DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund (CF)

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

(Dollars in Thousands)	FY 2016 Final	FY 2017 Annualized CR	FY2018 President's Budget
4D Nucleome	**24,680**	**27,940**	**19,476**
Technology Development, Biological Validation, Modeling and Pilot Mapping	9,968	10,169	7,955
Nucleomic, Imaging, and Computational Tool Development	9,968	9,991	6,912
4D Nucleome Coordination and Integration	4,744	7,779	4,608
Big Data to Knowledge (BD2K)	**62,666**	**74,136**	**34,855**
Extracellular RNA (ExRNA) Communication	**29,281**	**28,227**	**3,546**
Data Management and Resource/Repository (DMRR)	2,513	2,497	181
Reference Profiles of Human Extracellular RNA	4,074	4,043	3,223
Extracellular RNA Biogenesis, Biodistribution, Uptake, and Effector Function	7,533	7,223	48
Clinical Utility of Extracellular RNAs as Biomarkers and Therapeutic Agents	15,160	14,465	95
Gabriella Miller Kids First Pediatric Research	**13,128**	**12,970**	**12,944**
Health Care Systems Research Collaboratory	**11,774**	**11,335**	**4,528**
NIH-HMORN Coordinating Center	1,945	1,615	1,355
Expansion Activities	9,829	9,720	3,173
High-Risk, High-Reward Research	**163,432**	**153,465**	**153,804**
NIH Director's Pioneer Award	19,162	24,528	24,528
NIH Director's New Innovator Award Program	94,878	90,274	90,613
Transformative Research Award	28,566	17,557	17,557
NIH Director's Early Independence Award Program	20,826	21,106	21,106
Human BioMolecular Atlas Project (HuBMAP)	**0**	**0**	**5,680**
Illuminating the Druggable Genome (IDG)	**5,740**	**846**	**7,560**
Knowledge Management Network	3,219	560	1,307
Technology Development	2,521	15	0
Data and Resource Generation Centers	0	216	5,812
Dissemination and Outreach Hub	0	55	441
Metabolomics	**19,431**	**10,381**	**9,920**
Comprehensive Metabolomics Research Cores	9,176	5,840	9,920
Interdisciplinary Training in Metabolomics	3,274	15	0
Metabolomics Technology Development	1,995	30	0
Metabolomics Reference Standards Synthesis	1,929	1,946	0
Metabolomics Data Sharing and Program Coordination Core	3,057	2,550	0
Molecular Transducers of Physical Activity in Humans	**225**	**3,899**	**21,033**
Study Coordination and Data Management	180	1,542	3,127
Molecular Transducers of Physical Activity in Humans – Clinical Study	0	1,380	7,786
Chemical Analysis of Biological Samples	45	854	8,976
Characterization of Human Molecular Transducers of Physical Activity in Model Systems	0	123	1,144
Protein Capture Reagents	**207**	**1,005**	**2,000**
Antigen Production	50	0	0
Production of anti-TF antibodies	96	1,000	2,000
New Reagent Technology Development and Piloting	60	5	0
Regenerative Medicine Program (RMP)	**7,971**	**7,250**	**5,250**
NIH Center for Regenerative Medicine (NCRM)	54	0	0
Cell Therapy Projects	1,748	1,250	0
Stem Cell Translation Laboratory (SCTL)	6,169	6,000	5,250
Science of Behavior Change (SOBC)	**5,949**	**9,085**	**8,448**
Stimulating Peripheral Activity to Relieve Conditions (SPARC)	**21,267**	**42,068**	**37,781**
Functional and Anatomical Mapping of Five Organ Systems	14,960	21,890	15,855
Next Generation Tools	4,512	10,174	9,671
Off-Label Use of Existing Market-Approved Technology for Small Markets	1,713	7,866	7,385
Data Coordination	83	2,140	4,871
Strengthening the Biomedical Research Workforce	**6,602**	**6,684**	**2,447**
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	**0**	**0**	**6,080**
Undiagnosed Diseases Network (UDN)	**30,799**	**29,600**	**24,640**
Undiagnosed Diseases Program Network	29,899	28,785	24,640
Training in the Use of Contemporary Genomic Approaches to Rare Disease Diagnostics	900	815	0

Common Fund by Initiative
(Dollars in Thousands)

(Dollars in Thousands)	FY 2016 Final	FY 2017 Annualized CR	FY2018 President's Budget
Enhancing the Diversity of the NIH-Funded Workforce	**51,751**	**53,004**	**41,275**
BUILD Initiative	46,949	49,340	38,324
National Research Mentoring Network (NRMN)	1,434	2,436	1,963
Coordination and Evaluation Center (CEC)	3,368	1,228	988
Epigenomics	**4,322**	**4,000**	**73**
Genotype-Tissue Expression (GTEx)	**4,113**	**1,251**	**0**
Global Health	**13,303**	**15,530**	**12,741**
Medical Education Partnership Initiative (MEPI)	3,000	3,000	2,410
Human Heredity and Health in Africa (H3Africa)	8,478	10,182	8,493
Household Air Pollution Investigation Network (HAPIN)	1,825	2,348	1,838
Glycoscience	**19,836**	**20,552**	**17,319**
Health Economics	**5,317**	**3,406**	**54**
Changing Incentives for Consumers, Insurers, and Providers	84	146	41
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	2,427	1,567	0
Economics of Prevention	2,392	1,177	0
Data Infrastructure to Enable Research on Health Reform	415	517	14
Human Microbiome Project	**154**	**158**	**0**
Knockout Mouse Phenotyping Program	**8,000**	**11,000**	**8,850**
Data Coordination	1,262	1,262	1,011
Production, Characterization, Cryopreservation, Phenotyping, and Data Release	6,738	9,738	7,839
All of Us **Research Program** [1]	**130,000**	**129,753**	**0**
Single Cell Analysis	**14,330**	**45**	**0**
Pilot Studies to Evaluate Cellular Heterogeneity	6,026	22	0
Exceptionally Innovative Tools and Technologies for Single Cell Analysis	2,924	0	0
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	5,380	23	0
Single Cell Analysis Challenges	0	0	0
Library of Integrated Network-Based Cellular Signatures (LINCS)	**9,964**	**9,964**	**7,999**
Nanomedicine	**25**	**0**	**0**
Regulatory Science	**4,000**	**0**	**0**
Strategic Planning Funds	7,372	6,800	6,120
Subtotal Common Fund	675,639	674,355	454,423
New Initiatives in Common Fund	0	0	0
Total Common Fund	675,639	674,355	454,423

[1] Requested in the Office of the Director but outside the Common Fund in FY 2018.

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 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget	FY 2018 +/- FY 2017
BA	$675,639,000	$674,355,000	$454,423,000	-$219,932,000
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 Institutes and Centers (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 2018:

1. Fundamental Science
2. Treatments and Cures
3. Health Promotion and Disease Prevention
4. Enhancing Stewardship

Significant efforts are being made to evaluate programs during their lifetime, and outcomes are assessed as programs end. Continuous evaluation during program implementation allows flexibility to modify program management and/or budgets in response to rapidly evolving scientific landscapes, technical challenges, or other unforeseen challenges or opportunities. Funds freed as programs end, move to other sources of support, or require decreased support as indicated by evaluative data will be available in FY 2018 for new challenges and opportunities.

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

Overall Budget Policy: The FY 2018 President's Budget Request for the CF is $454.423 million, a decrease of $219.932 million compared to the FY 2017 Annualized Continuing Resolution level. This decrease reflects an overall budget reduction in accordance with the President's Budget, and the transition of the *All of Us* Research Program out of the CF but still within the Office of the Director. The CF will continue to support high-priority research with trans-NIH relevance in FY 2018. As mature programs transition out of the CF, new programs are being established through strategic planning activities that identify potentially transformative areas of research where limited-term CF 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 basic, translational, and clinical research. In accordance with the President's Budget Request, FY 2018 budgets for some CF programs are reduced by approximately 20 percent compared to the FY 2017 Annualized Continuing Resolution. Highlighted below are programs that exemplify the science to be supported in FY 2018, and/or which involve budget reductions significantly greater or less than 20 percent compared to FY 2017. Also included are CF programs that have achieved the goals set when program plans were originally developed, and have now identified additional scientific challenges and opportunities that will be addressed in a second stage of support. Several CF programs are planning to receive their final year of support in FY 2017, and thus are not requesting funds in FY 2018. These programs include Epigenomics[2], Genotype-Tissue Expression (GTEx)[3], and Health Economics[4]. Information on these programs and their accomplishments can be found on their program websites.

4D Nucleome

It is estimated that each human cell contains approximately 2 meters (6.5 feet) of linear DNA squeezed inside the cell's microscopic nucleus. We now know that DNA may not be randomly arranged within the nucleus. Research suggests that nuclear organization may play a role in cell function, but specific consequences of this organization are not well understood. The Common Fund's 4D (four dimensional) Nucleome program aims to understand principles underlying nuclear organization in space (three dimensions) and time (the fourth dimension), the role nuclear organization plays in gene expression and cellular function, and how changes in nuclear organization affect normal development as well as various diseases[5]. This program is developing technologies, resources, and data to enable the study of the 4D Nucleome. These include novel tools to explore the dynamic nuclear architecture and its role in gene expression, models to examine the relationship between nuclear organization and function in both normal

[2] https://commonfund.nih.gov/epigenomics/index
[3] https://commonfund.nih.gov/GTEx/index
[4] https://commonfund.nih.gov/Healtheconomics/index
[5] http://commonfund.nih.gov/4Dnucleome/index

development and disease, and reference maps of nuclear architecture in a variety of cells and tissues.

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[6]. 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. 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. The program is working to make big data software innovations available and more user-friendly. It is also supporting innovative approaches to advance biomedical science using crowdsourcing and interactive digital media. In FY 2018, the program will enter a second stage, and will pilot making NIH-funded large datasets and associated computational tools findable, accessible, interoperable, and reusable in a shared space that multiple scientists can access remotely, such as the cloud.

Extracellular RNA (ExRNA) Communication

Ribonucleic acid (RNA) was once thought to exist in a stable form only inside cells, where it regulates gene expression by serving as an intermediate product in the process by which cells translate the information coded in genes into proteins that carry out all cellular functions. However, research indicates that RNAs can play a role in a variety of complex functions, including mechanisms of cell-to-cell communication via RNAs that are exported from the cell. The impact of these extracellular RNAs, or exRNAs, is currently unknown. The CF's Extracellular RNA Communication program capitalized on the opportunity to understand entirely new paradigms of information exchange based on the release, transport, uptake, and regulatory role of exRNAs[7]. The Extracellular RNA Communication program supported awards with the following aims: 1) to determine the biological principles that guide exRNA generation, secretion, uptake, and function; 2) to develop a catalogue of exRNAs found in healthy human body fluids; 3) to identify exRNA biomarkers that can be used to diagnose and monitor disease progression and response to therapy; 4) to develop and demonstrate the potential for clinical utility of exRNAs as therapeutic agents; and 5) to develop a community-wide resource for exRNA standards, protocols, and data. In FY 2018, the success of several of the initiatives will allow them to transition to IC support while profiling and data coordination efforts will be maintained within the CF.

Gabriella Miller Kids First Pediatric Research

The Gabriella Miller Kids First Pediatric Research program (Kids First) aims to catalyze pediatric research by making large amounts of high-quality genetic and clinical data from pediatric patient cohorts widely available and easy to use for the entire biomedical research community[8]. The Kids First program will support a data resource that will integrate data from patients with childhood cancer or structural birth defects, conditions which have profound,

[6] https://commonfund.nih.gov/bd2k/index
[7] https://commonfund.nih.gov/Exrna/index
[8] https://commonfund.nih.gov/KidsFirst

lifelong effects on patients and their families. 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 cancer and can also lead to birth defects, we do not know how these mutations lead to disease. By sequencing the genomes of patients along with their parents, we will have a full picture of the genetic contributions to these conditions. This genetic information, in combination with other clinical data, will help researchers understand how genetic mutations lead to birth defects or to cancer, as well as understanding whether there are shared contributions to both conditions. There is considerable scientific evidence that examining childhood cancer and structural birth defects data together will uncover new connections between them that would not have been discovered if they were examined independently. Having these data sets together in a single, widely accessible resource is anticipated to facilitate new discoveries and novel ways of thinking about these conditions. Importantly, the Kids First Data Resource will aggregate Kids First-generated data together with many additional existing data sets, thus increasing researchers' ability to detect rare genetic changes that contribute to these conditions. In FY 2018, the program intends to support activities to establish and grow the Kids First Data Resource. This includes additional sequencing of 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 and analysis by the scientific community.

Health Care Systems Research Collaboratory

The Health Care Systems (HCS) Research Collaboratory program aims to strengthen the national capacity to implement cost-effective, large-scale research studies that engage health care delivery organizations as research partners[9]. This program will provide a framework of implementation methods and best practices that will enable the participation of many health care systems in clinical research. These methods and practices are being tested and honed within the context of pragmatic clinical trials, which measure the effectiveness of treatments in real world settings. A Coordinating Center serves as the central resource for the development of guidelines and best practices for the effective conduct of research studies in partnership with health care systems. The HCS Research Collaboratory also supports efficient, large-scale pragmatic clinical trials focused on the management of patients with multiple chronic health conditions. The pragmatic trials must address questions of major public health impact and test interventions that can be applied broadly to the patient population and are suitable for use in many health care systems, with the broad goal of determining whether the interventions improve health outcomes of patients with multiple chronic conditions. In FY 2018, CF support for HCS Research Collaboratory decreases with the planned ramping down of current pragmatic clinical trial efforts. IC support for a new round of pragmatic clinical trials will begin in FY 2018. Lessons learned from these trials will be disseminated to the broad biomedical research community.

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

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

Research (HRHR) 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.[10] 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 risky 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.

Partially 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 co-funded between the CF and ICs. This led to a gradual decrease in the CF 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 developed their own person-based awards to support outstanding researchers. To stabilize the HRHR budget, the Common Fund began 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.

Program Portrait: Human BioMolecular Atlas Project (HuBMAP)

FY 2017 Level: $0.000 million
FY 2018 Level: $5.680 million
Change: +$5.680 million

This program is set to launch in FY 2018 using funds made available by the planned ending, or scaling-down, of other Common Fund programs.

Cells are the fundamental unit of life, but until recently, they could only be studied in large groups. New technologies now provide the opportunity to analyze individual cells and how they interact with each other to form a healthy or diseased tissue. Cells that were thought to be the same are now known to be different, which could have profound impact on disease diagnostics and treatment. These observations suggest that more in-depth analyses of individual cells in tissues are necessary to understand normal biology and disease processes, and ultimately provide targeted diagnostic and therapeutic approaches. Anticipated to launch in FY 2018, the Human BioMolecular Atlas Project (HuBMAP) program will involve partnerships within the NIH and with other funding organizations, including the Chan Zuckerberg Initiative (CZI) and the Wellcome Trust, to establish an international effort to analyze the human body at a single cell level. The HuBMAP contribution to this effort will support data generation and technology development to explore the relationship between cellular location and function and the variability in tissue organization at the level of individual cells. Data from the Common Fund-supported awards and from other efforts will be integrated through a data platform to be developed in partnership with the CZI.

[10] https://commonfund.nih.gov/highrisk/index

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.[11] This program is focusing on hundreds of understudied proteins within select protein families that are commonly targeted for drug development. Designed as a two-stage program, the pilot stage of the program created 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. In FY 2018, IDG will launch a second stage that will capitalize on the information gathered and technologies developed in the pilot stage to elucidate the function of three key families of uncharacterized proteins – G-protein-coupled receptors, ion channels, and protein kinases. Ultimately, this program will catalyze discovery of previously unknown processes that occur within cells to change their function, potentially leading to new candidates for therapeutic development.

Metabolomics
Metabolites are small molecules that are produced or consumed in the chemical reactions that take place in the body and 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, effects of the environment, infection, health, and disease status. Recent advances in metabolomics technology have yielded important clues about disease mechanisms which suggest new opportunities for 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 standards for identifying the vast number of unknown metabolites. The Metabolomics program is intended to establish the needed resources, training, and technology development to catalyze the field of metabolomics to advance basic scientific discovery and its use in clinical practice.[12] It also facilitates the dissemination of data generated by the program through an informatics component and by working with the international community. This will ensure that CF investments are also leveraging investments in other countries, resulting in increased data sharing, a uniform system to name metabolites, reduced redundancy of effort, and faster translation toward improvements in health. In FY 2018, a second stage of the Metabolomics program will begin. As the research facilities established in the first stage move to a fee-for-service model of sustainability, the Common Fund investments in the second stage will focus on establishing the data infrastructure for metabolomics data sharing. A data hub will be established with the goal of making all NIH-supported metabolomics data publicly available, and computational tools will facilitate analysis and interpretation of the complex data sets.

Molecular Transducers of Physical Activity in Humans
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

[11] https://commonfund.nih.gov/idg/index
[12] https://commonfund.nih.gov/metabolomics/index

physical activity are realized. A better understanding of the molecules that underlie the benefits of physical activity could lead to the development of improved, personalized exercise recommendations as well as therapies for individuals who are unable to exercise due to illness or disability. 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[13]. This program will extensively catalogue the biological molecules affected by physical activity in people, identify some of the key molecules that underlie the systemic effects of physical activity, and characterize the function of these key molecules. After a planning year in FY 2017, the awardees will ramp up their efforts significantly in FY 2018.

Protein Capture Reagents

The Protein Capture Reagents program is developing resources and tools necessary to better understand the critical roles proteins within cells play in development, health, and disease[14]. Monoclonal antibodies are currently used to capture proteins so they can be studied, but many monoclonal antibodies do not target a single specific protein, are not reliably reproduced, and only represent a small subset of all human proteins. A renewable resource of protein capture reagents is needed to advance the study of human proteins 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 an important class of proteins called human transcription factors, and tested renewable, next generation capture technologies. The effort produced 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 making them available to the research community.

Regenerative Medicine Program (RMP)

The Regenerative Medicine Program (RMP) aims to work through scientific and regulatory hurdles to the development of induced pluripotent stem cells (iPSCs) for clinical use[15]. iPSCs are generated by coaxing adult cells into reverting back to an embryonic stem cell-like state, which then can generate many different cell types for use in screening or developing therapies. The goal of RMP is to serve as a national resource for stem cell science to accelerate the development of new medical applications and cell-based therapies. RMP is pursuing this goal through two initiatives. In the first initiative, RMP is supporting a Therapeutic Challenge award to advance efforts to develop iPSCs as therapy for age-related macular degeneration, a leading cause of blindness in the elderly. Additionally, in the second initiative, RMP is supporting the Stem Cell Translation Laboratory (SCTL) at the National Center for Advancing Translational Science. The SCTL will establish quality control standards, methods, and reagents to enable the

[13] https://commonfund.nih.gov/MolecularTransducers
[14] https://commonfund.nih.gov/proteincapture/index
[15] https://commonfund.nih.gov/stemcells/index

research community to generate and study iPSCs, moving the field of iPSC research closer to therapeutic applications.

Science of Behavior Change (SOBC)
Unhealthy human behaviors, such as smoking, drug and alcohol abuse, over-eating, and 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 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[16]. Research funded by the first stage 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. Interventions are designed to engage the specific targets identified in the first stage of the program, and engagement of those targets is assessed via reliable and validated assays. This approach provides a more reliable way to develop behavioral interventions, as well as a more robust way to measure their effectiveness. The program includes a focus on adherence to medical regimens, a problem area that could benefit from this target engagement approach. In FY 2018, existing SOBC awardees will begin to disseminate information about validated targets and assays to the greater behavioral research community, and new awards will enable researchers to incorporate this rigorous approach across a wide range of behavioral health studies.

Stimulating Peripheral Activity to Relieve Conditions (SPARC)
Bioelectronic medicine, which refers to neuromodulation 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, neural control of end-organ function is poorly understood. Consequently, efficacy of neuromodulation therapies has been inconsistent and side effects are difficult to predict. The Stimulating Peripheral Activity to Relieve Conditions (SPARC) program is a high-risk, goal-driven basic research endeavor to develop foundational knowledge and technologies for an entirely new class of therapeutic devices that have the potential to precisely treat a wide variety of diseases and conditions.[17] Launched in FY 2015, the SPARC program supports interdisciplinary teams of investigators to deliver neural circuit maps that illustrate how peripheral nerves control organ function, along with technologies to isolate, measure, and manipulate nerve-organ interactions and their functions. Because these activities are driven by an end goal to catalyze development of next-generation neuromodulation therapies, all SPARC comprehensive mapping projects involve validation in human tissues. 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

[16] https://commonfund.nih.gov/behaviorchange/index
[17] https://commonfund.nih.gov/sparc/index

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 and DARPA's ElectRx program, SPARC shares approaches with BRAIN and ElectRx so that all three programs will likely benefit from innovations made in the others. These initiatives are therefore being closely coordinated with NIH and DARPA staff. In FY 2018, SPARC will continue to progress toward its goals, investing in technology development, anatomical and functional mapping, exploring the utility of existing neuromodulation technologies for new purposes, leveraging partnerships with industry and physicians to learn from clinical studies in humans, and launching a publicly available online resource through which research tools and advancements will be shared.

Strengthening the Biomedical Research Workforce

The Strengthening the Biomedical Research Workforce program aims to enhance training opportunities for early career scientists to prepare them for a variety of career options in the dynamic biomedical research workforce landscape[18]. This program is supporting the Broadening Experiences in Scientific Training (BEST) awards to develop innovative approaches to complement traditional research training in biomedical sciences. Awardee institutions are collaborating with non-academic partners to ensure that experts from a broad spectrum of research and research-related careers contribute to coursework, rotations, internships, and other forms of exposure for trainees. Awardee institutions are working together to define needs and share best practices so that proven approaches can be broadly disseminated and adopted by the biomedical research training community. NIH is taking an active role in evaluating the approaches developed by this program by conducting an evaluation across all BEST sites in order to share this evidence base with the training community. The first cohort of grantees from the Workforce program will receive their final year of funding in FY 2017, leaving the remaining cohort of grantees to receive their final year of funding in FY 2018.

Program Portrait: Transformative High Resolution Cryo-Electron Microscopy (CryoEM)

FY 2017 Level: $0.000 million
FY 2018 Level: $6.080 million
Change: +$6.080 million

This program is set to launch in FY 2018 using funds made available by the planned ending, or scaling-down, of other Common Fund programs.

Structure determines function in biology. Therefore, knowing the structures of biological molecules is essential to understanding how they work normally to confer health and how they go awry to produce disease. Recent advances in a technology called high resolution cryo-electron microscopy (cryoEM) have revolutionized the field of structural biology. CryoEM allows visualization of frozen biological samples without using dyes or fixatives that can alter the structure of molecules, enabling researchers to get a more accurate picture of these molecules and better understand their function. The structure determination of proteins and protein complexes once thought to be too daunting have now become feasible. However, adoption of cryoEM in the US, and therefore the ability of the US to stay at the forefront in structural biology, is limited by access to the necessary high-end cryo-electron microscopes and by the expertise to use them effectively. The Transformative High Resolution Cryo-Electron Microscopy (CryoEM) program works to build the national capacity and infrastructure for cryoEM through the development of comprehensive resource centers and by creating training opportunities to develop a large expert workforce in the

[18] https://commonfund.nih.gov/workforce/index

most recent cryoEM advances. The program also will invest in improving technologies to make them more sensitive, practical and affordable.

Undiagnosed Disease Network (UDN)

It is estimated that rare diseases affect 25 to 30 million Americans. Often times, because their diseases are so uncommon or have never been described before, these individuals go for long periods of time without a diagnosis, as do those with rare variants of common diseases. To aid in the diagnosis of rare and new diseases, the CF's Undiagnosed Diseases Network (UDN) established clinical and research sites at academic centers across the country.[19] The UDN builds upon the experience and expertise of the NIH intramural Undiagnosed Diseases Program, established in 2008, and its cross-disciplinary approach to diagnosing both rare and new diseases. This Network is catalyzing the field of rare disease research by bringing state of the art medical and genomic approaches to bear on a myriad of diseases, bringing together basic and clinical researchers to elucidate underlying biological mechanisms, identify treatments and disease management strategies, and train the next generation of clinical researchers to use these approaches in disease diagnosis. The insights gained from understanding rare diseases may provide important clues about the pathology and potential treatments of a host of common diseases as well. In FY 2017, funding for the successful first stage of the UDN ended. In the second stage of the program, starting in FY 2018, the program will test additional diagnostic approaches and evaluate the long term sustainability of those approaches.

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 1 planning), and the articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic identified in Phase 1 (Phase 2 planning). Phase 1 strategic planning involves gathering broad input from external stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Phase 2 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, discuss new challenges, and develop strategies to adapt as part of routine program management.

[19] https://commonfund.nih.gov/Diseases/index

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, expert opinion, and the analysis of bibliometric data such as citation analyses.

Funds Available for New Programs

As mature initiatives end or transition out of the CF, or as information gathered through evaluations indicates a need for decreased support of existing programs, funds are available to address new challenges. As described above, three existing CF programs are planning to launch a second stage of support beginning in FY 2018 (Illuminating the Druggable Genome, Metabolomics, and the Undiagnosed Disease Network). Additionally, two new programs, the Human BioMolecular Atlas Project (HuBMAP) and Transformative High Resolution Cryo-Electron Microscopy (CryoEM), are planned to launch in FY 2018. These programs were identified through the strategic planning process as being high priority for the NIH as a whole.