DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund (CF)

NATIONAL INSTITUTES OF HEALTH
Common Fund

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2017 Final		FY 2018 Annualized CR		FY 2019 President's Budget		FY 2019 +/- FY 2018 CR	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	263	$169,549	198	$131,768	223	$169,701	25	$37,933
Administrative Supplements	*(45)*	25,038	*(5)*	1,529	*(4)*	2,375	*(-1)*	846
Competing:								
Renewal	1	396	0	0	0	0	0	0
New	121	150,110	124	154,227	110	135,913	-14	-18,314
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	122	$150,506	124	$154,227	110	$135,913	-14	-$18,314
Subtotal, RPGs	385	$345,094	322	$287,524	333	$307,989	11	$20,465
SBIR/STTR	0	0	0	0	0	0	0	0
Research Project Grants	385	$345,094	322	$287,524	333	$307,989	11	$20,465
Research Centers:								
Specialized/Comprehensive	28	$38,053	27	$36,484	24	$33,189	-3	-$3,295
Clinical Research	10	16,001	14	21,658	12	18,666	-2	-2,992
Biotechnology	2	4,022	1	2,075	0	516	-1	-1,559
Comparative Medicine	0	0	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	40	$58,076	42	$60,217	36	$52,371	-6	-$7,846
Other Research:								
Research Careers	19	$3,170	3	$475	3	$431	0	-$44
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	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	126	186,534	169	249,511	93	137,604	-76	-111,907
Other Research	145	$189,703	172	$249,986	96	$138,035	-76	-$111,951
Total Research Grants	570	$592,873	536	$597,727	465	$498,395	-71	-$99,332
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	196	23,810	176	21,826	125	15,530	-51	-6,296
Total Research Training	196	$23,810	176	$21,826	125	$15,530	-51	-$6,296
Research & Develop. Contracts	0	$27,446	0	$25,034	0	$52,000	0	$26,966
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Intramural Research	0	15,943	0	13,181	0	13,685	0	504
Res. Management & Support	0	35,385	0	21,061	0	19,171	0	-1,890
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	0	$695,456	0	$678,829	0	$598,781	0	-$80,048

[1] All items in italics and brackets are non-add entries.

Major Changes in the Fiscal Year 2019 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 mechanism and activity detail and these highlights will not sum to the total change for the FY 2019 President's Budget for the Common Fund, which is $80.048 million less than the FY 2018 Annualized Continuing Resolution Level, for a total of $598.781million. The FY 2019 President's Budget reflects the Administration's fiscal policy goals for the Federal Government. Within that framework, the Common Fund will pursue its highest research priorities through strategic investments and careful stewardship of appropriated funds.

Research Project Grants (+$20.465 million; total $307.989 million): The Common Fund expects to support a total of 333 Research Project Grant (RPG) awards in FY 2019. Plans include 223 Noncompeting RPGs and the award of 110 Competing RPGs. In general, the $307.989 million requested for RPGs represents a 7.0 percent increase in comparison to the FY 2018 Annualized CR Level.

Research Centers (-$7.846 million; total $52.371 million): The estimated decrease in Common Fund support for Research Centers reflects a general reduction in the Common Fund budget in accordance with the FY 2019 President's Budget Request.

Other Research (-$111.951 million; total $138.035 million): The estimated decrease in Common Fund support for the Other Research mechanism reflects the transfer of the *All of Us* Research Program out of the Common Fund to a separate *All of Us* Research Program office in the Office of the Director, resulting in a reduction in the use of Other Transactions within the Common Fund. The remaining budget for Other Transactions will be used by the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program, the Data Commons within the Big Data to Knowledge (BD2K) program, and the Human BioMolecular Atlas Program (HuBMAP).

Research and Development Contracts (+$26.966 million; total $52.000 million): Several activities contribute to the change in support for Research and Development Contracts. A contract within the *All of Us* Research Program is no longer supported by the Common Fund in FY 2019 as this program transfers elsewhere in the Office of the Director. Meanwhile, the Common Fund is launching a new Innovation Prize Program (described below) in FY 2019 using Research and Development Contracts.

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

	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
4D Nucleome	**27,940**	**27,841**	**25,085**
Technology Development, Biological Validation, Modeling and Pilot Mapping	10,169	9,982	8,965
Nucleomic, Imaging, and Computational Tool Development	10,149	10,076	9,054
4D Nucleome Coordination and Integration	7,621	7,784	7,066
Acute to Chronic Pain Signatures	**0**	**5,600**	**6,314**
All of Us Research Program	**129,994**	**129,117**	**0**
Big Data to Knowledge (BD2K)	**55,161**	**22,198**	**16,916**
Enhancing the Diversity of the NIH-Funded Workforce	**50,514**	**50,817**	**47,513**
BUILD Initiative	44,557	47,554	36,892
National Research Mentoring Network (NRMN)	1,776	1,798	9,110
Coordination and Evaluation Center (CEC)	4,181	1,465	1,511
Epigenomics	**4,003**	**78**	**0**
Extracellular RNA Communication	**28,222**	**6,912**	**5,241**
Data Management and Resource/Repository (DMRR)	2,489	2,714	54
Reference Profiles of Human Extracellular RNA	4,285	4,055	0
Extracellular RNA Biogenesis, Biodistribution, Uptake, and Effector Function	7,694	71	0
Clinical Utility of Extracellular RNAs as Biomarkers and Therapeutic Agents	13,753	71	5,187
Gabriella Miller Kids First Pediatric Research	**13,105**	**993**	**12,952**
Genotype-Tissue Expression (GTEx) Resources	**1,725**	**577**	**509**
Global Health	**15,527**	**15,837**	**13,948**
Medical Education Partnership Initiative (MEPI)	3,000	3,000	2,706
Human Heredity and Health in Africa (H3Africa)	10,179	10,491	9,126
Cookstove Initiative	2,348	2,346	2,116
Glycoscience	**23,164**	**20,345**	**17,571**
Health Care Systems Research Collaboratory	**11,835**	**5,624**	**1,579**
NIH-HMORN Coordinating Center	2,115	1,623	1,579
Expansion Activities	9,720	4,001	0
Health Economics	**3,289**	**60**	**0**
Changing Incentives for Consumers, Insurers, and Providers	146	44	0
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	1,544	0	0
Economics of Prevention	1,177	0	0
Data Infrastructure to Enable Research on Health Reform	423	17	0
High-Risk Research	**179,489**	**166,090**	**172,192**
NIH Director's Pioneer Award	24,886	34,696	39,956
NIH Director's New Innovator Award Program	115,395	88,472	86,697
Transformative Research Award	17,560	22,759	26,737
NIH Director's Early Independence Award Program	21,648	20,163	18,802
Human BioMolecular Atlas Project (HuBMAP)	**0**	**7,479**	**13,536**
Technology Development	0	2,105	3,738
Human Tissue Mapping	0	2,697	6,564
Data Coordination and Integration	0	2,676	3,233
Human Microbiome	**210**	**0**	**0**
Illuminating the Druggable Genome	**7,846**	**9,400**	**11,184**
Knowledge Management Network	560	1,574	3,264
Technology Development	15	0	0
Data and Resource Generation Centers	7,216	7,284	7,429
Dissemination and Outreach Hub	55	542	492
Knockout Mouse Phenotyping Program	**12,566**	**11,000**	**9,922**
Data Coordination	1,262	1,335	1,138
Production, Characterization, Cryopreservation, Phenotyping, and Data Release	11,304	9,665	8,784
Library of Integrated Network-Based Cellular Signatures (LINCS)	**9,964**	**10,000**	**9,020**

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

	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Metabolomics	**10,374**	**12,401**	**11,188**
Comprehensive Metabolomics Research Cores	6,035	0	0
Interdisciplinary Training in Metabolomics	15	0	0
Metabolomics Technology Development	30	0	0
Metabolomics Reference Standards Synthesis	1,946	0	0
Metabolomics Data Sharing and Program Coordination Core	2,347	5,350	4,828
Metabolomics Data Analysis	0	7,051	6,360
Molecular Transducers of Physical Activity	**5,587**	**24,990**	**33,166**
Study Coordination and Data Management	1,526	4,370	4,359
Molecular Transducers of Physical Activity in Humans – Clinical Study	2,130	8,920	9,463
Chemical Analysis of Biological Samples	1,809	10,262	17,945
Characterization of Human Molecular Transducers of Physical Activity in Model Systems	123	1,437	1,399
NIH Center for Regenerative Medicine (NCRM)	**7,242**	**5,600**	**6,855**
NIH Center for Regenerative Medicine (NCRM)	0	0	0
Cell Therapy Projects	1,248	600	541
Stem Cell Translation Laboratory (SCTL)	5,995	5,000	6,314
Protein Capture	**1,358**	**5**	**0**
Production of anti-TF antibodies	1,353	0	0
New Reagent Technology Development and Piloting	5	5	0
Science of Behavior Change	**8,968**	**12,445**	**11,381**
Single Cell Analysis	**47**	**0**	**0**
Pilot Studies to Evaluate Cellular Heterogeneity	22	0	0
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	25	0	0
Single Cell Analysis Challenges	0	0	0
Somatic Cell Genome Editing	**0**	**19,370**	**35,315**
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	**41,710**	**47,068**	**41,734**
Functional and Anatomical Mapping of Five Organ Systems	23,033	19,705	18,856
Next Generation Tools	10,205	12,079	9,091
Off-Label Use of Existing Market-Approved Technology for Small Markets	3,381	9,153	8,303
Data Coordination	5,091	6,132	5,483
Strengthening the Biomedical Research Workforce	**6,566**	**2,985**	**0**
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	**0**	**26,255**	**13,440**
National Centers for Cryo-Electron Microscopy	0	25,602	12,849
Training Cryo-electron Microscopists	0	653	591
Undiagnosed Diseases Network	**31,787**	**28,900**	**26,068**
Undiagnosed Diseases Program Network	30,972	28,900	26,068
Training in the Use of Contemporary Genomic Approaches to Rare Disease Diagnostics	815	0	0
Strategic Planning Funds	7,262	6,800	6,153
Subtotal Common Fund	695,456	676,785	548,781
New Initiatives in Common Fund	0	2,044	50,000
Total Common Fund	695,456	678,829	598,781

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 2017 Final	FY 2018 Annualized Continuing Resolution level	FY 2019 President's Budget	FY 2019 +/- FY 2018
BA	$695,456,000	$678,829,325	$598,781,000	-$80,048
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 2019:

1) Tackling Complex Challenges by Leveraging Partnerships
2) Supporting Basic Research to Drive New Understanding of Health and Disease in Living Systems
3) Investing in Translational and Clinical Research to Improve Health
4) Fostering a Diverse & Talented Biomedical Research Workforce for Today & Tomorrow

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.

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

Funds will be available in FY 2019 for new challenges and opportunities as programs end, move to other sources of support, or require decreased support as indicated by evaluative data.

Overall Budget Policy: The FY 2019 President's Budget Request for the CF is $598.781million, a decrease of $80.048 million or 11.8 percent compared to the FY 2018 Annualized Continuing Resolution level. This decrease reflects the transition of the *All of Us* Research Program out of the CF but still within the Office of the Director, and also allows for the launch of a new $50 million Innovation Prize Program in FY 2019. The CF will continue to support high-priority research with trans-NIH relevance in FY 2019. 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 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 aiming 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. The paragraphs below focus on new programs for FY 2019, programs requesting a second stage of support, and/or those in which the budget is changed by $5 million or more from the FY 2018 Annualized Continuing Resolution level. One CF program, Strengthening the Biomedical Research Workforce, will receive its final year of support in FY 2018; funds are therefore not requested in FY 2019. Information on this program and its accomplishments can be found on the program website.[2]

Program Portrait: Acute to Chronic Pain Signatures

FY 2018 Level: $5.600 million
FY 2019 Level: $6.314 million
Change: +$0.714 million

In many individuals, acute pain from injury, surgery, or disease persists beyond the initial insult and may last for months, years, or throughout life. The mechanisms driving the transition from acute pain to a chronic state are poorly understood. Developing tools to predict who is at risk and who is resilient to transition to a chronic pain state is a crucial step toward appropriate treatment of acute pain to prevent chronic pain, as well as potentially reversing chronic pain that is already established. Launching as a pilot in FY 2018, this program will focus on identifying mechanistic "signatures" predictive of the transition from acute to chronic pain and for an established chronic pain state. Understanding and identifying at-risk patients could result in preventive treatment plans that may greatly reduce the prevalence of chronic pain and reduce reliance on opioids. The major goal of the program would be to put forward a discovery-focused clinical trial to identify objective signatures (composed of genetic, imaging, molecular, biochemical, and psychosocial data) that associate with the transition from acute to chronic pain. However, feasibility of the study will be demonstrated initially through pilot activities in FY 2018. If the pilot is successful, funds requested in FY 2019 will be used to initiate a full-scale clinical trial.

[2] https://commonfund.nih.gov/workforce

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.[3] With the first awards made in 2014, the expectation is that BD2K will result in cultural changes in the way the biomedical research community shares, accesses, queries, cites, and analyzes data. The first stage of BD2K focused on facilitating broad use of biomedical big data, developing and disseminating analysis methods and software, enhancing training relevant for large-scale data analysis, and establishing centers of excellence for big data. The second stage of BD2K, launched in FY 2017, builds from the innovative tools, methods, and data management strategies that were developed in the first phase to establish and test an NIH Data Commons. This project is established as a pilot to test ways to store, access, and share biomedical big data and associated tools in a shared cloud environment. This effort will enable interoperability of data sets, and if the pilot phase is successful, it will enhance access to and use of all NIH data sets. In FY 2019, several Stage 1 initiatives will ramp down, including efforts in software and analysis methods, training, data coordination, sustainability, and the centers of excellence. It is anticipated that completed activities within these initiatives will have achieved their goals, and the tools and resources developed will have been disseminated for use by the broader biomedical research community. The remaining activities within these initiatives will focus on making the products of research usable, discoverable, and disseminated to intended end-users. Other ongoing efforts in BD2K will continue support of the Data Commons Pilot.

Budget Policy: The FY 2019 President's Budget Request is $16.916 million for the BD2K program, a decrease of $5.282 million or 23.8 percent compared to the FY 2018 Annualized Continuing Resolution level. This funding will support the Data Commons, as well as enhancing the usability and impact of products developed during the first stage of BD2K.

Enhancing the Diversity of the NIH Funded Workforce

Enhancing the Diversity of the NIH-Funded Workforce, also known as the Diversity Program Consortium (DPC), is a trans-NIH program funded by the CF and managed by the National Institute of General Medical Sciences (NIGMS).[4] Through this national collaborative, NIH works together with institutions and professional societies to advance the DPC's overarching goal of developing, implementing, assessing and disseminating innovative, effective approaches to research training and mentoring. Unique aspects of this program include: focusing on three levels of impact - student, faculty and institutional; integrating social science research and psychosocial interventions with the process of training and mentoring students and faculty; and rigorously assessing and evaluating the training and mentoring interventions implemented across the program. The DPC consists of three integrated initiatives: Building Infrastructure Leading to Diversity (BUILD), the National Research Mentoring Network (NRMN), and the Coordination and Evaluation Center (CEC). The BUILD initiative supports a set of 10 awards granted to undergraduate institutions, each of which developed quantitative approaches intended to determine the most effective ways to engage and retain students from diverse backgrounds in biomedical research, and to prepare students to become future contributors to the NIH-funded research enterprise. The NRMN is developing a national network of mentors and mentees from

[3] https://commonfund.nih.gov/bd2k
[4] https://www.nigms.nih.gov/training/dpc/Pages/default.aspx

all biomedical disciplines relevant to the NIH mission to provide mentorship, professional development, mentor/mentee training, networking and resources to individuals from the undergraduate to early career faculty levels. The CEC is responsible for coordinating and evaluating the outcomes of DPC activities. In FY 2019, the DPC will complete the first stage of the program and launch a second stage to determine efficacy of the new training and mentoring approaches that the program has developed.

Budget Policy: The FY 2019 President's Budget Request is $47.513 million for the DPC, a decrease of $3.304 million or 6.5 percent compared to the FY 2018 Annualized Continuing Resolution level. The level of support will be used to determine efficacy of the novel training and mentoring approaches developed in the first stage of the program.

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 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.[5] In the first stage, this 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. The success of these initiatives allowed several exRNA program investigators to garner additional non-CF IC support. As of September 2017, the exRNA Atlas contained 2,067 exRNA profiles and 21 billion RNA sequence reads across multiple body fluids from both healthy and various disease states. Since the launch of the exRNA Atlas, there have been over 29,400 downloads of datasets by 1,355 users across six continents, demonstrating the broad utility of data generated from the program. In addition to the exRNA Atlas, several bioinformatic tools have been made widely available so that researchers everywhere are able to analyze exRNA data. Translational success is evidenced by the fact that seven program awardees have met with FDA representatives to discuss preliminary biomarker qualification or pre-Investigational New Drug submissions. A review of the first stage of this program demonstrated enthusiasm for a second stage of support, including potential initiatives for validation of datasets to understand inter- and intra-individual exRNA variability over time; development of enabling resources, tools, and technologies; and improved data coordination, analysis, and outreach. Funds requested in FY 2019 will support these activities in the second stage.

Budget Policy: The FY 2019 President's Budget Request is $5.241 million for the Extracellular RNA Communication program, a decrease of $1.671 million or 24.2 percent compared to the FY 2018 Annualized Continuing Resolution level. A review of the first stage of this program

[5] https://commonfund.nih.gov/exrna

indicated additional scientific opportunities ripe for investment, and FY 2019 funds will be used to launch a second stage of support.

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.[6] The Kids First program supports a data resource that will integrate data from patients with childhood cancer or structural birth defects, conditions which have profound, lifelong effects on patients and their families. 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. To date, the Kids First program is supporting sequencing of 23 cohorts, for a total of 18,024 genomes to be sequenced. These cohorts include a wide variety of childhood cancers and structural birth defects, including lymphoma, neuroblastoma, Ewing sarcoma, hearing loss, cleft lip/palate, and diaphragmatic hernia. In FY 2019, the Kids First program will continue to support the Data Resource, and will also launch new demonstration projects to mine Kids First data for novel scientific insights about genetic contributions to childhood cancer and structural birth defects.

Budget Policy: The FY 2019 President's Budget Request is $12.952 million for the Kids First program, an increase of $11.959 million or 1,204.9 percent compared to the FY 2018 Annualized Continuing Resolution level. Programmatic funding remains at the $12.600 million statutory level in FY 2019, with additional requested funds to support research management activities. The decrease in FY 2018 funding levels was due to a lack of funds available in the Pediatric Research Initiative Fund in FY 2018. With a new transfer of funds into this account in FY 2019, funding for Kids First has been restored to the statutory level. FY 2019 funding for this program will support the developing Data Resource and launch new demonstration projects.

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 (HRHR) program takes a different approach by supporting exceptionally creative scientists proposing innovative and transformative research in any scientific area within the NIH

[6] https://commonfund.nih.gov/KidsFirst

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 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. Independent evaluations found Pioneer and New Innovator awardees produce more innovative, risky, and impactful research than is funded by typical R01 awards. Examples of innovative research from HRHR awardees include: tracking the Ebola outbreak using genetics and identification of the single animal to human transmission event, discovery of an off-switch for CRISPR-Cas9 gene editing that helps prevent unintended genome changes, creation of a 20-cent replacement for thousand-dollar lab centrifuges designed after a children's toy, and discovery of a promising new antibiotic with no identifiable drug-resistance from pathogens.

Budget Policy: The FY 2019 President's Budget Request is $172.192 million for the HRHR program, an increase of $6.102 million or 3.7 percent compared to the FY 2018 Annualized Continuing Resolution level. This increase in support will allow NIH to continue to support high-risk research with the potential for extraordinary impact.

Human BioMolecular Atlas Program (HuBMAP)

In living organisms consisting of multiple cell types, diverse cells with different functions and structures develop as we grow and age. The Human BioMolecular Atlas Program (HuBMAP) aims to catalyze development of an open, global framework for comprehensively mapping the human body at the level of individual cells.[8] HuBMAP will show proof of principle via preliminary mapping activities of a few organs and distributed systems with existing and emerging technologies, it will establish and validate innovative technologies, and it will demonstrate the utility of these data. HuBMAP will work with the broader community to establish the tools, infrastructure and standards with the expectation that the research community will continue to build upon these maps in the future. Ultimately, these maps will form part of a resource - conceptually like Google Maps for the human body - and as this data resource grows over time, will result in a complete human body map at the cellular level. These maps will enable and encourage future studies and new insights into inter-individual variation and tissue changes across the lifespan and health/disease continuum. This program is expected to establish and leverage close partnerships with other funding agencies so that multiple funding sources are coordinated for this global challenge. Launched in FY 2018, HuBMAP will begin set-up and then move to a scale-up phase in FY 2019. Support for HuBMAP will increase as initiatives for technology development, tissue mapping, and data and coordination ramp up.

Budget Policy: The FY 2019 President's Budget Request is $13.536 million for the HuBMAP program, an increase of $6.057 million or 81.0 percent compared to the FY 2018 Annualized

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

Continuing Resolution level. This increase in funding will support ramping up of the HuBMAP program in FY 2019.

Molecular Transducers of Physical Activity

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. 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.[9] 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.

Budget Policy: The FY 2019 President's Budget Request is $33.166 million for the Molecular Transducers of Physical Activity program, an increase of $8.176 million or 32.7 percent compared to the FY 2018 Annualized Continuing Resolution level. This increase in funding will support the large, complex clinical study required to discover the molecular mechanisms that underlie the wide range of benefits from physical activity.

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

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.[10] SPARC 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 Transaction Authority for selected initiatives, which allows high levels of flexibility, responsiveness to adjust program components, and ability to engage with non-

[9] https://commonfund.nih.gov/MolecularTransducers/
[10] https://commonfund.nih.gov/sparc

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.

Budget Policy: The FY 2019 President's Budget Request is $41.734 million for the SPARC program, a decrease of $5.334 million or 11.3 percent compared to the FY 2018 Annualized Continuing Resolution level. This level of support will allow SPARC to continue supporting efforts towards developing functional and anatomical neural circuit maps of peripheral organs, tool development, leveraging existing technologies for novel applications, and data coordination.

Program Portrait: Somatic Cell Genome Editing

FY 2018 Level: $19.370 million
FY 2019 Level: $35.315 million
Change: +$15.945 million

Recent developments in genome editing techniques to precisely change specific sequences in the human genome raise the possibility of a fundamentally new approach to treat genetic diseases, as well as opportunities to impact common diseases. Editing the genomes of somatic cells can be done outside the body (ex vivo) with subsequent transplantation of the edited cells into the patient. Alternatively, cells can be modified within the body (in vivo). However, efficacy, specificity, and delivery remain challenges, especially for approaches that target cells in vivo, which lag behind ex vivo approaches in development even though they are applicable to many more diseases. The Somatic Cell Genome Editing program aims to improve the efficacy and specificity of in vivo genome editing approaches.[11] This program could transform the practice of medicine and reduce the burden of both rare and common diseases. The program will be a coordinated effort towards the development of effective delivery methods and more precise technologies for accurate ("on-target") genome editing, while limiting "off-target" genetic changes and unintended consequences such as altered cells becoming cancerous, provoking an immune response, or causing long term physiological abnormalities. The major goal of the program is to develop enabling tools and technologies to facilitate the filing of successful Investigational New Drug applications, especially applications perceived to have little financial reward by industry.

Transformative High Resolution Cryo-Electron Microscopy

Knowing the structure of a molecule reveals important information about how it functions and can provide insight into potential drug targets for fighting disease. Cryo-electron microscopy (cryo-EM) is a method used to image frozen biological molecules in their natural state and offers considerable advantages in sample requirements over other techniques. Until recently, cryo-EM has been substantially limited in the level of structural detail that can be obtained, but technological advances in the past few years have dramatically extended cryo-EM resolution, making it possible to image proteins and "cellular machinery" in great detail. However, the high cost of cryo-EM instrumentation limits the method's availability to researchers. The Transformative High Resolution Cryo-Electron Microscopy program aims to provide nationwide access for researchers to cryo-EM through the creation of national service centers, improvement of technology, and the development of an expert workforce.[12] In FY 2019, the Transformative

[11] https://commonfund.nih.gov/editing
[12] https://commonfund.nih.gov/CryoEM

High Resolution Cryo-Electron Microscopy program will support national service centers to provide biomedical researchers access to state-of-the-art equipment, technical support, and instruction for the production and analysis of high-resolution cryo-EM data, as well as training for cryo-EM microscopists.

Budget Policy: The FY 2019 President's Budget Request is $13.440 million for the Transformative High Resolution Cryo-Electron Microscopy program, a decrease of $12.815 million or 48.8 percent compared to the FY 2018 Annualized Continuing Resolution level. The FY 2018 budget reflected substantial start-up equipment purchases. The FY 2019 level of support will continue the operations of national cryo-EM service centers while expanding support for training.

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 often 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 often 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.

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. The CF plans to launch a new program in FY 2019:

- **Common Fund Innovation Prize Program** – Beginning in FY 2019, the CF will administer an Innovation Prize Program, using up to $50 million to accelerate research in defined areas of need across the NIH. Use of an Innovation Prize Program has several advantages: the ability to establish a goal without predetermination of the most likely way to achieve the goal; paying only for results; increasing the number and diversity of individuals or organizations that address a specific problem or challenge; stimulating private sector investment so the winning result could be greater than the value of the prize; and attracting more interest and attention to a defined program, activity, or issue of concern. This program will be administered by the Common Fund, but all ICs as well as Common Fund programs can propose ideas for potential Innovation Prize competitions.