DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund (CF)

NOTE: The FY 2016 Enacted funding amounts cited throughout this chapter reflect the effects of OAR HIV/AIDS Transfers.

NATIONAL INSTITUTES OF HEALTH
FY 2017 Congressional Justification
Common Fund

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2015 Actual		FY 2016 Enacted		FY 2017 President's Budget[3]		FY 2017 +/- FY 2016	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	264	$162,896	281	$173,095	339	$208,948	58	$35,853
Administrative Supplements	*(66)*	11,549	*(47)*	8,262	*(37)*	6,436	*(-10)*	-1,826
Competing:								
Renewal								
New	155	151,807	171	167,326	171	167,449		123
Supplements								
Subtotal, Competing	155	$151,807	171	$167,326	171	$167,449		$123
Subtotal, RPGs	419	$326,253	452	$348,683	510	$382,833	58	$34,150
SBIR/STTR								
Research Project Grants	419	$326,253	452	$348,683	510	$382,833	58	$34,150
Research Centers:								
Specialized/Comprehensive	35	$78,163	28	$62,159	28	$62,480		$321
Clinical Research	10	22,715						
Biotechnology	3	5,773	1	2,651	1	3,000		349
Comparative Medicine	3	9,237						
Research Centers in Minority Institutions								
Research Centers	51	$115,887	29	$64,810	29	$65,480		$670
Other Research:								
Research Careers	31	$4,727	28	$4,237	17	$2,617	-11	-$1,620
Cancer Education								
Cooperative Clinical Research								
Biomedical Research Support								
Minority Biomedical Research Support								
Other	95	41,932	309	136,449	365	161,397	56	24,948
Other Research	126	$46,659	337	$140,686	382	$164,014	45	$23,328
Total Research Grants	596	$488,799	818	$554,179	921	$612,327	103	$58,148
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards								
Institutional Awards	81	12,681	169	26,381	191	29,823	22	3,442
Total Research Training	81	$12,681	169	$26,381	191	$29,823	22	$3,442
Research & Develop. Contracts		$11,387		$50,063		$86,676		$36,612
(SBIR/STTR) (non-add)[2]								
Intramural Research		$15,008		$17,419		$15,900		-$1,519
Res. Management & Support		17,764		27,598		30,914		3,316
Res. Management & Support (SBIR Admin) (non-add)[2]								
Office of the Director - Appropriation[2]								
Office of the Director - Other								
ORIP/SEPA (non-add)[2]								
Common Fund (non-add)[2]								
Buildings and Facilities								
Appropriation								
Type 1 Diabetes								
Program Evaluation Financing								
Cancer Initiative Mandatory Financing								
Other Mandatory Financing						-210,000		-210,000
Subtotal, Labor/HHS Budget Authority		**$545,639**		**$675,639**		**$565,639**		**-$110,000**
Interior Appropriation for Superfund Res.								
Total, NIH Discretionary B.A.		**$545,639**		**$675,639**		**$565,639**		**-$110,000**
Type 1 Diabetes								
Proposed Law Funding								
Cancer Initiative Mandatory Financing								
Other Mandatory Financing						210,000		210,000
Total, NIH Budget Authority		**$545,639**		**$675,639**		**$775,639**		**$100,000**
Program Evaluation Financing								
Total, Program Level		**$545,639**		**$675,639**		**$775,639**		**$100,000**

[1] All Subtotal and Total numbers may not add due to rounding.
[2] All numbers in italics and brackets are non-add.
[3] Includes mandatory financing.

Major Changes in the Fiscal Year 2017 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 2017 President's Budget for the Common Fund, which is $100.000 million more than the FY 2016 Enacted level, for a total of $775.639 million. The increase is requested to expand the Precision Medicine Initiative Cohort Program.

Research Project Grants (+$34.150 million; total $382.833 million): The Common Fund expects to support a total of 510 Research Project Grant (RPG) awards in FY 2017. Noncompeting RPGs will increase by 58 awards and $35.853 million. New RPGs will be awarded in Common Fund programs to be launched in FY 2017 as well as in new initiatives within ongoing Common Fund programs, including the Precision Medicine Initiative Cohort Program.

Other Research (+$23.328 million; total $164.014 million): The estimated increase in Common Fund support for the Other Research mechanism includes a request to increase use of Other Transaction Authority (OTA) by the Precision Medicine Initiative Cohort Program and the Stimulating Peripheral Activity to Relieve Conditions (SPARC) Program.

Research and Development Contracts (+$36.612 million; total $86.676 million): The estimated increase in Common Fund support for Research and Development Contracts is intended to support efforts under the Precision Medicine Initiative Cohort Program.

National Institutes of Health
Common Fund by Initiative
(Dollars in Thousands)

(Dollars in Thousands)	FY 2015 Actual	FY 2016 Enacted	FY 2017 President's Budget
Big Data to Knowledge (BD2K)			
Big Data to Knowledge (BD2K)	40,792	62,961	69,136
Pediatric Research Program			
Gabriella Miller Kids First Research Act	12,726	13,108	12,994
Genotype-Tissue Expression (GTEx) Resources			
Genotype-Tissue Expression (GTEx) Resources	11,101	4,114	1,289
Global Health			
Medical Education Partnership Initiative (MEPI)	3,000	3,000	3,000
Human Heredity and Health in Africa (H3Africa)	9,602	8,478	3,262
Cookstoves Initiative	0	1,825	2,325
Subtotal, Global Health	12,602	13,303	8,587
Glycoscience			
Accelerating Translation of Glycoscience: Integration and Accessibility	9,337	19,862	19,877
Health Economics			
Changing Incentives for Consumers, Insurers, and Providers	70	84	167
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	2,346	2,474	1,547
Economics of Prevention	2,622	2,392	1,180
Data Infrastructure to Enable Research on Health Reform	78	415	525
Subtotal, Health Economics	5,117	5,365	3,419
High-Risk Research			
NIH Director's Pioneer Award	23,984	10,877	10,871
NIH Director's New Innovator Award Program	87,723	91,797	90,300
Transformative R01's	44,486	39,432	30,748
NIH Director's Early Independence Award Program	21,069	19,217	21,546
Subtotal, High-Risk Research	177,262	161,323	153,465
Illuminating the Druggable Genome			
Knowledge Management Network	3,305	3,222	0
Technology Development	3,046	2,586	0
Subtotal, Illuminating the Druggable Genome	6,351	5,808	0
Knockout Mouse Phenotyping Program			
Production, Characterization, and Cryopreservation	9,693	0	0
Phenotyping and Data Release	6,507	0	0
Data Coordination	525	1,262	1,262
Production, Characterization, Cryopreservation, Phenotyping, and Data Release	0	6,738	9,738
Subtotal, Knockout Mouse Phenotyping Program	16,725	8,000	11,000
Metabolomics			
Comprehensive Metabolomics Research Cores	10,917	9,890	4,785
Interdisciplinary Training in Metabolomics	4,409	3,555	2,001
Metabolomics Technology Development	2,503	1,927	0
Metabolomics Reference Standards Synthesis	1,926	1,929	1,981
Metabolomics Data Sharing and Program Coordination Core	1,049	2,264	1,614
Subtotal, Metabolomics	20,804	19,565	10,381

National Institutes of Health
Common Fund by Initiative
(Dollars in Thousands)

(Dollars in Thousands)	FY 2015 Actual	FY 2016 Enacted	FY 2017 President's Budget
Molecular Transducers of Physical Activity			
Study Coordination and Data Management	0	0	887
Molecular Transducers of Physical Activity in Humans – Clinical Study	0	0	1,213
Chemical Analysis of Biological Samples	0	0	609
Characterization of Human Molecular Transducers of Physical Activity in Model Systems	0	0	113
Subtotal, Molecular Transducers of Physical Activity	0	0	2,821
Precision Medicine Initiative Cohort Program			
Precision Medicine Initiative Cohort Program	0	130,000	230,000
Protein Capture			
Antigen Production	71	50	50
Production of anti-TF antibodies	3,010	96	4,099
New Reagent Technology Development and Piloting	58	60	33
Subtotal, Protein Capture	3,138	207	4,182
Science of Behavior Change			
Mechanisms of Change	0	0	0
Science of Behavior Change 2	6,964	5,782	13,085
Subtotal, Science of Behavior Change	6,964	5,782	13,085
Single Cell Analysis			
Pilot Studies to Evaluate Cellular Heterogeneity	6,219	6,027	0
Exceptionally Innovative Tools and Technologies for Single Cell Analysis	4,535	2,893	0
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	7,600	5,335	0
Single Cell Analysis Challenges	96	0	0
Subtotal, Single Cell Analysis	18,449	14,255	0
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions			
Functional and Anatomical Mapping of Five Organ Systems	9	11,064	19,905
Next Generation Tools	3,092	8,077	11,079
Off-Label Use of Existing Market-Approved Technology for Small Markets	205	207	3,205
Data Coordination	79	83	2,079
Subtotal, S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	3,385	19,431	36,268
4D Nucleome			
Technology Development, Biological Validation, Modeling and Pilot Mapping	10,646	10,163	10,038
Nucleomic, Imaging, and Computational Tool Development	9,939	10,075	10,068
4D Nucleome Coordination and Integration	4,699	7,710	7,834
Subtotal, 4D Nucleome	25,285	27,948	27,940
Enhancing the Diversity of the NIH-Funded Workforce			
BUILD Initiative	44,508	47,786	48,419
National Research Mentoring Network (NRMN)	3,061	2,696	2,298
Coordination and Evaluation Center (CEC)	2,026	1,311	2,287
Subtotal, Enhancing the Diversity of the NIH-Funded Workforce	49,595	51,794	53,004
Epigenomics			
Mapping Centers	22	0	0
Human Health and Disease	2,960	54	0
Technology Development in Epigenetics	0	0	0
Pharmacology	4,519	3,946	4,000
Subtotal, Epigenomics	7,500	4,000	4,000

National Institutes of Health
Common Fund by Initiative
(Dollars in Thousands)

(Dollars in Thousands)	FY 2015 Actual	FY 2016 Enacted	FY 2017 President's Budget
Extracellular RNA Communication			
Data Management and Resource/Repository (DMRR)	3,437	2,513	2,375
Reference Profiles of Human Extracellular RNA	4,357	4,075	4,078
Extracellular RNA Biogenesis, Biodistribution, Uptake, and Effector Function	7,019	7,179	7,173
Clinical Utility of Extracellular RNAs as Biomarkers and Therapeutic Agents	13,927	16,057	16,132
Subtotal, Extracellular RNA Communication	28,740	29,823	29,757
Gulf Long-term Follow-up of Workers Study			
Gulf Long-term Follow-up of Workers Study	3,000	0	0
Health Care Systems Research Collaboratory			
NIH-HMORN Coordinating Center	2,384	2,445	1,800
Expansion Activities	10,427	9,985	10,285
Subtotal, Health Care Systems Research Collaboratory	12,811	12,430	12,085
Human Microbiome			
Sequence a Reference Set of Genomes	0	0	0
Evaluation of multi-'omic data in understanding the microbiome's role in health and disease	11,321	171	133
Subtotal, Human Microbiome	11,321	171	133
Library of Integrated Network-Based Cellular Signatures (LINCS)			
Perturbation-Induced Data and Signature Generation Centers (U54)	11,007	10,000	10,000
Nanomedicine			
Nanomedicine Development Centers	115	40	0
NIH Center for Regenerative Medicine (NCRM)			
NIH Center for Regenerative Medicine (NCRM)	206	0	0
Cell Therapy Projects	1,249	1,250	1,250
Cell-Based Screenings	3,000	6,750	6,750
Subtotal, NIH Center for Regenerative Medicine (NCRM)	4,455	8,000	8,000
Regulatory Science			
Microphysiological Systems for Drug Efficacy and Toxicity Testing	4,000	4,000	0
Undiagnosed Disease Program			
Undiagnosed Diseases Program Network	29,079	29,900	28,700
Training in the Use of Contemporary Genomic Approaches to Rare Disease Diagnostics	900	900	900
Subtotal, Undiagnosed Disease Program	29,979	30,800	29,600
Strengthening the Biomedical Research Workforce			
Director’s Workforce Innovation Award to Enhance Biomedical Research Training	6,256	6,750	6,750
Strategic Planning Funds	6,824	6,800	6,800
Subtotal Common Fund	545,639	675,639	764,572
New Initiatives in Common Fund	0	0	11,067
Total Common Fund	545,639	675,639	775,639

Justification of Budget Request

Common Fund

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

Budget Authority (BA):

	FY 2015 Actual	FY 2016 Enacted	FY 2017 President's Budget	FY 2017 +/- FY 2016
BA	$545,639,000	$675,639,000	$775,639,000	$100,000,000
FTE	0	0	0	0

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

Overview

The NIH Common Fund (CF) supports research in areas of emerging scientific opportunities, rising public health challenges, and knowledge gaps that deserve special emphasis; that would benefit from strategic coordination and planning across NIH ICs; and that are designed to address specific, high-impact goals and milestones within a 5- to 10-year timeframe.[1] Collectively, these programs represent strategic investments aimed at solving problems or building resources to affect research throughout the entire biomedical research enterprise. CF programs attempt to change the way science is conducted through the establishment of new scientific fields or paradigms, the development of new and innovative technologies that change the way scientists approach their work, or the generation of comprehensive data sets or other resources that catalyze all research and enable discovery.

Many CF programs support the NIH Director's priority themes for FY 2017:

1) Foundation for Discoveries: Basic Research
2) The Promise of Precision Medicine
3) Applying Big Data and Technology to Improve Health
4) Stewardship to Inspire Public Trust

Significant efforts are being made to evaluate programs during their lifetime, and outcomes are assessed as programs end. Funds freed as programs end or move to other sources of support will be available in FY 2017 for new challenges and opportunities.

[1] https://commonfund.nih.gov/

Overall Budget Policy: The FY 2017 President's Budget Request for CF is $775.639 million, an increase of $100.000 million or 14.8 percent compared to the FY 2016 Enacted level. CF will continue to support high-priority research with trans-NIH relevance in FY 2016. As mature programs transition out of CF, new programs are being established through strategic planning activities that identify potentially transformative areas of research where limited-term Common Fund investment can have a catalytic impact.

Selected Program Descriptions and Accomplishments

CF supports approximately 30 programs, most of which consist of a series of integrated initiatives that collectively address a set of goals that aim to transform the way research is conducted, the way that health and disease are understood, and/or the way that diseases are diagnosed or treated. These programs span a wide range of biomedical research fields, and encompass both basic and translational research. Highlighted below are programs that exemplify the science supported in FY 2017, and which involve budget shifts of $3 million or more compared to FY 2016. Also included are CF programs that may be supported in a second stage to address additional scientific challenges and opportunities.

Big Data to Knowledge (BD2K)

As biomedical tools and technologies rapidly improve, researchers are producing and analyzing an ever-expanding amount of complex biological data called "big data." As one component of an NIH-wide strategy, CF, in concert with NIH ICs, is supporting the Big Data to Knowledge (BD2K) program. The program goal is to facilitate broad use of biomedical big data, develop and disseminate analysis methods and software, enhance training in techniques associated with big data usage, and establish a network of collaborating centers of excellence.[2] The expectation is that implementation of BD2K will result in sweeping cultural changes in the way the biomedical research community shares, accesses, queries, cites, and analyzes data. In FY 2017, the program will support development of big data software, reference datasets, and data analysis and dissemination methods. The program will work to make big data software innovations available and user-friendly. It will also support innovative approaches to advance biomedical science using crowdsourcing and interactive digital media. The CF is also supporting NIH efforts through BD2K to create a comprehensive data commons for NIH data resources.

Budget Policy: The FY 2017 President's Budget Request is $69.136 million for the BD2K program from the Common Fund, an increase of $6.175 million or 9.8 percent compared to the FY 2016 Enacted level. This estimated increase in funding will be used to support activities described above.

Gabriella Miller Kids First Pediatric Research

In FY 2015, in accordance with the Gabriella Miller Kids First Research Act, Congress appropriated $12.600 million to the CF to support pediatric research. The Gabriella Miller Kids First Pediatric Research (Kids First) program is using big data approaches that will ultimately enable a more precise understanding of pediatric conditions. It is developing a "big data"

[2] https://commonfund.nih.gov/bd2k/index

resource for the pediatric research community that will also stimulate basic research.[3] This data resource will consist of well-curated clinical and genetic sequence data that will allow scientists to identify pathways underlying specific pediatric conditions and also to uncover shared pathways between seemingly disparate conditions. The Kids First program focuses on childhood cancers and structural birth defects. The fields of pediatric oncology and developmental biology, which studies disorders like birth defects, have made major discoveries that have advanced our understanding of disease and development. However, while we know that genetic mutations can lead to both cancer and birth defects, relatively few specific mutations that lead to these conditions in children have been identified. We also have a poor understanding of how the mutations result in disease. The pediatric data resource will put genetic data and clinical data for these conditions together and researchers will be able to mine the data for insights into the complex role of genetics in childhood cancer and structural birth defects. In FY 2017, the program intends to support activities to establish and grow the data resource. This includes a call for applications to sequence the genomes of participants in childhood cancer or structural birth defect research cohorts as well as support for the DNA sequencing center. It also includes an initiative to develop, build, and maintain a user-friendly interface that will facilitate data mining by the scientific community.

Budget Policy: The FY 2017 President's Budget Request is $12.994 million for Pediatric Research, a decrease of $0.114 million or 0.9 percent below the FY 2016 Enacted level. This estimated decrease in funds reflects lower anticipated program administration costs. Programmatic funding remains at the $12.600 million statutory level.

Genotype-Tissue Expression (GTEx)

The GTEx program provides data on how human DNA variation (or genotype) correlates with differences in gene expression levels in various tissues.[4] This information is important because many diseases involve changes in DNA where it is difficult to determine how the change leads to disease, especially for variants that lie outside of protein-coding regions but that can nonetheless affect gene expression levels. GTEx data show which tissues are most affected by a particular DNA variant, and researchers can use these data to identify potential pathways that lead to disease and possible new targets for therapies. The GTEx program has been highly successful in recruiting samples, extracting high quality RNA from tissues, and obtaining data from its gene expression array and RNA sequencing experiments. Data and biospecimens are being made available to the research community. The GTEx program aims to achieve its goals in FY 2017, delivering biospecimens, gene variation and expression data, and statistical methods for use by the research community.

Budget Policy: The FY 2017 President's Budget Request is $1.289 million for the GTEx program, a decrease of $2.825 million or 68.7 percent compared to the FY 2016 Enacted level. The estimated decrease reflects the planned winding down of the program and will support activities related to archiving and preserving GTEx resources.

[3] https://commonfund.nih.gov/KidsFirst/
[4] https://commonfund.nih.gov/GTEx/index

Global Health
NIH has a longstanding commitment to address both infectious and noninfectious diseases around the world, including in low- and middle-income nations that face a persistent cluster of infectious disease, malnutrition, and a growing incidence of chronic diseases and disabilities. Strategic investment by the Global Health program is intended to build capacity for research in Africa, since research in Africa is vital not only for health of Africans but for our understanding of human genetic diversity and the impact this has on health and disease everywhere.[5] This program fosters teamwork among scientists and health organizations, builds infrastructure, and increases capacity to improve medical training and retention of trained personnel to understand and treat disease more aggressively. It is supporting the development of a robust genetics and genomics research community in Africa, enabling big data approaches to the analysis of communicable and non-communicable diseases. It also provides support for medical education with an emphasis on research as part of the training program, and supports high priority research projects.

Budget Policy: The FY 2017 President's Budget Request is $8.587 million for the Global Health program, a decrease of $4.716 million or 35.5 percent compared to the FY 2016 Enacted level. This level of funding reflects the planned completion of several initiatives, including collaborative centers individual research grants, and a bioinformatics network. Additional initiatives may be launched in FY 2017 if an NIH review determines a second stage would allow the initiative to address new and important scientific challenges and opportunities.

Health Economics
The Health Economics program aims to support basic and applied research to understand how innovations in treatments, diagnosis, and preventive strategies can be most effectively implemented in a health care setting.[6] Research supported by this program falls within the objectives identified through a recent effort to develop an NIH taxonomy of high priority Health Economics research topics. This program will identify factors determining diffusion and optimal adoption and implementation of highly effective health technologies, innovations, and discoveries, so that past and future investments by NIH may have greater public health impact. The program seeks to analyze factors that are likely to affect the adoption of personalized medicine approaches, including research to understand individual characteristics and preferences of patients and their families, as well as factors influencing health care provider decisions. Understanding these responses will inform the development of future treatments, diagnostic, and preventive strategies to ensure that innovations are implementable in a real world environment. The Health Economics program also aims to build research capacity in health economics so that future NIH-supported research can be informed by economic analysis of factors that influence health and the uptake and adoption of NIH-supported innovations.

Budget Policy: The FY 2017 President's Budget Request is $3.418 million for the Health Economics program, a decrease of $1.947 million or 36.3 percent compared to the FY 2016 Enacted level. This level of funding reflects the planned completion of two awards and reductions in five other awards as they enter their final year.

[5] https://commonfund.nih.gov/globalhealth/index
[6] https://commonfund.nih.gov/Healtheconomics/index

High-Risk, High-Reward Research

Research that aims to transform science is inherently difficult and risky but necessary to accelerate the pace of scientific discovery and advance human health. While all CF programs encourage risk-taking to overcome significant challenges in biomedical research, most programs designate funds for particular high-risk objectives or methods. The High-Risk, High-Reward Research program takes a different approach by supporting exceptionally creative scientists proposing innovative and transformative research in any scientific area within the NIH mission through four complementary initiatives: the Pioneer Award, New Innovator Award, Transformative Research Award, and Early Independence Award.[7] The Pioneer Award supports extraordinarily creative scientists who propose bold approaches to addressing major challenges in biomedical and behavioral research. The New Innovator Award supports exceptionally creative, early career investigators who propose innovative, high-impact projects. The Transformative Research Award supports unconventional, paradigm-shifting research projects that are inherently risk and untested and allows teams of principal investigators when appropriate. The Early Independence Award bypasses the traditional post-doctoral training period by helping establish independent scientific careers for newly graduated scientists with the intellect, creativity, drive, and maturity to flourish independently.

In part as a response to an evaluation of the Pioneer program that demonstrated high levels of innovation and impact, we initiated a budget policy for the HRHR program in 2013 in which Pioneer and Transformative Research Awards were to be co-funded between the Common Fund and the ICs. This led to a gradual decrease in the Common Fund HRHR budget, as ICs paid non-competing commitments on new awards. Although this policy reflected enthusiasm voiced by IC Directors about these initiatives, the budget policy has been difficult to implement in practice, since the work supported by these grants often falls at the interface of multiple ICs. In addition, some ICs have been more focused on developing their own HRHR awards. To stabilize the HRHR budget, the Common Fund is beginning in FY 2016 to once again fully fund Pioneer and Transformative Research Awards. As new awards are issued each year, costs for each cohort will build on top of commitments from prior year awards. This will result in a gradual increase in the HRHR budget over the next few years to reach a steady state of approximately $192 million in FY 2020.

Budget Policy: The FY 2017 President's Budget Request is $153.465 million for the High-Risk High-Reward program, a decrease of $7.858 million or 4.87 percent compared to the FY 2016 Enacted level. This will support competing costs for FY 2017 awards as well as all non-competing commitments for FY 2016 awards. However, since ICs will continue to provide non-competing costs for prior year cohorts, the HRHR budget shows a small decrease.

Illuminating the Druggable Genome (IDG)

The overarching goal of the Illuminating the Druggable Genome (IDG) program is to improve knowledge of the properties and functions of understudied proteins that are related to known drug targets, and are thus likely candidates to be drug targets themselves.[8] This program is

[7] https://commonfund.nih.gov/highrisk/index
[8] https://commonfund.nih.gov/idg/index

focusing on hundreds of understudied proteins within four protein families that are commonly targeted for drug development – G-protein-coupled receptors, nuclear receptors, ion channels, and protein kinases. Designed as a two-phase program, the pilot phase of the program is creating a data resource that will catalog known information about these protein families and establish strategies for obtaining further information about the function of these proteins so that investigators can determine whether a given protein is a likely target for a disease or condition of interest. Ultimately, this program will catalyze discovery of truly new biological pathways and targets and provide a wealth of new candidates for therapeutic development.

Budget Policy: The FY 2017 President's Budget Request does not fund the Illuminating the Druggable Genome program, which reflects the planned completion of the pilot stage of the program. However, IDG is being considered for a second stage of support in FY 2017. Pending a favorable review, a second stage is anticipated to encompass data coordination and high throughput approaches to analyze protein function.

Knockout Mouse Phenotyping Program (KOMP2)

Recognizing the value and utility of a readily-accessible, genome-wide collection of mouse mutants for determining how mammalian genes function, several international programs were launched to develop mutant mouse strains. Collectively, these basic research programs have generated more than 8,000 mutant mouse strains, in which individual genes have been removed or "knocked out" to allow researchers to determine their function. The CF has joined together with multiple NIH ICs to support the Knockout Mouse Phenotyping Program (KOMP2), which builds upon this existing resource by expanding the efforts to characterize, or phenotype, the mutant strains, including mutations that result in embryonic lethality.[9] The data are being made rapidly available to the entire research community through an international data coordinating center as a way to catalyze additional analyses of how or whether specific genes contribute to health and disease conditions. Some of the genes to be characterized are expected to suggest novel drug targets and increase understanding of genetic pathways that drugs may affect. In FY 2017, CF will continue to support a second stage of KOMP2 that builds upon the success of the first stage, expanding the program to add 3,000 more knockouts. This will be accomplished using a broad-based phenotyping platform, studying male and female mice in all tests, continued embryo phenotyping where applicable, and adding a cohort of older mice that are more reflective of human disease development times. To meet program goals and manage costs, the program is shifting to newly developed technology, called Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR). CRISPR technology has the ability to induce mutations in a variety of species, including mice, and has sparked a transformation in genetic research by offering significant savings in time and cost.

Budget Policy: The FY 2017 President's Budget Request is $11.000 million for the KOMP2 program, an increase of $3.000 million or 37.5 percent compared to the FY 2016 Enacted level. This level of funding reflects the planned increase to the mouse production and phenotyping awards.

[9] https://commonfund.nih.gov/KOMP2/index

Metabolomics

Metabolites are small molecules that are produced or consumed in the chemical reactions that take place in the body to sustain life. The sum of all metabolites at any given moment – the metabolome – is a form of big data "chemical read out" of the state of health of the cell or system, and provides a wealth of information about nutrition, environmental insult, infection, health, and disease status. Recent advances in metabolomics technology have yielded important clues about disease mechanisms which suggest new treatment strategies. However, the use of these technologies is limited by the number of research centers that have the necessary equipment and expertise to conduct the studies, and the lack of uniform standards for identifying unknown metabolites. The Metabolomics program is intended to establish the needed resources, training, technology development, and standards to catalyze the field of metabolomics to advance basic scientific discovery and clinical practice.[10] It also facilitates the dissemination of data generated by the program through an informatics component and through the establishment of an international consortium. This consortium will ensure that CF investments are also leveraging investments made in other countries, resulting in increased data sharing, reduced redundancy of effort, and faster translation toward improvements in health.

Budget Policy: The FY 2017 President's Budget Request is $10.381 million for the Metabolomics program, a decrease of $9.184 million or 46.9 percent compared to the FY 2016 Enacted level. The estimated decrease in funding reflects the planned completion of initiatives in training, technology development, and operations of the Data Repository and Coordinating Center.

Program Portrait: Molecular Transducers of Physical Activity in Humans

FY 2016 Level: $0.000 million
FY 2017 Level: $2.199 million
Change: +$2.199 million

Physical activity has been demonstrated to contribute to health via a wide variety of measures, and lack of physical activity is at the root of many common chronic health problems. Despite this, we have a poor understanding of the molecular mechanisms by which the benefits of physical activity are realized. The development of a "molecular map" of physical activity is a daunting task but is now made possible because of recent advances in several powerful high-throughput analytic approaches, including metabolomics, proteomics, genomics, transcriptomics, and epigenomics. The Molecular Transducers of Physical Activity in Humans Consortium (MoTrPAC) will leverage these advances to improve our understanding of the molecular mechanisms by which physical activity improves health.[11] Support for the program will be slightly delayed from initial plans so that awards will start in early FY 2017 rather than late FY 2016..

[10] https://commonfund.nih.gov/metabolomics/index
[11] https://commonfund.nih.gov/MolecularTransducers

Program Portrait: Precision Medicine Initiative Cohort Program

FY 2016 Level: $130.000 million
FY 2017 Level: $230.000 million
Change: +$100.000 million

The PMI Cohort Program will build a national research cohort of one million or more U.S. volunteers, providing a transformative platform for expanding our knowledge of precision medicine approaches. Precision medicine is an approach to disease prevention and treatment that seeks to maximize effectiveness by taking into account individual variability in genes, environment, and lifestyle. Precision medicine seeks to redefine our understanding of disease onset and progression, effective prevention, treatment response, and health outcomes through the more precise measurement of molecular, environmental, and behavioral factors that contribute to health and disease. This understanding will lead to more accurate diagnoses, more rational disease prevention strategies, better treatment selection, and the development of novel therapies. Coincident with advancing the science of medicine is a changing culture of medical practice, and research that engages individuals as active partners – not just as patients or research subjects. The combination of a highly engaged population and rich biological, health, behavioral, and environmental data will usher in a new and more effective era of American healthcare. FY 2016 marks the start of the Cohort Program and the budget reflects partial year funding in a pilot (startup) phase. Support for the program will increase significantly in FY 2017 as awardees move toward full implementation of the required infrastructure and programmatic operations needed for the cohort to support initial enrollees.

Protein Capture Reagents

The Protein Capture Reagents program is developing resources and tools necessary to better understand the critical role the multitude of cellular proteins play in development, health, and disease. Monoclonal antibodies are currently used to capture proteins, but many monoclonal antibodies do not target a single specific protein, are not reliably reproduced, and only represent a small subset of proteins comprising the human proteome. A renewable resource of protein capture reagents – specifically designed to meet research and clinical demands ranging from protein isolation and high-throughput assays to diagnostics and biomarker development – is needed to advance the field of proteomics and fuel biomedical research. To have the maximum benefit, such reagents would need to be high quality, affordable, reliable, and represent the wide range of possible proteins within cells and tissues. The Protein Capture Reagents program piloted an effort focused on producing such reagents for human transcription factors and tested renewable, next generation capture technologies. The effort produced sorely needed reagents and established a community resource capable of generating protein capture reagents for future research. Currently, the program is focused on validating the generated human transcription factor reagents and disseminating them to the research community.

Budget Policy: The FY 2017 President's Budget Request is $4.182 million for the Protein Capture Reagents program, an increase of $3.975 million compared to the FY 2016 Enacted level. This level of funding reflects an effort to enhance the utility of the reagents generated by the program by having these reagents validated by anindependent contractor.

Science of Behavior Change

Unhealthy human behaviors, such as smoking, drug and alcohol abuse, over-eating, and a failure to exercise, all contribute to negative health outcomes and common diseases. However, it is extremely difficult not only to implement healthy behavior changes, but also to maintain positive changes over an extended period of time. Uncovering the basic foundations of how motivation changes across a broad array of health-related behaviors can lead to more effective and efficient

approaches to behavioral interventions, with the ultimate goal of improving the Nation's health. The first stage of the Science of Behavior Change (SOBC) program aimed to improve understanding of the basic mechanisms of human behavior change across a broad range of health-related behaviors and use this knowledge to develop more effective behavioral interventions. Research funded by the first phase led to the identification of three broad classes of intervention targets that are highly relevant to understanding the mechanisms of behavior change: self-regulation, stress reactivity and resilience, and interpersonal and social processes. The second stage of the SOBC program, which began in FY 2015, is developing measures and techniques that afford a more mechanistic, experimental medicine approach to behavior change, where interventions are designed to engage the putative targets identified in stage one and engagement of those targets is routinely assessed via reliable and validated assays. The program will also include an important new focus on adherence to medical regimens and other high priority health behaviors that could benefit from this target engagement approach.

Budget Policy: The FY 2017 President's Budget Request is $13.085 million for the Science of Behavior Change program, an increase of $7.303 million or 126.31 percent compared to the FY 2016 Enacted level. This level of funding reflects the planned expansion of the program and builds upon ongoing efforts, including new awards to improve adherence interventions and to facilitate the transition of lead projects from the CF to the ICs.

Single Cell Analysis

Cells are the basic unit of life, yet individual cells are difficult to study in their natural environments. Most analyses in cell biology and biochemistry are performed using groups of cells because of limitations with the sensitivity of the techniques; however, individual cells within the same population may differ dramatically from one another with important consequences for the health and function of the entire population. In order to uncover fundamental biological principles and ultimately improve the detection and treatment of disease, new approaches that permit analyses at the single cell level are needed. The Single Cell Analysis program seeks to overcome the scientific and technological hurdles in understanding how cells vary and operate within cell populations in tissue.[12] In particular, the program addresses basic research challenges in systematically describing cell "states," defining normal cell-to-cell variation, measuring the impact of environmental changes, understanding cellular responses within tissues, and overcoming limitations in measurement approaches.

Budget Policy: The FY 2017 President's Budget Request does not fund the Single Cell Analysis, which reflects the planned completion of the program.

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

Modulation of peripheral nerve signals to control organ function has been recognized as a potentially powerful way to treat many diseases and conditions, such as hypertension, heart failure, gastrointestinal disorders, type II diabetes, inflammatory disorders, and more. However, the mechanisms of action for neuromodulation therapies are poorly understood, and consequently efficacy is minimal and side effects are frequent. The Stimulating Peripheral Activity to Relieve Conditions (SPARC) program is a high-risk, goal-driven basic research

[12] https://commonfund.nih.gov/Singlecell/index

endeavor to develop foundational knowledge and technologies for an entirely new class of neural control devices that have the potential to precisely treat a wide variety of diseases and conditions.[13] Launched in FY 2015, the SPARC program supports interdisciplinary teams of investigators to deliver neural circuit maps of several organ systems, novel electrode designs, minimally invasive surgical procedures, and stimulation protocols, driven by an end goal to develop new neuromodulation therapies. The program is designed to be iterative and dynamic, with the novel technologies informing mapping efforts, and mapping results defining new technology requirements. This program uses Other Transaction Authority for selected initiatives, which allows high levels of flexibility, responsiveness to adjust program components, and ability to engage with non-traditional partners as needed to address specific, high-risk goals within this complex, interdisciplinary, and rapidly evolving area of science. While distinct from the NIH BRAIN initiative, SPARC shares approaches with BRAIN and both initiatives will likely benefit from innovations made in the other; these initiatives are therefore being closely coordinated by NIH staff.

Budget Policy: The FY 2017 President's Budget Request is $36.268 million for the SPARC program, an increase of $16.837 million or 86.65 percent compared to the FY 2016 Enacted level. This increase reflects plans for SPARC to expand ongoing efforts to develop neural circuit maps and generate next generation tools to stimulate peripheral nerves. Additionally, SPARC will augment existing and launch new activities to explore the utility of existing neuromodulation devices to address new indications.

Strategic Planning and Evaluation

The CF's 10-year restriction on support for any given program is designed to create a churn of funds so that new challenges and opportunities may be addressed each year. Strategic planning is therefore a critical activity for the CF. Conducted annually, the strategic planning process allows CF to be nimble and adaptive to the changing scientific landscape. This process is a collaborative activity between the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)/Office of Strategic Coordination (OSC) and the ICs. CF strategic planning encompasses both the identification of broadly relevant scientific challenges and opportunities for strategic investments using the CF (Phase I planning), and the articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic identified in Phase I (Phase II planning). Phase I strategic planning involves gathering broad input from external stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Phase II strategic planning involves more specific consultations with external experts, analysis of NIH and worldwide portfolios of research on the given topic, and literature reviews to articulate specific gaps and areas of research where opportunities for transformative progress are possible.

Since CF programs are goal driven, evaluation is critical and increasingly important as more programs near the end of their support period. Evaluation is conducted as a partnership between DPCPSI/OSC and the ICs, and it includes both formal and informal evaluative activities. Informal evaluation involves convening grantees and NIH-wide teams to review progress,

[13] https://commonfund.nih.gov/sparc/index

discuss new challenges, and develop strategies to adapt as part of routine program management. It also involves gathering input from external consultants and using their input, together with internal analysis, to help guide the implementation of the program. Formal evaluations involve the development of baseline data for new programs and the development of multiple metrics of outcomes. The utility of data, resources, technologies, and other program outputs is assessed through surveys and the analysis of bibliometric data such as citation analyses.

Budget Policy: The FY 2017 President's Budget Request is $6.80 million, which is the same as the FY 2016 Enacted level. The funds will be used to implement a strategic planning process to identify areas of scientific opportunity that are ripe for short-term, catalytic support from the Common Fund. Funds will also be used to evaluate the outputs and outcomes of both ongoing and mature programs and to fund the operating cost for OSC to manage the Common Fund.

Funds Available for New Programs

As mature initiatives end or transition out of the CF, funds are available to address new challenges. As described above, two existing CF programs will be considered for a second stage of support beginning in FY 2017 (H3Africa and Illuminating the Druggable Genome). These programs are undergoing assessments with respect to achievements of the initial support period, and proposals for a second phase of support will be considered pending available funds.

Budget Policy: The FY 2017 President's Budget Request is $11.067 million to support new programs and initiatives within the Common Fund and/or to provide a second phase of funding for those initiatives completing an initial phase.