DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

COMMON FUND (CF)

BUDGET MECHANISM TABLE

(Dollars in Thousands)	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 +/- FY 2020	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	245	$183,110	257	$200,823	284	$221,994	27	$21,171
Administrative Supplements	*(50)*	13,107	*(6)*	1,697	*(3)*	868	*(-3)*	-829
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	145	159,892	136	150,486	122	125,132	-14	-25,354
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	145	$159,892	136	$150,486	122	$125,132	-14	-$25,354
Subtotal, RPGs	390	$356,109	393	$353,006	406	$347,994	13	-$5,012
SBIR/STTR	0	0	0	0	0	0	0	0
Research Project Grants	390	$356,109	393	$353,006	406	$347,994	13	-$5,012
Research Centers:								
Specialized/Comprehensive	33	$38,885	23	$26,785	22	$25,692	-1	-$1,093
Clinical Research	10	19,068	7	13,036	6	10,815	-1	-2,221
Biotechnology	1	772	0	0	0	0	0	0
Comparative Medicine	4	5,721	3	4,159	4	5,804	1	1,645
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	48	$64,445	33	$43,980	32	$42,311	-1	-$1,669
Other Research:								
Research Careers	0	$0	0	$0	0	$0	0	$0
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	118	150,062	151	192,504	132	168,277	-19	-24,227
Other Research	118	$150,062	151	$192,504	132	$168,277	-19	-$24,227
Total Research Grants	556	$570,616	577	$589,490	570	$558,582	-7	-$30,908
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	469	12,711	538	14,884	447	12,350	-91	-2,534
Total Research Training	469	$12,711	538	$14,884	447	$12,350	-91	-$2,534
Research & Develop. Contracts	0	$1,183	0	$577	0	$0	0	-$577
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Intramural Research		15,251		13,129		6,969		-6,160
Res. Management & Support		19,404		21,031		18,566		-2,465
Res. Management & Support (SBIR Admin)		*(0)*		*(0)*		*(0)*		*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	**556**	**$619,166**	**577**	**$639,111**	**570**	**$596,467**	**-7**	**-$42,644**

MAJOR CHANGES IN THE 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 2021 President's Budget for the Common Fund, which is $42.6 million less than the FY 2020 Enacted level, for a total of $596.5 million. The FY 2021 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 (-$5.0 million; total $348.0 million): The Common Fund expects to support a total of 406 Research Project Grant (RPG) awards in FY 2021. Estimated awards for FY 2021 include 284 Noncompeting RPGs and 122 Competing RPGs.

Other Research (-$24.2 million; total $168.3 million): The estimated decrease in Common Fund support for the Other Research mechanism reflects planned decreases to activities within several programs. These include decreased support for national service centers in the Transformative High Resolution Cryo-Electron Microscopy program and chemical analysis sites within the Molecular Transducers of Physical Activity program. Additionally, within the Stimulating Peripheral Activity to Relieve Conditions program, there are planned decreases in the anatomical and functional mapping initiative and a technology development initiative, resulting in a reduction in use of Other Transactions Authority.

Intramural Programs (-$6.2 million; total $7.0 million): The estimated decrease in support for Intramural Programs reflects the planned completion of the Common Fund's Regenerative Medicine Program.

BUDGET BY INITIATIVE

(Dollars in Thousands)	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
4D Nucleome	$27,997	$28,860	$27,485
Acute to Chronic Pain Signatures	2,094	16,636	14,648
Big Data to Knowledge (BD2K)	2,605	0	0
Enhancing the Diversity of the NIH-Funded Workforce	52,656	53,713	47,401
Extracellular RNA Communication	6,728	5,846	10,497
Gabriella Miller Kids First Pediatric Research	13,482	13,000	13,000
Genotype-Tissue Expression (GTEx) Resources	772	0	0
Global Health	15,569	11,565	9,261
Glycoscience	19,435	13,362	5,191
Health Care Systems Research Collaboratory	1,988	1,750	1,694
High-Risk, High-Reward Research	206,110	193,100	186,001
NIH Director's Pioneer Award	*45,446*	*54,265*	*51,293*
NIH Director's New Innovator Award Program	*102,692*	*77,815*	*79,795*
Transformative Research Award	*35,149*	*38,402*	*34,659*
NIH Director's Early Independence Award Program	*22,823*	*22,618*	*20,255*
Human BioMolecular Atlas Program (HuBMAP)	15,005	27,031	31,040
Illuminating the Druggable Genome	12,970	13,390	12,971
Knockout Mouse Phenotyping Program	13,757	11,000	0
Library of Integrated Network-Based Cellular Signatures (LINCS)	9,946	87	0
Metabolomics	12,403	12,401	12,000
Molecular Transducers of Physical Activity	44,744	46,126	42,609
New Models of Data Stewardship	199	0	0
NIH Center for Regenerative Medicine (NCRM)	7,597	5,700	0
Protein Capture	1,334	0	0
Science of Behavior Change	12,674	222	0
Somatic Cell Genome Editing	33,324	38,937	44,232
Stimulating Peripheral Activity to Relieve Conditions (SPARC)	51,559	47,268	41,883
Strengthening the Biomedical Research Workforce	56	0	0
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	14,895	51,800	36,290
Undiagnosed Diseases Network	29,207	24,401	21,683
Strategic Planning, Evaluation, and Infrastructure	10,061	22,917	21,129
Subtotal Common Fund	619,166	639,111	579,017
New Initiatives in Common Fund	0	0	17,450
Total Common Fund	**$619,166**	**$639,111**	**$596,467**

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 2019 Final	FY 2020 Enacted Level	FY 2021 President's Budget	FY 2021 +/- FY 2020
BA	$619,166,000	$639,111,000	$596,467,000	-$42,644,000
FTE	0	0	0	0

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

COMMON FUND NARRATIVE

Overview

The NIH Common Fund (CF) supports research in areas of emerging scientific opportunities, 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 achieve specific, high-impact goals and milestones within a 5-10 year timeframe.[125] CF programs aim to change the way science is conducted through the establishment of new scientific fields or paradigms, development of new and innovative technologies, or the generation of data or other resources that catalyze research and enable discovery across the entire spectrum of biomedical research.

Designed as short-term investments with defined goals and deliverables, many CF programs have achieved notable successes during their lifespan that continue to enable biomedical research, including:

- Molecular Libraries and Imaging – Prior to this program, academic researchers did not have access to high-throughput molecular screening facilities that enable the identification of chemical compounds that can be used as research tools and/or that may have novel therapeutic potential. This program established this type of infrastructure within academic institutions and supported screening projects to identify novel compounds with diverse functions.[126] Research from the Molecular Libraries and Imaging program led to the development of a drug currently pending FDA review as a novel treatment for multiple sclerosis. The program also generated many resources that continue to be used by the scientific community, including numerous small molecule

[125] https://commonfund.nih.gov/
[126] https://commonfund.nih.gov/molecularlibraries/index

compounds and probes, several research databases, and PubChem, a widely used web resource for chemical information.[127] Now, five years after CF support for this program ended, the infrastructure that was established continues via support from NIH ICs and from other entities. The program transformed the research enterprise, since it is now relatively straightforward to screen for small molecule probes with specific functions.

- Human Microbiome Project (HMP) – When the HMP began, there was little understanding of the census of microbes that live in and on humans, or how they might contribute to health and disease. HMP transformed our understanding of the human body as an ecosystem including both human and microbial cells by defining the normal human microbiome composition, studying the interplay of microbial and human host biological properties in several diseases/conditions, developing tools and technologies to enable microbiome research, and laying the foundation for an explosion of microbiome research around the globe.[128] This research is informing the development of novel therapies that manipulate the microbial ecosystem and suggests that future probiotic therapies could have powerful and diverse benefits.
- Patient-Reported Outcomes Measurement Information System (PROMIS) – PROMIS created new paradigms for how clinical research information is collected, used, and reported.[129] This program addressed a need in the clinical research community for a rigorously tested tool to measure patient-reported outcomes such as pain, fatigue, physical functioning, emotional distress, and social role participation. The PROMIS tool is now widely used in clinical and research settings.

CF programs often address areas of science that are particularly timely, where breakthrough technologies, public health needs, or scientific challenges create new opportunities for strategic investment. Current examples include:

- The Somatic Cell Genome Editing program is leveraging recent advances in precision genome editing technology to develop broadly useful tools and resources to accelerate the development of new therapies for a variety of genetic diseases.[130]
- The Human BioMolecular Atlas Program (HuBMAP) is capitalizing on recent advances in single cell technology, including advances enabled by the CF's Single Cell Analysis program, to develop a platform to map the human body at single-cell resolution.[131,132]
- Several CF activities are exploring new frontiers in pain research and align with the goals of NIH's Helping to End Addiction Long-term (HEAL) Initiative, a trans-NIH effort to speed scientific solutions to stem the national opioid public health crisis. These activities are supported by the CF, and thus represent an additional NIH commitment beyond HEAL investment to address the opioid public health crisis.
    - The Acute to Chronic Pain Signatures program is developing a set of objective biomarkers to predict if chronic pain is likely to develop after acute pain.[133]

[127] https://pubchem.ncbi.nlm.nih.gov/
[128] https://commonfund.nih.gov/hmp
[129] https://commonfund.nih.gov/promis/index
[130] https://commonfund.nih.gov/editing
[131] https://commonfund.nih.gov/HuBMAP
[132] https://commonfund.nih.gov/Singlecell
[133] https://commonfund.nih.gov/pain

    - An initiative within the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program is generating anatomical and functional datasets from nerve cells that mediate visceral pain.[134]
- Finally, the CF is taking advantage of advances in cloud computing to make CF-supported data resources more useful for the research community through support of a cloud-based data ecosystem.[135] This aligns with the broader NIH efforts to make data Findable, Accessible, Interoperable, and Reusable (FAIR) and increase accessibility of cloud computing. The CF is working closely with the NIH Office of Data Science Strategy to ensure that CF efforts are aligned with and inform broader NIH activities.

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 will be available in FY 2021 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 2021 President's Budget request for the CF is $596.5 million, a decrease of $42.6 million or 6.7 percent compared to the FY 2020 Enacted level. This decrease reflects the planned ramping down of several programs and initiatives and allows support for high-priority activities within existing programs. Several potential new programs are also being considered for an FY 2021 launch: 1) Harnessing Data Science for Health Discovery and Innovation in Africa, 2) Design and Use of Artificial Intelligence Platforms for Biomedical and Behavioral Research, 3) Faculty Institutional Recruitment for Sustainable Transformation (FIRST), and 4) Precision Nutrition.

Description of Activities

The 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. Highlighted below are programs that exemplify the science to be supported in FY 2021, and/or which involve significant budget shifts compared to FY 2020.

Several CF programs will receive their last year of support in FY 2020; funds are therefore not requested in FY 2021. These include Knockout Mouse Phenotyping Program,[136] Library of Integrated Network-based Cellular Signatures (LINCS),[137] Regenerative Medicine Program (NIH Center for Regenerative Medicine),[138] and Science of Behavior Change.[139] Information on these programs and their accomplishments can be found on the program websites.

[134] https://commonfund.nih.gov/SPARC
[135] https://commonfund.nih.gov/dataecosystem
[136] https://commonfund.nih.gov/KOMP2
[137] https://commonfund.nih.gov/LINCS
[138] https://commonfund.nih.gov/stemcells
[139] https://commonfund.nih.gov/behaviorchange

Program Portrait: 4D Nucleome

FY 2020 Level: $28.9 million
FY 2021 Level: $27.5 million
Change: -$1.4 million

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 know the organization of the nucleus is tightly controlled, and research suggests this organization plays an important role in cell function. However, specific consequences of this organization are not well understood. The 4D Nucleome program is examining how the three-dimensional organization of the nucleus over time (the 4th dimension) affects human health, development, and disease.[140] The first stage of this program has generated a variety of publicly available tools and resources, including nearly 2000 datasets from hundreds of experiments, 52 software packages for data analysis and visualization, and 23 protocols and reagents. Building on the success of the first stage of this program, 4D Nucleome is launching a second stage in FY 2020, aimed at delivering data and tools to the broad biomedical research community to address the role of nuclear organization in health and disease. By enabling research on nuclear organization, the 4D Nucleome program will enhance our understanding of normal cell development and function, and catalyze discovery of new targets for the treatment of human diseases caused by abnormal nuclear organization. Funds requested in FY 2021 will support research on the dynamics and function of genetic material and associated proteins; data integration, modeling, and visualization; transition of research into more biologically relevant cells, tissues, and organisms; an organizational hub; and a data coordination and integration center.

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.[141] 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. The DPC consists of several integrated initiatives: Building Infrastructure Leading to Diversity (BUILD), which aims to determine the most effective ways to engage and retain students from diverse backgrounds in biomedical research; National Research Mentoring Network (NRMN), which is developing a national network of mentees and mentors from diverse backgrounds and disciplines; and the Coordination and Evaluation Center (CEC), which coordinates and evaluates DPC activities. Now in its second stage, the DPC is determining the efficacy of the new training and mentoring approaches developed in the first stage of the program. Additionally, two new activities have recently been added to the DPC. One effort aims to establish or enhance Offices of Sponsored Programs at academic institutions to enrich biomedical research and/or research training. The second effort provides an opportunity for institutions who are not currently part of the DPC to employ methods piloted by

[141] https://www.nigms.nih.gov/training/dpc/Pages/default.aspx

the DPC to better understand the effectiveness of these experimental training and mentoring approaches.

Budget Policy:
The FY 2021 President's Budget Request is $47.4 million, a decrease of $6.3 million or 11.8 percent compared to the FY 2020 Enacted level. This level of funding will allow for continued support of the planned DPC efforts in training, mentoring, evaluation, and dissemination.

Extracellular RNA Communication

Ribonucleic acid (RNA) was once thought to exist in a stable form only inside cells, where it plays a key role in translating information coded in genes into proteins that carry out cellular functions. However, we now know that RNA can play additional roles, including roles in cell-to-cell communication via RNAs that are exported from the cell and travel throughout the body. The Extracellular RNA Communication program seeks to understand new paradigms of cellular information exchange based on these extracellular RNAs.[142] Since its founding in 2013, the program has established data standards, a data portal, and tools and reagents available to the scientific community. The program has catalogued extracellular RNA molecules found in human body fluids such as blood plasma, saliva and urine from over 2000 donors. It has also identified potential extracellular RNA biomarkers for nearly 30 diseases, including cardiovascular disease, pregnancy complications, glaucoma, diabetes, and multiple types of cancer. Increased support for this program in FY 2021 will enable development of approaches to rapidly sort complex mixtures of extracellular RNAs associated with various carrier molecules into different populations. It will also enable development of methods to isolate individual members of a specific class of extracellular RNA carriers called extracellular vesicles. The ability to isolate and sort different types of RNAs and associated carriers will allow researchers to investigate their distinct roles in human health and disease and may also ultimately lead to the development of a novel class of therapies that use RNA to alter cell function.

Budget Policy:
The FY 2021 President's Budget Request is $10.5 million, an increase of $4.7 million or 79.6 percent compared to the FY 2020 Enacted level. This increase will enable development of novel approaches to better sort and isolate specific types of extracellular RNAs and their carriers, allowing researchers to decipher the specific roles that different extracellular RNAs may play in health and disease.

Gabriella Miller Kids First Pediatric Research Program

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.[143] The Kids First program supports a data resource that integrates data from patients with childhood cancer or structural birth defects. Researchers analyze these data to understand how genetic mutations lead to birth defects or to cancer, and to discover whether there are shared

[142] https://commonfund.nih.gov/exrna
[143] https://commonfund.nih.gov/KidsFirst

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. To date, the program has sequenced more than 20,000 samples from childhood cancer and structural birth defects cohorts, and clinical and genetic sequence data from 9 datasets are publicly available. Because investigators funded through this program are dedicated to translating the knowledge gained from these data sets to new therapeutic approaches as quickly as possible, end-user support is an important focus. Funds requested in FY 2021 from the Pediatric Research Initiative Fund will be used to support pediatric research, consistent with the Gabriella Miller Kids First Research Act, and remain constant at statutory level set by this legislation. Requested funds will be used to continue support for the Kids First Data Resource, genetic sequencing of patient cohorts, and research projects to demonstrate the value of the Kids First data to the broader research community.

Budget Policy:
The FY 2021 President's Budget Request is $13.0 million, unchanged from the FY 2020 Enacted level. Programmatic funding from the Pediatric Research Initiative Fund remains constant at the $12.6 million statutory level. The remainder of the funds are requested in the regular CF appropriation to support research management activities.

Glycoscience

The Glycoscience program aims to create new resources, tools, and methods to make the study of glycans (sugars) more accessible to the biomedical research community.[144] Glycans are present on a number of biologically important molecules and play critical roles in a wide range of activities, including fighting viruses and bacteria, movement of proteins within cells to carry out important functions, and growth of neurons. However, due to their complex nature, the study of glycans has been largely inaccessible to many researchers. Important contributions of the Glycoscience program to date include development of techniques for identifying glycans that are especially difficult to study, probes to study glycans in bacterial cell walls, standards for glycan chemical synthesis, methods for high-throughput glycan studies, and glycoscience educational materials. The Glycoscience program, having developed valuable tools, methods, and resources to facilitate the study of glycans across a wide range of scientific fields, winds down activities in FY 2021.

Budget Policy:
The FY 2021 President's Budget Request is $5.2 million, a decrease of $8.2 million or 61.2 percent compared to the FY 2020 Enacted level. This decrease in support reflects the planned ramping down of the program in FY 2021.

[144] https://commonfund.nih.gov/Glycoscience

High-Risk, High-Reward Research Program

The High-Risk, High-Reward Research (HRHR) program supports 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.[145] These awards are intended to support transformative science that is inherently difficult and risky, but necessary to accelerate the pace of scientific discovery and advance human health. Independent evaluations found that Pioneer and New Innovator awardees produce more innovative, risky, and impactful research compared to typical R01 awards. Additionally, the HRHR program has served as the model for many other high-risk, high-reward awards across NIH ICs, demonstrating trans-NIH commitment to fostering innovation and risk-taking in pursuit of transformative discoveries. The HRHR program has supported numerous fundamental discoveries and the development of novel tools that are now demonstrating wide-spread impact. Examples include:

- Expansion microscopy – Developed by Pioneer Awardee Dr. Edward Boyden, expansion microscopy is a groundbreaking technique that allows researchers to expand biological samples up to 100-fold.[146] This allows visualization of cells and tissues on a scale that surpasses the limits of conventional light microscopy, enabling exploration of cellular structures and biological molecules that otherwise would not be possible. This technique has been used to explore a wide range of research questions because of its applicability in numerous biological models that range from bacteria to human brain tissue.
- Novel antibiotics – Addressing the growing public health crisis of antibiotic-resistant bacteria, research by Transformative Research Awardee Kim Lewis led to the discovery of teixobactin, a novel antibiotic effective against a wide variety of bacteria including those with resistance to other antibiotics. Since publication, this discovery has generated over 1400 citations, providing an entirely novel option in the fight against antibiotic-resistant bacteria.

Funds requested in FY 2021 will be used to support additional high-risk projects with the potential for extraordinary impact.

Budget Policy:

The FY 2021 President's Budget Request is $186.0 million, a decrease of $7.1 million or 3.7 percent compared to the FY 2020 Enacted level. This level of support will allow NIH to continue to invest in high-risk research projects with the potential to achieve remarkable scientific breakthroughs and advance human health.

Human BioMolecular Atlas Program

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.[147] Understanding the specialization, spatial organization, and interaction of cells is critical to fully comprehending the health and function of all our organs and tissues. HuBMAP will map

[145] https://commonfund.nih.gov/highrisk
[146] https://www.ncbi.nlm.nih.gov/pubmed/?term=25592419
[147] https://commonfund.nih.gov/HuBMAP

a small percentage of the human body (tens of millions of cells out of the trillions in the human body), but it will work with the broader community to establish tools, infrastructure, and standards with the expectation that the research community will continue to build upon these maps in the future. As this data resource grows over time, it will result in a complete human body map at the cellular level, ultimately contributing to a resource like Google Maps for the human body. If successful, these maps will enable and encourage future studies and new insights into individual variation and tissue changes across the lifespan and health/disease continuum. This program is expected to leverage close partnership with companies and international agencies so that multiple funding sources are applied to this global challenge. HuBMAP continues to grow in FY 2021, using requested funds to continue efforts in tissue mapping and technology development, while increasing support for data coordination and launching a new initiative to support data analysis.

Budget Policy:
The FY 2021 President's Budget Request is $31.0 million, an increase of $4.0 million or 14.8 percent compared to the FY 2020 Enacted level. The increased level of support will allow continuation of several HuBMAP activities while supporting increased data coordination and new efforts in data analysis.

Somatic Cell Genome Editing

Recent developments in genome editing techniques are allowing researchers to precisely change specific sequences in the human genome. These advances raise the possibility of a fundamentally new approach to treat genetic disorders, including common diseases such as cancer and diabetes, as well as rare conditions such as Duchenne muscular dystrophy, Huntington's disease, and cystic fibrosis. The Somatic Cell Genome Editing program aims to develop quality tools to perform safe and effective genome editing in human patients, ultimately reducing the time and cost to develop new therapies for diseases caused by changes to the genetic code.[148] These tools will need to function specifically on the disease gene to minimize unintended consequences. They will also need to be delivered selectively to the cells within the body that are affected by the disease, avoiding unaffected cells and reproductive cells so that changes are not passed on to future generations. In FY 2021, requested funds will be used for increased support to develop improved and validated gene delivery systems capable of targeting specific cells and tissues safely and effectively. Support will also continue for efforts to develop an expanded set of gene editing technologies, better animal models, approaches to assess unintended biological effects, and a coordination and dissemination center.

Budget Policy:
The FY 2021 President's Budget Request is $44.2 million, an increase of $5.3 million or 13.6 percent compared to the FY 2020 Enacted level. This increase in support will allow development and refinement of a comprehensive suite of resources to speed the translation of gene editing approaches into the clinic.

Stimulating Peripheral Activity to Relieve Conditions

[148] https://commonfund.nih.gov/editing

The Stimulating Peripheral Activity to Relieve Conditions (SPARC) program aims to accelerate development of therapeutic devices that modulate electrical activity in nerves to improve organ function.[149] Therapeutic manipulation of nerve function could be a novel approach to treat diverse diseases and conditions, such as hypertension, heart failure, gastrointestinal disorders, type 2 diabetes, and more. However, there is an urgent need to better understand the precise pattern of end-organ neural circuitry, so that the correct nerves can be targeted and the most beneficial amounts and types of stimulation can be applied. SPARC is a high risk, goal-driven basic research endeavor to develop foundational knowledge and technologies for an entirely new class of neuromodulation devices. SPARC supports interdisciplinary teams of investigators to develop neural circuit maps and models, along with technologies to measure and manipulate nerve-organ interactions. Through partnerships with industry and physicians, the program supports human clinical studies that will serve to validate or refine neural circuit maps built from animal data. The mapping data, models, technologies, and protocols generated will be publicly available through an online resource to share tools and advancements. 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.

Budget Policy:
The FY 2021 President's Budget Request is $41.9 million, a decrease of $5.4 million or 11.4 percent compared to the FY 2020 Enacted level. This level of support reflects a planned decrease in mapping efforts and tool development, while maintaining support for data coordination, partnerships to pursue clinical studies, and studies on neural circuity mediating visceral pain.

Transformative High Resolution Cryo-Electron Microscopy

Knowing the structure of a biological molecule reveals important information about how it functions and can provide insight into potential drug targets for fighting disease. However, techniques commonly used to investigate molecular structure often use harsh chemicals or treatments that can change the structure, producing inaccurate or incomplete results. Cryo-electron microscopy enables researchers to determine the structures of a wide range of biological molecules with greater accuracy, which helps identify new therapeutic targets for vaccines and drugs. However, the high cost of cryo-electron microscopes means that access to this technology is out of reach for many scientists. The Transformative High Resolution Cryo-Electron Microscopy program (CryoEM) aims to broaden access to cryo-electron microscopy for biomedical researchers through support of national service centers, improvement of technology, and training.[150] In FY 2021, the requested budget will support efforts to increase access to cryo-electron tomography, a related technology that enables improved imaging of molecules within intact cells and tissues in three dimensions, as well as continued support for CryoEM service centers and training.
Budget Policy:

[149] https://commonfund.nih.gov/sparc
[150] https://commonfund.nih.gov/CryoEM

The FY 2021 President's Budget Request is $36.3 million, a decrease of $15.5 million or 29.9 percent compared to the FY 2020 Enacted level. This level of support reflects a planned decrease in funding for cryo-electron microscopy national service centers, while maintaining support for broadening access to state-of-the-art technologies in cryo-electron tomography.

Strategic Planning, Evaluation, and Infrastructure

Management of the CF requires that certain activities be undertaken for the benefit of the CF as a whole. Strategic planning and evaluation, described below, have been long-standing costs. However, as data-intensive strategies are increasingly undertaken to achieve the goals of CF programs, infrastructure to address challenges facing all data management centers has become necessary. This infrastructure, referred to as the Common Fund Data Ecosystem, will help to ensure that all CF data sets are FAIR, provide training for users to operate on the data in a cloud environment, and ensure that CF data continue to be available after individual programs are completed. This Data Ecosystem will amplify the impact of several CF programs by enabling researchers to interrogate multiple disparate data sets, and thereby make new kinds of scientific discoveries that were not possible before.

Strategic planning is undertaken every year to identify new scientific challenges and opportunities. CF strategic planning encompasses both the identification of broadly relevant scientific challenges and opportunities for strategic investments (Phase 1 planning), and the articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic (Phase 2 planning). Phase 1 strategic planning often involves gathering broad input from stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Phase 2 strategic planning often involves specific consultations with external experts, analysis of NIH and worldwide research portfolios, 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 to monitoring progress and developing strategies to adapt program management. Evaluation 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 Initiatives

Planning for potential new FY 2021 programs involved discussions with NIH Leadership, NIH IC Directors, and editors from diverse and well-respected scientific journals, who have a broad view of the scientific landscape. From these discussions, several promising ideas emerged, and selected concepts are currently undergoing planning for a potential launch in FY 2021 (pending

availability of funds). One potential new program, Harnessing Data Science for Health Discovery and Innovation in Africa, would explore whether advances in data science applied in the African context can spur new health discoveries and catalyze innovation in healthcare and health research on the continent. A second program, Design and Use of Artificial Intelligence Platforms for Biomedical and Behavioral Research, would implement catalytic, time-limited initiatives in response to recommendations from the NIH Advisory Committee to the Director. This program would support strategic investments to generate broadly useful data sets in a way that will be amenable to artificial intelligence approaches; it will also catalyze formation of "bilingual" teams that bring health research expertise and artificial intelligence expertise together for high priority research questions. Third, the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program would aim to create cultures of inclusive excellence at NIH-funded institutions, establishing and maintaining scientific environments that can cultivate and benefit from a full range of talent. This potential program would establish a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address bias, faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts. Finally, a potential program in Precision Nutrition would aim to understand individual responses to diet, enabling tailored dietary recommendations to be provided by physicians as well as development of tools to allow individuals to make more informed decisions about healthy food choices. The focus and scope of these potential programs may change as additional planning activities are conducted.