type 1 Diab Current Law Proposed	eetes Mandatory: -\$150,000,000	-\$96,575,000	\$0	\$96,575,000
Extension Total	<u>\$0</u> -\$150,000,000	- <u>\$53,425,000</u> - <u>\$150,000,000</u>	<u>-\$150,000,000</u> <u>-\$150,000,000</u>	-\$96,575,000 <u>\$0</u>
Labor/HHS: FTEs	\$2,025,511,000 621	\$2,115,146,000 660	\$1,924,211,000 660	-\$190,935,000 0

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 affects 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. Estimates of chronic kidney disease (CKD) show that about 37 million Americans are affected, and over 787,000 people were treated for irreversible kidney failure in the Nation in 2016. Many urologic diseases, such as urinary incontinence, urinary tract infections, and benign prostatic hyperplasia, are also highly prevalent. Digestive diseases accounted for an estimated 66.4 million ambulatory care visits to doctor's offices, outpatient

<sup>&</sup>lt;sup>1</sup> Centers for Disease Control and Prevention (CDC). National Diabetes Statistics Report, 2017. Atlanta, GA: CDC, Department of Health and Human Services (HHS); 2017.

<sup>&</sup>lt;sup>2</sup> CDC. Chronic Kidney Disease in the United States, 2019. Atlanta, GA: CDC HHS, 2019.

<sup>&</sup>lt;sup>3</sup> U.S. Renal Data System, USRDS 2018 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, NIH, NIDDK, Bethesda, Maryland, 2018.

<sup>&</sup>lt;sup>4</sup> Urological Diseases in America. NIDDK/NIH Publication Number 12-7865, 2012.

hospital clinics, and emergency departments in 2016,<sup>5</sup> as well as 15.9 million hospitalizations with a primary or secondary diagnosis.<sup>6</sup> Obesity affects nearly 40 percent of U.S. adults and over 18 percent of children and adolescents.<sup>7</sup> It is a strong risk factor for type 2 diabetes, fatty liver disease, including nonalcoholic steatohepatitis, 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 its vigorous pursuit of research to combat the diseases and disorders within its mission, being guided by the NIDDK Director's priorities: maintain a vigorous investigator-initiated research portfolio, support pivotal clinical studies and trials, promote a steady and diverse pool of talented new investigators, foster exceptional research training and mentoring opportunities, and ensure knowledge dissemination through outreach and communications.

#### The State of Research 20 Years Ago

There has been tremendous progress in NIDDK mission areas since 2000. At that time, there was no known way to treat or prevent type 2 diabetes, and there were many fewer treatment options for both type 1 and type 2 diabetes. There was no way to treat the root cause of cystic fibrosis (CF), and the median predicted life expectancy of a child born with CF was about 33 years of age.<sup>8</sup> There was a much more limited understanding of the genetic, physiological, and neurological bases for obesity, the major forms of diabetes mellitus, kidney and glomerular diseases, inflammatory bowel disease, non-alcoholic steatohepatitis, and other major NIDDK mission diseases.

#### The State of the Science Today

Revolutionary advances supported by NIDDK in the last 20 years have reshaped our understanding of diseases across the entire spectrum of the Institute's mission and in many cases have led to dramatic improvements in prevention and treatment. For example, the landmark Diabetes Prevention Program (DPP) clinical trial showed type 2 diabetes could be prevented or substantially delayed in many people at high risk for the disease. Translational research proved that an adaptation of the DPP lifestyle intervention can be delivered affordably, at scale, for millions of Americans with prediabetes, leading to the decision for Medicare to cover a program based upon this version of the DPP intervention for eligible beneficiaries. While those advances were making it possible to prevent or delay the disease, new oral and injected medications including improved insulins as well as technologies like the artificial pancreas and superior methods to monitor blood glucose control have transformed care of people with both type 1 and type 2 diabetes. According to a 2017 report from the Cystic Fibrosis

<sup>&</sup>lt;sup>5</sup> National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, CDC. <a href="https://www.cdc.gov/nchs/ahcd/index.htm">www.cdc.gov/nchs/ahcd/index.htm</a>

<sup>&</sup>lt;sup>6</sup> Healthcare Cost and Utilization Project, National Inpatient Sample, Agency for Healthcare Research and Quality. <a href="https://www.hcup-us.ahrq.gov/nisoverview.jsp">www.hcup-us.ahrq.gov/nisoverview.jsp</a>

<sup>&</sup>lt;sup>7</sup> Hales CM, et al. 2017. CDC. National Center for Health Statistics Data Brief No. 288.

<sup>&</sup>lt;sup>8</sup> www.cff.org/CF-Community-Blog/Posts/2017/Survival-Trending-Upward-but-What-Does-This-Really-Mean/

<sup>&</sup>lt;sup>9</sup> Knowler WC, et al. N Engl J Med 346: 393-403, 2002.

<sup>&</sup>lt;sup>10</sup> Ackermann RT, et al. Am J Prev Med 35: 357-363, 2008.

<sup>11</sup> www.govinfo.gov/content/pkg/FR-2017-11-15/pdf/2017-23953.pdf

<sup>&</sup>lt;sup>12</sup> Hermayer KL, et al. <u>Cleve Clin J Med</u> 83: S18-S26, 2016.

<sup>&</sup>lt;sup>13</sup> Mathieu C, et al. Nat Rev Endocrinol 13: 385-399, 2017.

<sup>&</sup>lt;sup>14</sup> Boughton CK, et al. Sci Transl Med 11: eaaw4949, 2009.

<sup>&</sup>lt;sup>15</sup> Rodbard D, et al. <u>Diabetes Technol Ther</u> 11:551-565, 2009.

Foundation, half of U.S. CF patients born between 2013 and 2017 will live for at least 44 years, an estimate that does not take into account potential benefits of new treatments continuing to enter the market.<sup>16</sup> Indeed, a new therapy was approved by the Food and Drug Administration (FDA) in October 2019 for 90 percent of CF patients age 12 or older based in part on work supported by industry as well as NIDDK and others.<sup>17</sup> Exponential growth in our knowledge of the microbiome has reshaped our understanding of its effects on digestive and metabolic health. For example, a recent study has shown that women with lean body types who eat high-fiber diets have complex, highly interactive bacterial networks in their gut microbiomes, and subsequent experiments in mice showed that these bacteria can impart resistance to obesity for several weeks on a high fat diet.<sup>18</sup> The NIDDK is supporting research to develop three-dimensional "chips" about the size of a thumb drive—that replicate the structure and function of human organs/tissues in a laboratory setting, such as islet, liver, kidney, intestinal, and pancreatic chips. These chips are among the latest technological advances that are rapidly increasing our understanding of key tissues and accelerating drug discovery. NIDDK's ReBuilding a Kidney Program, <sup>19</sup> for example, is using these technologies as a springboard to enhance renal repair and promote the generation of new nephrons with the goal of one day being able to restore function in people with kidney disease. The Accelerating Medicines Partnership Type 2 Diabetes Program is building on the long-term investment NIDDK has made in studying the genetics of type 2 diabetes to identify new targets for pharmaceutical development.<sup>20</sup>

#### **Vision for the Future**

Recent NIDDK-supported scientific discoveries are advancing progress toward prevention of type 1 diabetes.<sup>21</sup> Research on development and transplantation of insulin-producing beta cells may lead to a new era in therapy for type 1 diabetes that could greatly reduce the burden of the disease by restoring glucose-dependent insulin release from the pancreas. Future research may improve on type 2 diabetes prevention strategies and make it possible to target those approaches to those most likely to benefit. Progress in understanding the human gut microbiome, including how it changes over time in people with inflammatory bowel disease, is yielding important clues to the causes of the disease and identifying targets for therapy.<sup>22</sup> Indeed, recent results from a multi-center clinical study identified several patient characteristics, such as their clinical, genetic, and microbial profiles, that can predict how well children with ulcerative colitis, a form of inflammatory bowel disease, will respond to treatment, which opens doors to more personalized approaches for treating the disease.<sup>23</sup> Fundamental research on organ function and development, and production of "organoids" in a laboratory may usher in an era when it is possible to replace intestines damaged by inflammatory bowel disease, liver damaged by cirrhosis, or kidneys damaged by polycystic kidney disease using laboratory-generated, tissue-matched organs, without the need for a donor. For example, scientists have discovered that intestinal stem cells

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<sup>&</sup>lt;sup>16</sup> www.cff.org/Research/Researcher-Resources/Patient-Registry/2017-Cystic-Fibrosis-Foundation-Patient-Registry-Highlights.pdf

<sup>&</sup>lt;sup>17</sup> Keating, et al. N Engl J Med 379: 1612-1620, 2018.

<sup>&</sup>lt;sup>18</sup> Dugas LR, et al. <u>Sci Rep</u>:8: 17135, 2018.

<sup>19</sup> www.rebuildingakidney.org/

<sup>&</sup>lt;sup>20</sup> www.nih.gov/research-training/accelerating-medicines-partnership-amp/type-2-diabetes and www.type2diabetesgenetics.org/informational/about

<sup>&</sup>lt;sup>21</sup> Herold KC, et al. N Engl J Med 381: 603-613, 2019.

<sup>&</sup>lt;sup>22</sup> Lloyd-Price J, et al. Nature 569: 655-662, 2019.

<sup>&</sup>lt;sup>23</sup> Hyams JS, et al. <u>Lancet</u> 393: 1708-1720, 2019.

interact with nearby immune cells in a bi-directional manner that affects both the renewal of this stem cell source and remodeling of the intestinal lining during infection.<sup>24</sup>

Overall Budget Policy: The FY 2021 President's Budget request is \$1,924.2 million, excluding mandatory Type 1 Diabetes funding, a decrease of \$190.9 million or 9.0 percent 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**

#### 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.

In FY 2021, 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. Recent discoveries from such efforts include new insights into the link between diabetes and higher risk of dementia from research on a mouse model, which showed that insulin and the related hormone IGF-1 act in multiple parts of the brain to regulate blood sugar levels, memory, and other vital mind and body processes. Another study, with more than 300,000 individuals, found genetic factors combined to have a large impact on eventual weight gain during childhood, so that by middle age people in the highest 10 percent of genetic risk for obesity were 13 kg (about 28.5 pounds) heavier, on average, and had a 25-fold higher risk for severe obesity than the 10 percent of people in the lowest-risk group. NIDDK seeks to accelerate progress in obesity research by funding development of new quantitative assays to detect proteins involved in the body's maintenance of energy balance, including regulation of appetite, calorie burning, and other biological processes relevant to obesity.

With FY 2021 resources, NIDDK will continue major clinical and translational research studies in diabetes, endocrinology, and metabolic diseases. In a recent study involving thousands of women and children, researchers have found that elevated maternal blood glucose levels even below those meeting traditional gestational diabetes (GDM) diagnostic criteria increase the risk of future type 2 diabetes in mothers<sup>28</sup> and impaired glucose metabolism<sup>29</sup> and greater excess fat<sup>30</sup> in children 10 to 14 years post-delivery. NIDDK is cultivating new research in this area by establishing a new consortium that will employ cutting edge technology to ascertain the "profile"

<sup>&</sup>lt;sup>24</sup> Biton M, et al. Cell 175:1307-1320, 2018.

<sup>&</sup>lt;sup>25</sup> Soto M, et al. <u>PNAS</u> 116: 6379-6384, 2019.

<sup>&</sup>lt;sup>26</sup> Khera AV, et al. Cell 17: 587-596.e9, 2019.

<sup>&</sup>lt;sup>27</sup> www.grants.nih.gov/grants/guide/rfa-files/RFA-dk-19-001.html

<sup>&</sup>lt;sup>28</sup> Lowe WL, et al. <u>JAMA</u> 320: 1005-1016, 2018.

<sup>&</sup>lt;sup>29</sup> Lowe WL, et al. <u>Diabetes Care</u> 42: 372-380, 2019.

<sup>&</sup>lt;sup>30</sup> Lowe WL, et al. <u>Diabetologia</u> 62: 598-610, 2019.

of blood glucose levels in women across the span of pregnancy. <sup>31</sup> Such information could help lay the foundation for future clinical studies and trials evaluating new approaches to GDM screening, diagnosis, and intervention, with the goal of improving the health of women and their children. In major recent cystic fibrosis advances, researchers examined, in an animal model, whether it might be possible to maximize the clinical value of existing therapies by starting treatment before birth; <sup>32</sup> tested new, triple drug combinations in clinical trials with participants who have the  $\Delta F508$  mutation, one of which recently obtained FDA approval for use in people 12 and over with the most common CF-causing mutation; <sup>33,34,35</sup> and developed new candidate corrector drugs that could potentially raise CFTR channel levels in the majority of people with CF to normal or near-normal levels. <sup>36</sup>

Budget Policy: The FY 2021 President's Budget request for this program is \$662.5 million, a decrease of \$69.1 million or 9.4 percent compared with the FY 2020 Enacted level. With FY 2021 resources, NIDDK will continue major diabetes clinical trials. NIDDK will also continue its support of an ancillary study to the Glycemia Reduction Approaches in Diabetes (GRADE) study to examine how the correlation between hemoglobin A1c and average blood glucose differs by racial/ethnic heritage. NIDDK's plans for FY 2021 include continuing research that examines changes in blood glucose levels over the course of pregnancy that could inform future strategies for combating GDM, and research comparing bariatric surgery versus non-surgical approaches for treating type 2 diabetes to inform clinical decision making. In FY 2021, NIDDK will continue funding for research centers to advance research relevant to diabetes and to cystic fibrosis and other genetic metabolic diseases. NIDDK will also continue to fund translational research and support health information dissemination activities to bring scientific discoveries in diabetes and obesity to real-world medical practice and other community settings, along with other efforts as part of an overall balanced research program.

#### **Digestive Diseases and Nutrition**

The objectives of this program are to enhance understanding of liver and other digestive diseases, nutrition and obesity, and to develop and test strategies for disease prevention and treatment. This program supports basic, 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.

In FY 2021, NIDDK will continue to support research aimed at improving the prevention and treatment of diseases associated with the digestive system. For example, NIDDK's highly productive Inflammatory Bowel Disease Genetics Consortium will continue to gain further insights into the disease and potential ways to treat it.<sup>37</sup> Recent NIDDK-supported research has shown that components of a blood coagulation pathway are hyper-activated in people with

 $<sup>\</sup>frac{31}{2} \frac{\text{www.grants.nih.gov/grants/guide/rfa-files/rfa-dk-18-018.html and www.grants.nih.gov/grants/guide/rfa-files/rfa-dk-18-019.html}{2}$ 

<sup>&</sup>lt;sup>32</sup> Sun X, et al. Sci Transl Med 11: eaau7531, 2019.

<sup>&</sup>lt;sup>33</sup> Davies JC, et al. N Engl J Med 379: 1599-1611, 2018.

<sup>&</sup>lt;sup>34</sup> Keating D, et al. N Engl J Med 379: 1612-1620, 2018.

<sup>35 &</sup>lt;u>www.fda.gov/news-events/press-announcements/fda-approves-new-breakthrough-therapy-cystic-fibrosis</u>

<sup>&</sup>lt;sup>36</sup> Veit G, et al. <u>Nat Med</u> 24: 1732-1742, 2018.

<sup>&</sup>lt;sup>37</sup> www.grants.nih.gov/grants/guide/rfa-files/RFA-DK-16-029.html

inflammatory bowel disease, particularly those with active symptoms who do not respond to one of the major classes of medication used to treat the disease; this result points to a potential new avenue for treatment.<sup>38</sup>

Other NIDDK-supported digestive disease researchers have identified risk factors for rapid progression of pediatric pancreatitis<sup>39</sup> and showed that the progression of pediatric and adult forms of the disease can be very similar despite notable differences in these risk factors.<sup>40</sup> Among advances in research on liver diseases, scientists have identified gene variants present in infants with biliary atresia splenic malformation syndrome that may increase susceptibility to this severe and potentially deadly childhood liver disease, 41 and, in the largest, international druginduced liver injury genetic study to date, found that a genetic variant implicated in autoimmune diseases increases the risk of liver injury triggered by a range of drugs.<sup>42</sup> Through other studies, researchers have identified for the first time a direct line of communication between the gut and the brain that allows for rapid signaling of sensory information about food intake<sup>43</sup> and shown that despite similar weight loss, teens who underwent a form of bariatric surgery called Roux-en-Y gastric bypass were significantly more likely to have remission of type 2 diabetes and high blood pressure compared to adults who had the same procedure.<sup>44</sup> Advances such as these will pave the way for improvements in the prevention, diagnosis, and treatment of digestive diseases in FY 2021 and beyond.

#### Program Portrait: The Childhood Liver Disease Research Network (ChiLDReN)

FY 2020 Level: \$8.5 million FY 2021 Level: \$7.9 million Change: - \$0.6 million

Cholestatic liver diseases, in which bile cannot flow properly from the liver, are clinically devastating and potentially life-threatening in children. The causes and progression of these diseases are poorly understood, making them difficult to predict, diagnose, and treat with medication; therefore, they are the most common reasons for pediatric liver transplants. Furthermore, the rarity of these diseases presents a major hurdle to finding effective treatments because it is difficult for a single research center to recruit enough participants to conduct effective studies. To support larger multi-center studies that facilitate the discovery of new diagnostic, etiologic, and treatment options for children with liver diseases, the NIDDK established ChiLDReN<sup>45</sup> in FY 2009. This network continues, expands, and merges the Biliary Atresia Research Consortium and the Cholestatic Liver Disease Consortium while incorporating new studies on cystic fibrosis-associated liver disease. It is also training the next generation of investigators specializing in pediatric liver diseases. The Network's collaborative team of doctors, nurses, research coordinators, medical facilities, and patient support organizations has clinical sites and research labs across the United

<sup>&</sup>lt;sup>38</sup> Kaiko GE, et al. Sci Transl Med. 11: eaat0852, 2019.

<sup>&</sup>lt;sup>39</sup> Liu QY, et al. <u>J Pediatr Gastroenterol Nutr</u>. 69:206-211, 2019.

<sup>&</sup>lt;sup>40</sup> Schwarzenberg SJ, et al. <u>J Pediatr Gastroenterol Nutr.</u> 68:566-573, 2019.

<sup>&</sup>lt;sup>41</sup> Berauer JP, et al. Hepatology 70:899-910, 2019

<sup>&</sup>lt;sup>42</sup> Cirulli ET, et al. Gastroenterology 156:1707-1716, 2019.

<sup>&</sup>lt;sup>43</sup> Kaelberer MM, et al. <u>Science</u> 361: 1219-1227, 2018.

<sup>&</sup>lt;sup>44</sup> Inge TH, et al. N Engl J Med 380: 2136-2145, 2019.

<sup>45</sup> www.childrennetwork.org/

States and Canada. These sites are working together to improve the lives of children and families dealing with rare liver diseases.

ChiLDReN conducts natural history studies aimed at acquiring information and data that will provide a better understanding of pediatric liver conditions such as cholestasis, mitochondrial liver diseases, and cystic fibrosis-associated liver disease. The Network also conducts clinical trials to test treatments for liver diseases, including biliary atresia and Alagille Syndrome. Prior accomplishments of this Network include: the evaluation of the safety and efficacy of steroid use following hepatoportoenterostomy (surgery to restore bile flow) in children newly diagnosed with biliary atresia<sup>46</sup>; the assessment of the effectiveness of fat-soluble vitamin supplements in biliary atresia<sup>47</sup>; an evaluation of the safety and feasibility of an antibody-based therapy for biliary atresia<sup>48</sup>; and a clinical trial to test the efficacy and safety of a drug to treat excessive itching in Alagille Syndrome patients.<sup>49</sup> (Because results from this trial were promising, the long-term safety, tolerability, and durability of effect of this drug is under evaluation.) Additionally, ChiLDReN developed a robust biospecimen repository with biliary atresia patient DNA specimens, liver tissue samples from the range of liver diseases under study, and bile duct tissue samples from children with biliary atresia. Basic science advances from the Network include insights into the genetics of pediatric liver diseases. For example, scientists participating in ChiLDReN recently identified gene variants present in infants with biliary atresia splenic malformation syndrome (BASM) that may increase susceptibility to this potentially deadly childhood liver disease. This study offers clues into the causes of BASM and could help identify children who would be at risk.<sup>50</sup>

The Network also receives funding for specific studies from the Cystic Fibrosis Foundation and the Alpha-1 Foundation. NIDDK support of the Network was renewed in FY 2014 and again in FY 2019.

Budget Policy: The FY 2021 President's Budget request for this program is \$555.4 million, a decrease of \$57.9 million or 9.4 percent compared with the FY 2020 Enacted level. In FY 2021, NIDDK will continue major clinical research networks to help understand and treat liver diseases. Among its obesity-related efforts in FY 2021, NIDDK will continue to pursue research to understand factors in infancy and early childhood that influence obesity development. NIDDK will also use FY 2021 funds to support an ongoing clinical trial comparing three treatments for fecal incontinence toward informing clinical decision making by patients and their health care providers. Research on intestinal stem cells and the lymphatic system in digestive health and disease, which can benefit a variety of digestive diseases, will continue in FY 2021, along with other efforts as part of an overall balanced research program.

#### 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. Basic, clinical, and translational research, as well as research training, are supported in the areas of 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/bladder pain syndrome, stones, impotence, congenital urologic disorders, and urinary tract infections; and disorders of the blood and blood-forming

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<sup>&</sup>lt;sup>46</sup> Bezerra JA, et al. JAMA. 311:1750-1759, 2014.

<sup>&</sup>lt;sup>47</sup> Shneider BL, et al. Pediatrics 130:e607-614, 2012.

<sup>&</sup>lt;sup>48</sup> Mack CL, et al. <u>J Pediatr Gastroenterol Nutr</u> 68:495-501, 2019.

<sup>&</sup>lt;sup>49</sup> Shneider BL, et al. Hepatol Commun 2:1184-1198, 2018.

<sup>&</sup>lt;sup>50</sup> Berauer JP, et al. <u>Hepatology</u> 70:899-910, 2019.

organs, including sickle cell disease, Cooley's anemia, hemochromatosis, and the anemia of inflammation and chronic disease.

In recent kidney disease research, NIDDK-supported scientists found that known biomarkers of damage to the kidney's filtration units were associated with mortality but not with cardiovascular risk.<sup>51</sup> In women's urology research, it was discovered that the presence of fungi in urine samples was a predictor of symptom severity in interstitial cystitis/bladder pain syndrome.<sup>52</sup> Findings in men's urology included that individuals with benign prostatic hyperplasia whose symptoms worsen despite treatment with two standard drugs might have a form of the condition characterized by prostate fibrosis;<sup>53</sup> and that in a mouse model prostate fibrosis can result from an *E. coli* infection of the urinary tract.<sup>54</sup> Investigators have also developed a laboratory culture method for dramatically expanding numbers of blood stem cells from mice, a finding which might one day transform bone marrow transplant therapies if shown to be effective in humans as well.<sup>55</sup> Such robust progress in the kidney, urologic, and hematologic diseases will continue in FY 2021.

Activities in this portfolio will support the Administration's focus on advancing kidney health with patients with CKD and kidney failure. The HHS initiative to transform kidney health will focus on reducing the risk of kidney failure through research and prevention, improving access to quality treatment options, and increasing access to kidney transplantation. In support of these ends, the NIDDK issued a notice of special interest on Next-Generation Approaches to Renal Replacement Therapy Including Vascular Access, <sup>56</sup> which seeks to elicit small business grant applications to develop innovative approaches to treating ESRD and addressing critical accompanying challenges such as vascular access and fluid management during dialysis. Other efforts described below, including the APOL1 Long-term Kidney Transplantation Outcomes Network and the Kidney Precision Medicine Program, also support the overall goal of HHS to transform the way we prevent and treat kidney diseases.

#### Program Portrait: The APOL1 Long-term Kidney Transplantation Outcomes Network (APOLLO)

FY 2020: \$3.9 million FY 2021: \$3.6 million Change: -\$0.3 million

African Americans have higher rates of ESRD than European Americans, but for many years the reasons for this health disparity were largely unknown. In 2008, researchers reported that genetic variations on chromosome 22, later revealed to be in the *apolipoprotein LI (APOL1)* gene, were linked to a greater incidence of non-diabetic kidney disease among African Americans. These *APOL1* variants are among the only known genetic factors contributing to the well-appreciated health disparities in kidney diseases, and their identification is arguably the most important discovery about the pathogenesis of chronic kidney disease over the past several decades.

<sup>&</sup>lt;sup>51</sup> Jotwani VK, et al. Am J Nephrol. 49:346-355, 2019.

<sup>&</sup>lt;sup>52</sup> Nickel JC, et al. World J Urol. doi: 10.1007/s00345-019-02764-0, 2019. [Epub ahead of print]

<sup>&</sup>lt;sup>53</sup> Macoska JA, et al. <u>J Urol</u>. 2019 Jun 12:101097JU0000000000385, 2019. [Epub ahead of print]

<sup>&</sup>lt;sup>54</sup> Bell-Cohn A, et al. Am J Physiol Renal Physiol 316:F682-F692, 2019.

<sup>&</sup>lt;sup>55</sup> Wilkinson AC, et al. Nature 571:117-121, 2019.

<sup>&</sup>lt;sup>56</sup> https://grants.nih.gov/grants/guide/notice-files/NOT-DK-19-027.html

In the years since the initial groundbreaking discovery of APOL1 risk variants, numerous NIDDKsupported studies have shed light on their important roles in disease risk, as well as the underlying mechanisms of APOL1 protein function. Some evidence suggested that kidneys donated from people with high-risk APOL1 variants fare poorly after transplantation. However, the studies on recipient health have been limited, and the potential long-term risks to a living kidney donor carrying these APOL1 risk variants has been unclear. To comprehensively assess effects of APOL1 gene variants on the risk of kidney transplant failure, the NIDDK, with additional support from the National Institute of Allergy and Infectious Diseases and the National Institute on Minority Health and Health Disparities in 2016 launched the APOL1 Long-term Kidney Transplantation Outcomes Network, or APOLLO. The study will measure in kidney transplant recipients the rates of changes in kidney function, transplant rejection, and return to dialysis. APOLLO will also study the impact of APOL1 variants on the health of living kidney donors. The results of APOLLO will inform clinical practice by letting patients, transplant physicians, and potential kidney donors know whether individuals with APOL1 variants should be considered as living kidney donors, for their own health or the recipient's health. More precise quantification of the risks of poor outcomes related to donor/recipient APOL1 variant status will enhance the efficacy of the allocation of precious donor kidneys. Patient recruitment for APOLLO began in FY 2019 and will continue in FY 2021; the median recipient follow-up time will be four years.

Budget Policy: The FY 2021 President's Budget request for this program is \$430.3 million, a decrease of \$44.9 million or 9.4 percent compared with the FY 2020 Enacted level. In FY 2021, NIDDK will continue support for ongoing major clinical studies of CKD in adults and children. NIDDK also plans to continue its Kidney Precision Medicine Project to improve the scientific knowledge base of kidney diseases, the clinical utility of kidney biopsies, and the pipeline of new drugs for treatment, toward a long-term goal of personalizing care for people with kidney disease. NIDDK also plans to continue its support of research networks focused on enhancing understanding of glomerular diseases, urologic chronic pelvic pain syndrome (UCPPS), and lower urinary tract symptoms. Centers focused on kidney, urologic, and hematologic research will receive continued funding. FY 2021 funds will also be used to support research to understand normal kidney function and disease progression, and research to generate or repair nephrons that can function within the kidney, along with other efforts as part of an overall balanced research program.

#### **Special Statutory Funding Program for Type 1 Diabetes Research**

Complementing efforts of the Diabetes, Endocrinology, and Metabolic Disease program, the overarching goal of the Special Diabetes Program (SDP) 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; 2) preventing or reversing the disease; 3) developing cell replacement therapy; 4) improving management and care; 5) preventing or reducing diabetes complications; and 6) attracting new talent and applying new technologies to research. Although focused on type 1 diabetes, aspects of this research are relevant to type 2 diabetes and other autoimmune disorders. For example, people with type 2 diabetes could benefit from research developing novel artificial pancreas technologies and other diabetes management technologies. In a study with even broader applicability, researchers investigating possible causes of type 1

diabetes have published new details about how environmental factors such as breastfeeding affect the microbes in the gut (*i.e.* the gut "microbiome") as children age. <sup>57,58</sup>

Recent efforts supported by SDP are greatly expanding our understanding of autoimmunity in type 1 diabetes. Research using a sophisticated novel imaging technology enabled scientists to measure over 30 cellular markers simultaneously, allowing them to visualize different pancreatic cell types and immune cells involved in the autoimmune attack in type 1 diabetes that destroys insulin-producing beta cells. Results from these studies confirmed that there were significant differences in the number and types of cells found in the pancreases of different individuals with type 1 diabetes, indicating the heterogeneity of the disease. Sp,60 Clinical research is also showing that patients may benefit from therapies that interfere with autoimmunity: a clinical trial found that treatment with an anti-CD3 monoclonal antibody (teplizumab) that targets the immune system slowed the progression to clinical type 1 diabetes by two or more years in high-risk individuals—the first demonstration that clinical type 1 diabetes can be delayed. Additional research could build on this result to determine the long-term effects of this treatment and its mechanism of action and to further understand the role of autoimmunity in type 1 diabetes.

<u>Budget Policy</u>: The FY 2021 President's Budget request for the Special Statutory Funding Program for Type 1 Diabetes Research proposes an extension of the program providing \$150.0 million in FY 2021.

#### **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. Recently, IRP scientists compared the effects of a diet of ultra-processed food with a diet of unprocessed or minimally-processed foods and found that people consumed more calories per day and gained weight on the ultra-processed diet, while losing weight on the unprocessed food diet;<sup>62</sup> determined the three-dimensional structure of a protein complex that copies DNA—a fundamental molecular process required by all biological organisms; 63 calculated the rate of anticipated and unanticipated mutations generated by use of emerging DNA editing methods, providing important information to consider when deciding which technology to choose for research and, potentially, for future clinical use in repairing errors in the genetic code;<sup>64</sup> and contributed to discovering the cause of a rare inherited disease, while demonstrating that some

<sup>&</sup>lt;sup>57</sup> Stewart CJ, et al. Nature 562: 583-588, 2018.

<sup>&</sup>lt;sup>58</sup> Vatanen T, et al.. Nature 562: 589-594, 2018.

<sup>&</sup>lt;sup>59</sup> Damond N, et al. Cell Metab 29: 755-768.e5, 2019.

<sup>&</sup>lt;sup>60</sup> Wang YJ, et al. Cell Metab 29: 769-783.e4, 2019.

<sup>&</sup>lt;sup>61</sup> Herold KC, et al. N Engl J Med 381: 603-613, 2019.

<sup>&</sup>lt;sup>62</sup> Hall KD, et al. Cell Metab. 30: 67-77, 2019.

<sup>63</sup> Gao Y, et al. <u>Science</u> 363: pii: eaav7003, 2019.

<sup>&</sup>lt;sup>64</sup> Lee HK, et al. Nat Commun 9: 4804, 2018.

disease causing mutations will not be found by rapid methods that analyze only protein encoding parts of the genome but many can still be discovered by analyzing regions around genes as well.<sup>65</sup> In FY 2021, the Intramural Research Program will continue to advance research in these and other areas.

<u>Budget Policy</u>: The FY 2021 President's Budget request for this program is \$200.0 million, a decrease of \$15.0 million or 7.0 percent compared with the FY 2020 Enacted level.

#### **Research Management and Support**

Research Management and Support (RMS) activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, research 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 its administrative support of meritorious basic, clinical, and translational research and research training efforts, and continues its communication of research-based health information to patients, health professionals, and the public.<sup>66</sup>

<u>Budget Policy</u>: The FY 2021 President's Budget request for this program is \$76.0 million, a decrease of \$4.0 million or 5.0 percent compared with the FY 2020 Enacted level.

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<sup>&</sup>lt;sup>65</sup> van Kuilenburg ABP, et al. <u>N Engl J Med</u> 380: 1433-1441, 2019.

<sup>66</sup> www.niddk.nih.gov/health-information

# Budget Authority by Object Class<sup>1</sup> (Dollars in Thousands)

		FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Total con	mpensable workyears:			
	Full-time equivalent	660	660	0
	Full-time equivalent of overtime and holiday hours	1	1	0
	Average ES salary	\$198	\$201	\$3
	Average GM/GS grade	12.0	12.0	0.0
	Average GM/GS salary	\$115	\$117	\$2
	Average salary, grade established by act of July 1,	\$104	¢107	¢2
	1944 (42 U.S.C. 207)	\$104	\$107	\$3
	Average salary of ungraded positions	\$154	\$156	\$2
	OBJECT CLASSES	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
	Personnel Compensation			
11.1	Full-Time Permanent	44,453	44,961	508
11.3	Other Than Full-Time Permanent	40,327	40,789	462
11.5	Other Personnel Compensation	3,155	3,191	36
11.7	Military Personnel	1,115	1,150	35
11.8	Special Personnel Services Payments	13,001	12,001	-1,000
11.9	Subtotal Personnel Compensation	\$102,051	\$102,092	\$41
12.1	Civilian Personnel Benefits	31,270	32,980	1,710
12.2	Military Personnel Benefits	817	843	26
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	\$134,138	\$135,915	\$1,777
21.0	Travel & Transportation of Persons	2,460	2,180	-280
22.0	Transportation of Things	179	157	-22
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	0	0	0
23.3	Communications, Utilities & Misc. Charges	318	280	-38
24.0	Printing & Reproduction	13	11	-2
25.1	Consulting Services	620	495	-125
25.2	Other Services	29,143	22,412	-6,731
25.3	Purchase of goods and services from government accounts	189,060	181,513	-7,547
25.4	Operation & Maintenance of Facilities	2,340	1,800	-540
25.5	R&D Contracts	18,954	14,807	-4,147
25.6	Medical Care	1,060	900	-160
25.7	Operation & Maintenance of Equipment	4,796	4,185	-611
25.8	Subsistence & Support of Persons	45	41	-4
25.0	Subtotal Other Contractual Services	\$246,017	\$226,152	-\$19,865
26.0	Supplies & Materials	13,258	10,150	-3,108
31.0	Equipment	11,616	10,154	-1,462
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	1,707,146	1,539,211	-167,935
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	\$1,981,009	\$1,788,297	-\$192,712
	Total Budget Authority by Object Class	\$2,115,146	\$1,924,211	-\$190,935

 $<sup>^{\</sup>mbox{\scriptsize 1}}$  Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

# 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)	\$44,453	\$44,961	\$508
Other Than Full-Time Permanent (11.3)	40,327	40,789	462
Other Personnel Compensation (11.5)	3,155	3,191	36
Military Personnel (11.7)	1,115	1,150	35
Special Personnel Services Payments (11.8)	13,001	12,001	-1,000
Subtotal Personnel Compensation (11.9)	\$102,051	\$102,092	\$41
Civilian Personnel Benefits (12.1)	\$31,270	\$32,980	\$1,710
Military Personnel Benefits (12.2)	817	843	26
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	\$134,138	\$135,915	\$1,777
Travel & Transportation of Persons (21.0)	\$2,460		-\$280
Transportation of Things (22.0)	179	157	-22
Rental Payments to Others (23.2)	0	0	0
Communications, Utilities & Misc. Charges (23.3)	318	280	-38
Printing & Reproduction (24.0)	13	11	-2
Other Contractual Services:			
Consultant Services (25.1)	570	450	-120
Other Services (25.2)	29,143	22,412	-6,731
Purchases from government accounts (25.3)	126,856	117,206	-9,650
Operation & Maintenance of Facilities (25.4)	2,340	1,800	-540
Operation & Maintenance of Equipment (25.7)	4,796	4,185	-611
Subsistence & Support of Persons (25.8)	45	41	-4
Subtotal Other Contractual Services	\$163,749	\$146,093	-\$17,656
Supplies & Materials (26.0)	\$13,258	\$10,150	-\$3,108
Subtotal Non-Pay Costs	\$179,977	\$158,871	-\$21,106
Total Administrative Costs	\$314,115	\$294,786	-\$19,329

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

	]	FY 2019 Fina	l	FY 2020 Enacted		FY 2021 President's Budget			
OFFICE/DIVISION	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Diabetes, Endocrinology, and Metabolic Diseases									
Direct:	27	-	27	30	-	30	30	-	30
Reimbursable:	3	-	3	3	-	3	3	-	3
Total:	30	-	30	33	-	33	33	-	33
Division of Digestive Diseases and Nutrition									
Direct:	23	2	25	26	2	28	26	2	28
Division of Extramural Activities									
Direct:	66	-	66	73	-	73	73	-	73
Division of Intramural Research Programs									
Direct:	337	8	345	352	8	360	352	8	360
Division of Kidney, Urologic, and Hematologic Diseases									
Direct:	24	-	24	27	-	27	27	-	27
Office of the Director									
Direct:	131	-	131	139	-	139	139	-	139
Total	611	10	621	650	10	660	650	10	660
Includes FTEs whose payroll obligations are supported by the N	NIH Common	Fund.							
FISCAL YEAR	Average GS Grade								
2017	12.0								
2018	12.0								
2019	12.0								
2020		12.0							
2021		12.0							

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

GRADE	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	192,254	197,637	200,661
GM/GS-15	60	64	64
GM/GS-14	63	66	66
GM/GS-13	102	105	105
GS-12	71	75	76
GS-11	34	35	35
GS-10	0	0	0
GS-9	21	23	23
GS-8	14	16	16
GS-7	13	14	14
GS-6	3	3	3
GS-5	3	3	3
GS-4	1	4	3
GS-3	2	3	3
GS-2	0	0	0
GS-1	2	1	1
Subtotal	389	412	412
Grades established by Act of July 1, 1944 (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	4	6	6
Senior Grade	0	0	0
Full Grade	2	2	2
Senior Assistant Grade	2	2	2 2
Assistant Grade	0	0	0
Subtotal	8	10	10
Ungraded	228	242	242
Total permanent positions	383	407	407
Total positions, end of year	626	665	665
Total full-time equivalent (FTE) employment, end of year	621	660	660
Average ES salary	192,254	197,637	200,661
Average GM/GS grade	12.0	12.0	12.0
Average GM/GS salary	111,901	115,034	116,794

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