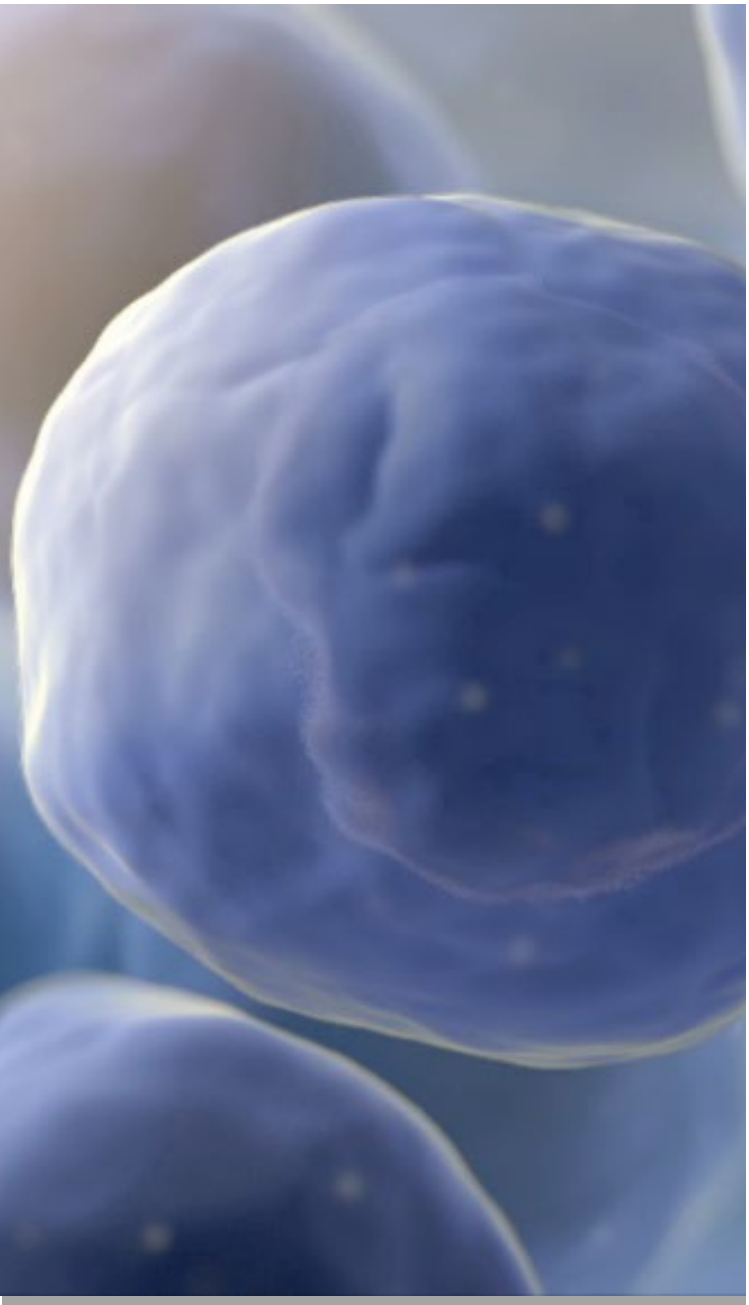

NIH Common Fund

CONGRESSIONAL JUSTIFICATION

FY 2022

Department of Health and Human Services

National Institutes of Health

NIH National Institutes of Health
Office of Strategic Coordination - The Common Fund

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NIH Common Fund

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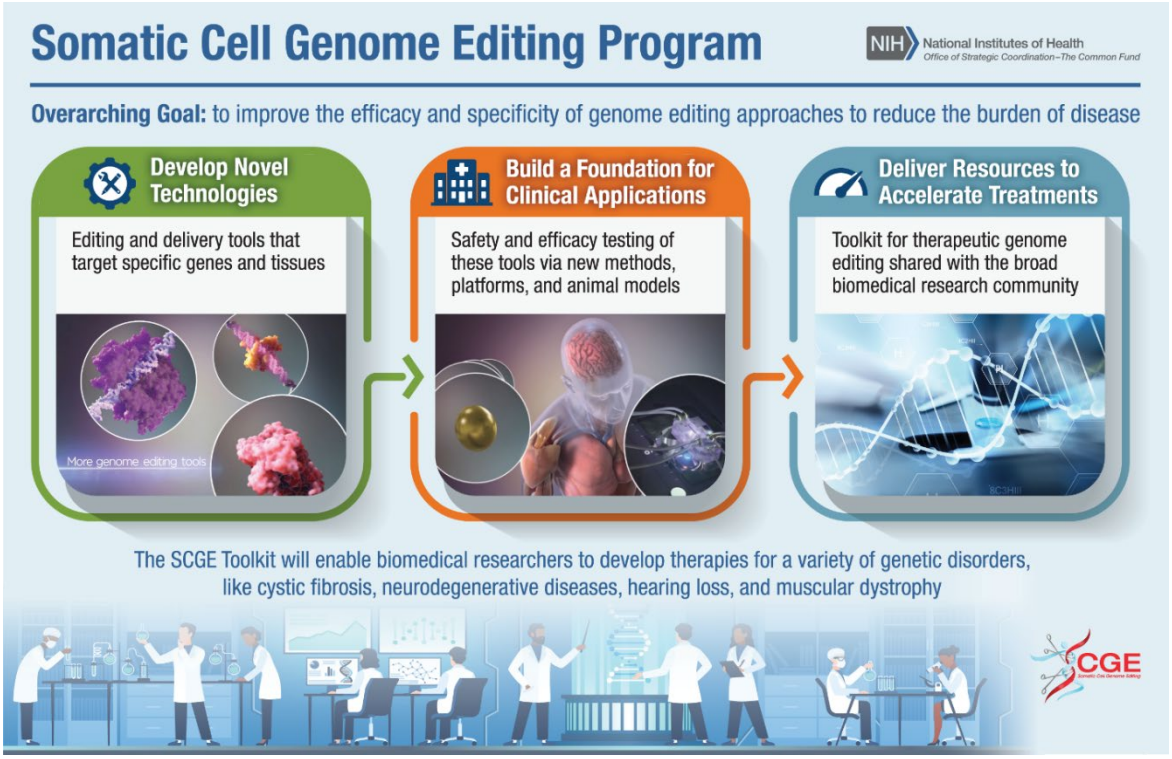
Director's Overview

Elizabeth Wilder, Ph.D., Director, Office of Strategic Coordination

The National Institutes of Health (NIH) Common Fund (CF) is a unique and exciting component of the NIH, specifically designed to address challenges and opportunities that are of high priority for the NIH as a whole. We support research in areas of emerging scientific opportunities, public health challenges, and knowledge gaps that deserve special emphasis; would benefit from strategic coordination and planning across NIH Institutes and Centers (IC); and are designed to achieve specific, high-impact goals and milestones within a 5-10 year timeframe.[233] These bold scientific programs often accelerate emerging science, enhance the biomedical research workforce, remove research roadblocks, or support high-risk, high-reward science in ways that no other entity is likely or able to do. Many CF programs are designed to produce specific deliverables, such as data sets, tools, technologies, or fundamental scientific paradigms. We intend for these deliverables to spur subsequent scientific advances that would not be possible without our strategic investment.

Often, CF programs assemble consortia of multidisciplinary, innovative researchers who collaborate to tackle a shared, ambitious goal. For example, researchers from the Somatic Cell



[233] commonfund.nih.gov/

Genome Editing[234] (SCGE) program (pictured above) are working together to improve the efficacy and specificity of gene editing approaches to help reduce the burden of diseases caused by genetic mutation. One initiative is developing improved human gene editing tools and targeted delivery systems to precisely transport editors to the correct cells and tissues. A complimentary initiative is developing new methods for assessing safety and efficacy, and applying these methods to test the novel tools and delivery systems developed in the first initiative. The tools, technologies, data, methods, and best practices developed through the program will make up the SCGE Toolkit, which will be broadly disseminated to the biomedical research community by another initiative focused on dissemination and coordination.

CF programs provide a venue for NIH to respond to critical needs and scientific opportunities using a trans-agency approach, complementing IC-specific programs and activities. CF programs play an important role in addressing NIH priority areas, including answering the call of urgent public health needs, diversifying the workforce, and capitalizing on foundational investments.

Answering the call of urgent public health needs

One of the purposes of the CF is to respond to public health challenges through interdisciplinary approaches that complement research supported by ICs. Since the inception of the CF, we have supported programs that address complex public health challenges, such as the need to engage health care systems in research that determines the best way to treat patients in real world settings, or the need to determine which patients are likely to suffer from chronic pain following surgery and may therefore be at higher risk for opioid use disorder.

The recent emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus and the disease it causes, coronavirus disease 2019 (COVID-19), have required an unprecedented scientific response to address this global pandemic. With $30 million provided by the Coronavirus Aid, Relief, and Economic Security (CARES) Act, 2020,[235] we are supporting research to prevent, prepare for, and respond to coronavirus, domestically or internationally. In FY 2020, we supported emergency competitive revisions to existing CF grants and cooperative agreements to conduct innovative research on COVID-19 and coronavirus. Projects funded through these supplements include research on host and viral genes influencing infection severity, generation of genetically diverse mouse models susceptible to SARS-CoV-2, rapid screening for neutralizing antibodies, and understanding causes of disparities in COVID-19 severity across socioeconomic groups.

We also issued new FY 2021 Funding Opportunity Announcements for the Transformative Research[236] and Early Independence Awards[237] to bring new, innovative perspectives to COVID-19 and coronavirus research. These awards, part of the High-Risk, High-Reward program, support highly innovative research that is expected to have exceptional impact. Any

[234] commonfund.nih.gov/editing
[235] www.congress.gov/116/plaws/publ136/PLAW-116publ136.pdf
[236] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-020.html
[237] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-021.html

relevant area of SARS-CoV-2 research is welcome, including behavioral/social science research, research on health disparities, novel therapeutics, and other related topics.

Diversifying the workforce and closing the gap in health disparities

The NIH has a long-standing interest in supporting a diverse scientific workforce that fosters contributions from creative and talented individuals from all backgrounds. Within the CF, we support several efforts designed to test new approaches for attracting and retaining biomedical researchers from groups underrepresented in the workforce, rigorously evaluate these approaches to determine their effectiveness in different contexts, and disseminate information about proven approaches so that institutions everywhere can implement strategies that are known to be effective.

The Enhancing the Diversity of the NIH-Funded Workforce program, also known as the Diversity Program Consortium (DPC),[238] is developing, implementing, assessing, and disseminating innovative and effective approaches to engaging, training, and mentoring students; enhancing faculty development; and strengthening institutional research training infrastructure to enhance the participation and persistence of individuals from underrepresented backgrounds in biomedical research careers. The DPC is comprised of several integrated initiatives: awards to undergraduate institutions to develop and implement approaches to engage, retain, and prepare students from diverse backgrounds in biomedical research; a national mentoring network; a coordination and evaluation center; support for Offices of Sponsored Programs at educational institutions; and awards to use DPC experimental methods to study the effectiveness of a training, mentoring, or capacity building intervention.

The Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program[239] aims to address the persistent challenge of achieving meaningful levels of diversity at the faculty level by targeting institutional culture change. The FIRST program aims 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 program is examining whether recruitment of a critical mass of investigators committed to diversity and inclusion will foster the institutional changes needed to create sustainable improvements in faculty diversity. FIRST supports a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts.

While NIH has long supported programs to improve the diversity of the scientific workforce, those efforts have not been sufficient to achieve racial equity across the biomedical research enterprise. Through a new initiative called UNITE[240], NIH has begun to identify short-term and long-term actions to end structural racism and racial inequities throughout the biomedical research enterprise. Part of ending racial inequities in biomedical research will be to ensure NIH-supported research benefits the health of all populations, especially those whose health is

[238] commonfund.nih.gov/diversity
[239] commonfund.nih.gov/first
[240] www.nih.gov/ending-structural-racism

negatively impacted by racism. For this reason, conducting new research into health disparities, minority health, and health inequities is an important goal of UNITE.

As part of UNITE, the Common Fund and UNITE team members are developing new initiatives to bolster innovation, solve challenges, and address emergent opportunities in health disparities research. In FY 2021, the Common Fund launched the Transformative Research to Address Health Disparities and Advance Health Equity initiative. This initiative supports innovative projects in developing, disseminating, or implementing effective interventions that prevent, reduce, or eliminate health disparities and health inequities, and also expands the research base dedicated to health disparities research at minority serving institutions.

Capitalizing on foundational investments

Science often advances by building upon previous discoveries, leveraging prior investments to propel research forward. CF programs are designed to be catalytic, either capitalizing on emerging scientific opportunities or removing research roadblocks to accelerate progress across a wide range of biomedical research fields. Many CF programs produce resources, such as data sets, tools, technologies, or methods, that are designed to spur subsequent biomedical advances. Additionally, CF programs often aim to establish new paradigms in biology, generating foundational knowledge to support new and emerging fields. Therefore, CF programs often represent foundational investments in biomedical research that are expected to have extraordinarily high impact.

Examples of foundational CF programs include:

- Human BioMolecular Atlas Program (HuBMAP) – HuBMAP is developing a framework for mapping the human body at cellular resolution as a basis for understanding human health and diagnosing, monitoring, and treating disease. This will be achieved through a globally coordinated effort to develop new technologies; generate foundational tissue maps; and make data findable, accessible, interoperable, and reusable.
- Molecular Transducers of Physical Activity in Humans – This program aims to uncover the molecules that underlie the health benefits of physical activity across many tissues/organs, and where possible, to associate these molecules with individual differences in response to exercise. This "molecular map" is anticipated to catalyze the development of therapeutic strategies that mimic components of the physical activity response and inform development of more specific exercise recommendations. Additional funding in FYs 2018 and 2019 enabled a more detailed analysis of human tissues after exercise, pilot analyses of how exercise may affect the microbiome, and analyses of how the microbiome may influence the health benefits of exercise.
- Extracellular RNA Communication (ERC) – The ERC program aims to generate new paradigms for cell-to-cell communication through the analysis of extracellular RNAs. Once thought to exist only inside cells, the evolving understanding that RNA is exported from cells hints at previously unknown processes through which cells in one tissue influence cells in another tissue to maintain or disrupt health. These extracellular RNAs may also provide new diagnostic or therapeutic strategies. Resources developed through the ERC program are catalyzing this emerging field of research.

We make significant efforts to evaluate programs during their lifetime and assess outcomes 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. New challenges and opportunities will be supported in FY 2022 from funds made available as other programs end, move to other sources of support, or require decreased support as indicated by evaluative data.

Overall Budget Policy. The FY 2022 President's Budget request for the CF is $658.5 million, an increase of $10.0 million from the FY 2021 Enacted level. This level of funding will support high-priority activities within existing programs and support the launch of the Nutrition for Precision Health, powered by the *All of Us* Research Program. This new program will develop algorithms to predict individual responses to diet through partnership with the *All of Us* program. Additionally, a program to explore somatic mosaicism in various human tissues is being considered for launch in FY 2022, as explained later in this narrative.

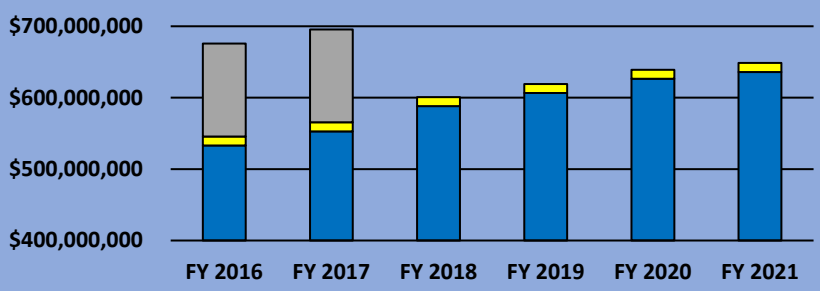
National Institutes of Health
Office of Strategic Coordination - The Common Fund

About the NIH Common Fund

The NIH Common Fund provides a dedicated source of support for trans-NIH scientific programs with the potential for extraordinary impact. Common Fund programs are time-limited, goal-driven investments that accelerate emerging science, remove research roadblocks, enhance the biomedical workforce, and/or support high-risk, high-reward science. These programs often involve multi-disciplinary, innovative researchers who work together to tackle a shared, ambitious goal. Common Fund programs span the NIH mission, addressing scientific opportunities and research challenges in some of the most cutting-edge areas of biomedical research, including genome editing, pain biomarkers, undiagnosed and rare diseases, data science, and bioelectronic medicine.

Elizabeth Wilder, Ph.D., has been the Director of the Office of Strategic Coordination since 2010. She received a Ph.D. in Molecular/Cellular Biology from Northwestern University and was a faculty member at the University of Pennsylvania School of Medicine before joining the NIH in 2002.

Common Fund Appropriations History



The FY 2022 President's Budget request is $658.5 million

Blue indicates Common Fund base appropriation; yellow indicates the Pediatric Research Initiative Fund; gray indicates the Precision Medicine Initiative (moved out of the Common Fund to the Office of the Director in FY 2018).

Common Fund Research Accomplishments

- The Genotype-Tissue Expression (GTEx) program is revolutionizing our understanding of how genes are expressed in different tissues in the body, how they are regulated, and how variations in gene expression result in a wide range of human diseases.
- The Undiagnosed Diseases Program (UDP) is establishing a new model for meeting the pressing need for diagnosis of rare diseases. In the first 20 months of operation, UDP accepted over 600 patients, provided a diagnosis in 35 percent of patients evaluated, and discovered 31 new syndromes.
- The Regenerative Medicine Program supported research leading to the first United States phase I/IIa clinical trial to test the safety of a novel stem cell therapy to treat age-related macular degeneration.
- The Knockout Mouse Phenotyping Program (KOMP2) systematically described genes with previously unknown function, providing information on hearing, embryonic development, metabolism, aging, and more.

Facts and Figures

- 21 Scientific Programs in FY 2020
- 561 Principal Investigators (PI)*
  - 175 High-Risk, High Reward awardees*
  - 104 early career High-Risk, High-Reward awardees*
- 139 competing Research Project Grants*
- In the past 10 years, Common Fund-supported researchers have published over 28,000 papers
- In FY 2020, Common Fund supported research in 38 states and 7 countries.

*Data represent yearly averages from FY 2016 – FY 2020

National Institutes of Health
Office of Strategic Coordination - The Common Fund

Current Activities

The Common Fund supports scientific programs that span the mission of the entire NIH. Examples of exciting ongoing activities include:

- **Somatic Cell Genome Editing** – working to improve the efficacy and specificity of gene editing approaches to help reduce the burden of common and rare diseases caused by genetic mutations.
- **Transformative Research to Address Health Disparities and Advance Health Equity –** developing, disseminating, and implementing innovative and effective interventions to prevent, reduce, or eliminate health disparities and health inequities.
- **Stimulating Peripheral Activity to Relieve Conditions** – accelerating the development of novel therapeutic devices that modulate nerve function by providing foundational data and tools

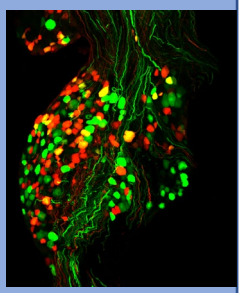


Image from the SPARC program shows sensory (vagal) neurons in a mouse

Future Initiatives

As Common Fund programs end, funds are freed to invest in new challenges and opportunities. One potential program is undergoing planning activities and may be implemented in FY 2022:

- **Somatic Mosaicism Across Human Tissues** - to investigate the causes and effects of genetically distinct cells within a single individual (mosaicism)

Image Credit: Darryl Leja, NHGRI

High-Risk, High-Reward Research Program

Science often advances step-by-step, with each new discovery adding a modest, yet important, piece in a complex biological puzzle. However, rapid scientific advancement also requires research that is innovative and flexible, allowing researchers to follow their ideas into novel territory. NIH provides dedicated support for this type of "high-risk, high-reward" research. The Common Fund's High-Risk, High-Reward (HRHR) Research program supports exceptionally creative scientists pursuing highly innovative and impactful research on any topic within the NIH mission. HRHR awardees are developing breakthrough technologies and making paradigm-shifting discoveries. For example, HRHR awardees are exploring how blood platelets could be engineered to fight cancer, whether a gut-brain connection may play a role in autism spectrum disorder, and what maps of all the neural networks involved in memory look like. In FY 2021, the Common Fund launched a new Transformative Research to Address Health Disparities and Advance Health Equity initiative to support research in developing, disseminating, or implementing innovative and effective interventions that prevent, reduce, or eliminate health disparities and inequities.

NIH DIRECTOR'S PIONEER AWARD

NIH DIRECTOR'S TRANSFORMATIVE RESEARCH AWARD

NIH DIRECTOR'S NEW INNOVATOR AWARD

NIH DIRECTOR'S EARLY INDEPENDENCE AWARD

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note there may be overlap between budget mechanisms and activity detail, and these highlights will not sum to the total change for the FY 2022 President's Budget Request for the Common Fund, which is $10.0 million more than the FY 2021 Enacted level, for a total of $658.5 million.

Research Project Grants (-$19.4 million; total $350.1 million): The Common Fund expects to support a total of 379 Research Project Grant (RPG) awards in FY 2022, down from 393 in FY 2021. Estimated awards for FY 2022 include 277 Noncompeting RPGs and 102 Competing RPGs. The decrease in RPGs reflect the planned ramping down of several programs. Additionally, a change in the funding approach for the NIH Director's New Innovator awards results in a temporary decline in funding levels while maintaining a similar number of New Innovator awards. Prior to FY 2021, New Innovator awards provided all five years of funding in the first fiscal year of the research project. However, to enhance financial stewardship, starting in FY 2021, New Innovator awards now provide support for years one to three of the project in the first fiscal year, and then provide support for years four and five in the fourth fiscal year.

Research Centers (+$31.9 million; total $88.2 million): The estimated increase in support for Research Centers is due to planned ramping up or launch of programs that include specialized/comprehensive centers, including Bridges to Artificial Intelligence (Bridge2AI), Cellular Senescence Network (SenNet), Faculty Institutional Recruitment for Sustainable Transformation (FIRST), Human BioMolecular Atlas Program (HuBMAP), and Nutrition for Precision Health (NPH) programs.

(Dollars in Thousands)	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		FY 2022 +/- FY 2021 Enacted	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	258	$197,806	262	$222,728	277	$233,054	15	$10,326
Administrative Supplements	*(34)*	5,265	*(40)*	6,164	*(53)*	8,273	*(13)*	2,109
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	137	146,739	131	140,582	102	108,763	-29	-31,819
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	137	$146,739	131	$140,582	102	$108,763	-29	-$31,819
Subtotal, RPGs	395	$349,810	393	$369,474	379	$350,090	-14	-$19,384
SBIR/STTR	0	0	0	0	0	0	0	0
Research Project Grants	395	$349,810	393	$369,474	379	$350,090	-14	-$19,384
Research Centers:								
Specialized/Comprehensive	26	$28,435	35	$38,286	65	$71,449	30	$33,163
Clinical Research	10	18,343	7	12,046	6	10,762	-1	-1,284
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	4	4,320	6	5,996	6	5,997	0	1
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	40	$51,097	48	$56,328	77	$88,208	29	$31,880
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	114	195,084	105	179,354	105	178,853	0	-501
Other Research	114	$195,084	105	$179,354	105	$178,853	0	-$501
Total Research Grants	549	$595,991	546	$605,156	561	$617,151	15	$11,995
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	430	10,268	526	12,758	439	10,631	-87	-2,127
Total Research Training	430	$10,268	526	$12,758	439	$10,631	-87	-$2,127
Research & Develop. Contracts		$577	0	$0	0	$0	0	$0
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Intramural Research	0	13,703	0	7,439	0	7,460	0	21
Res. Management & Support	0	18,572	0	23,186	0	23,297	0	111
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	549	$639,111	546	$648,539	561	$658,539	15	$10,000

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

BUDGET BY PROGRAM

Common Fund Program	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
4D Nucleome	28,614	28,394	28,378
Acute to Chronic Pain Signatures	16,636	15,132	6,432
Bridge to Artificial Intelligence (Bridge2AI)	0	0	32,000
Cellular Senescence Network (SenNET)	0	25,000	40,350
Enhancing the Diversity of the NIH-Funded Workforce	53,682	48,968	44,222
Extracellular RNA Communication	6,753	11,845	10,841
Faculty Institutional Recruitment for Sustainable Transformation (FIRST)	0	4,000	27,217
Gabriella Miller Kids First Pediatric Research	12,984	13,000	13,063
Global Health	11,376	9,567	0
Glycoscience	13,349	5,358	0
Harnessing Data Science for Health Discovery and Innovation in Africa (DSI-Africa)	525	12,493	12,455
Health Care Systems Research Collaboratory	1,750	1,750	225
High-Risk Research	196,948	197,140	173,830
NIH Director's Pioneer Award	*51,701*	*50,520*	*51,333*
NIH Director's New Innovator Award Program	*83,719*	*62,437*	*51,450*
Transformative Research Award	*38,249*	*38,664*	*40,248*
NIH Director's Early Independence Award Program	*23,280*	*21,519*	*20,799*
Transformative Health Disparities Research	*0*	*24,000*	*10,000*
Human BioMolecular Atlas Project (HuBMAP)	27,021	28,661	44,676
Illuminating the Druggable Genome	13,369	14,763	13,390
Knockout Mouse Phenotyping Program	10,981	429	0
Library of Integrated Network-Based Cellular Signatures (LINCS)	82	0	0
Metabolomics	12,397	12,397	106
Molecular Transducers of Physical Activity	46,089	44,007	40,493
Nutrition for Precision Health	0	0	22,549
NIH Center for Regenerative Medicine (NCRM)	5,736	0	0
Science of Behavior Change	168	0	0
Somatic Cell Genome Editing	34,449	45,695	50,433
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	45,000	42,623	25,000
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	51,769	37,490	19,890
Undiagnosed Diseases Network	24,389	22,400	16,400
Strategic Planning, Evaluation, and Infrastructure	25,043	27,428	25,386
Subtotal Common Fund	639,111	648,539	647,336
New Initiatives in Common Fund	0	0	11,203
Total Common Fund	639,111	648,539	658,539

NIH Common Fund

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

Budget Authority (BA):

	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
BA	$639,111,000	648,539,000	658,539,000	$10,000,000
FTE	0	0	0	0

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

PROGRAM DESCRIPTIONS

The CF supports over 20 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 – within five to ten years. Planned activities and budgets for Common Fund programs are strategically developed, with clear milestones defined throughout the lifetime of the program to enable measurement of progress towards pre-defined goals. Therefore, Common Fund programs often undergo planned budget shifts driven by the needs and activities for each program.

Two CF programs will receive their last year of support in FY 2021; funds are therefore not requested in FY 2022. These are Glycoscience[9] and Global Health.[10] Information on these programs and their accomplishments can be found on the program websites.

Highlighted below are programs that exemplify the science to be supported in FY 2022.

Acute to Chronic Pain Signatures (A2CPS)

As part of the NIH response to the growing opioid crisis, the A2CPS[11] program aims to further understanding of the transition from acute to chronic pain. Acute pain following injury resolves

[9] commonfund.nih.gov/Glycoscience
[10] commonfund.nih.gov/globalhealth
[11] commonfund.nih.gov/pain

in many patients, but the pain can become chronic for a large number of people, even after the injury itself has healed. This transition is poorly understood and therefore prevention or treatment is difficult. A2CPS is addressing this challenge by developing an objective set of biomarkers (a "signature") to predict susceptibility of transitioning from acute to chronic pain. The A2CPS program enhances the objectives of the NIH Helping to End Addiction Long-term[SM] (HEAL) Initiative, a trans-agency effort to speed scientific solutions to end the opioid public health crisis. A2CPS will benefit the HEAL research priority to enhance pain management. The decrease in funds requested for FY 2022 is driven by planned ramping down of clinical studies collecting data from patients following an acute pain event.

Budget Policy. The FY 2022 President's Budget request is $6.4 million, a decrease of $8.7 million or 57.5 percent compared to the FY 2021 Enacted level. This decrease reflects the planned ramping down of clinical studies and will support data generation, analysis, and integration.

Bridge to Artificial Intelligence (Bridge2AI)

Rapid advancements in artificial intelligence and machine learning hold great promise for biomedical research. Many NIH ICs are investing in these promising technologies, and the NIH is dedicating significant effort to developing strategic and cross-agency activities to accelerate the use of artificial intelligence in biomedical research, clinical research, and medicine. Based on recommendations from the NIH's Advisory Committee to the Director on how to capitalize on recent advances in artificial intelligence technologies, the Bridge2AI program is fostering the use of artificial intelligence strategies for biomedical and behavioral research through the generation of new biomedically relevant data sets amenable to machine learning analysis at scale. FY 2022 funds will be used to launch activities aiming to generate rubrics to measure amenability of data sets to machine learning approaches, develop tools to accelerate AI-readiness, enhance existing data generation efforts to improve AI-readiness, generate gold-standard data sets that adhere to these rubrics, and use the rubrics to evaluate and update select existing public biomedical research data.

Cellular Senescence Network (SenNET)

As we age, tissues throughout the body accumulate small numbers of specialized cells that no longer divide, called senescent cells. Under some conditions, senescent cells may accumulate and release molecules that can cause damage to nearby tissue, while in other conditions, senescent cells can protect health by preventing tumor growth or promoting the growth of new tissues. There are many unanswered questions about how, when, why, and where senescent cells form, but their rarity and diversity make them difficult to study. The SenNet program aims to comprehensively identify and characterize the differences in senescent cells across the body, across various states of human health, and across the lifespan. SenNet will provide publicly accessible atlases of senescent cells, the differences among them, and the molecules they secrete, using data collected from multiple human and model organism tissues. To identify and characterize these rare cells, SenNet will develop innovative tools and technologies that build upon previous advances in single cell analysis, such as those from the Common Fund's Human Biomolecular Atlas Program[12] and Single Cell Analysis Program.[13] Lastly, SenNet aims to unite cellular senescence researchers by developing common terms and classifications for senescent cells.

[12] commonfund.nih.gov/HuBMAP
[13] commonfund.nih.gov/Singlecell

Budget Policy. The FY 2022 President's Budget request is $40.4 million, an increase of $15.4 million or 61.4 percent from the FY 2021 Enacted level. The increase in funding will support ramping up of the tissue mapping centers, as well as technology development and application projects, and a consortium organization and data coordination center.

Harnessing Data Science for Health Discovery and Innovation in Africa (DS-I Africa)

The DS-I Africa program will leverage data science technologies and prior NIH investments to develop solutions to Africa's most pressing public health problems through a robust ecosystem of new partners from academic, government, and private sectors. Despite recent progress, Africa carries a disproportionate share of the global burden of disease. However, extensive mobile phone coverage in Africa has led to major innovations that could bring the clinic to the patient through data science technologies. This could have applications to rural and underserved populations in the United States and worldwide. Additionally, substantial investment in African research and research training by NIH ICs, the Common Fund, and other organizations has provided resources and expertise that can be leveraged to impact health in Africa and around the world. This program aims to promote sustainability of the African health research enterprise by encouraging these innovative partnerships, and will also consider ethical, legal, and social issues (ELSI) for data science research and its applications to public health in Africa. Funds requested in FY 2022 will support industry partnerships for innovation, training programs, an open data science platform and coordinating center, oversight and coordination activities, and ELSI research.

Faculty Institutional Recruitment for Sustained Transformation (FIRST)

As the nation's population grows increasingly diverse, there is an urgent need to ensure that scientific talent is nurtured, recognized, and supported in researchers from diverse backgrounds. The FIRST program aims to establish a more inclusive and diverse biomedical research workforce through support of faculty cluster hiring and institutional culture change efforts. Based on early results from other cohort-based hiring programs, FIRST will explore whether hiring a critical mass of faculty committed to diversity and scientific excellence will promote institutional culture changes necessary to foster inclusive environments that create meaningful improvements in researcher diversity. FIRST will support a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts. Funds requested in FY 2022 will be used to support hiring of the first round of faculty cohorts and ramping up of the coordination and evaluation center.

Budget Policy. The FY 2022 President's Budget request is $27.2 million, an increase of $23.2 million or 580.4 percent over the FY 2021 Enacted level. This increase in support will be used to hire the first round of faculty cohorts and ramp up coordination and evaluation activities.

Gabriella Miller Kids First Pediatric Research Program (Kids First)

The Kids First[14] program aims to generate new insights into childhood cancer and birth defects through development of a widely accessible data resource containing high-quality genetic and clinical data from pediatric patient cohorts, along with associated computational tools to facilitate data analysis. There is considerable evidence for undiscovered connections between childhood cancer and structural birth defects, and therefore examining these data sets together will facilitate new discoveries and novel ways of thinking about these conditions. Funds requested in FY 2022 will be used to support pediatric research, consistent with the Gabriella Miller Kids First Research Act, and remain constant at the statutory level set by this legislation. A small amount to support program management activities is requested from the general Common Fund appropriation. In FY 2022, the Kids First program will launch a second stage, building on the successes within the program thus far to strengthen the value of the Kids First Data Resource and sustain the resource after Common Fund support. During stage 2, Kids First will continue to generate data, develop new initiatives to identify underlying mechanisms of these pediatric conditions, and strengthen Kids First's ability to work with other data resources.

Budget Policy. The FY 2022 President's Budget request is $13.1 million, an increase of $0.1 million, or 0.5 percent from the FY 2021 Enacted level. Programmatic funding remains constant at the $12.6 million statutory level and will be used to conduct pediatric research in the second stage of this program. The remainder of the funds are requested in the regular CF appropriation to support research management activities.

High-Risk, High-Reward (HRHR) Research Program

The HRHR[15] program supports exceptionally creative scientists proposing innovative and transformative research in any scientific area within the NIH mission through complementary initiatives: the Pioneer Award, New Innovator Award, Transformative Research Award, and Early Independence Award. These awards are intended to support transformative science that is inherently difficult and may appear risky because preliminary data are not required, but is necessary to accelerate the pace of scientific discovery and advance human health. For all HRHR awards, "high risk" does not imply that additional risk is posed to research participants, as these awards use the same rigorous procedures to protect research participant safety as all other NIH-funded studies involving human subjects. Although the majority of HRHR funds are dedicated to innovative ideas on biomedical research topics proposed by the investigator, funds in FY 2021 were used to address to specific areas of pressing public health need: 1) COVID-19-related funding opportunities within the Transformative Research and Early Independence Awards,[16, 17] supported via the Coronavirus Aid, Relief, and Economic Security (CARES) Act, 2020, and 2) Accelerating Leading-edge Science in ALS (ALS^2) within the Transformative Research Awards.[18] Funds requested in FY 2022 will be used to support additional innovative, high priority projects with the potential for extraordinary impact.

[14] commonfund.nih.gov/KidsFirst
[15] commonfund.nih.gov/highrisk
[16] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-020.html
[17] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-021.html
[18] grants.nih.gov/grants/guide/notice-files/NOT-RM-20-019.html

Additionally, in FY 2021, the Common Fund launched a new Transformative Research to Address Health Disparities and Advance Health Equity initiative[19] to support research in developing, disseminating, or implementing innovative and effective interventions that prevent, reduce, or eliminate health disparities and health inequities. This initiative also aims to expand the capacity for health disparities research at minority serving institutions. This effort is part of NIH's UNITE[20] initiative, which is identifying short- and long-term actions to end structural racism and racial inequities throughout the biomedical research enterprise. Conducting new research into health disparities, minority health, and health inequities is an important goal of UNITE, and this Common Fund initiative is one component of the NIH-wide strategy to achieve this goal. Awards for this initiative were issued in FY 2021, using multiyear funding to provide support for the first two years of the awards and annual funding to support years three through five. An additional round of awards to support health disparities research at minority serving institutions will be funded in FY 2022.

Budget Policy. The FY 2022 President's Budget request is $173.8 million, a decrease of $23.3 million or 11.8 percent from the FY2021 Enacted level. The reduction in support reflects a change in funding approach for the NIH Director's New Innovator awards and does not reflect a decrease in the anticipated number of awards provided. To improve financial stewardship, starting in FY 2021, the New Innovator awards provide support for years one through three of the project in the first fiscal year, and then provide support for years four and five in the fourth fiscal year. Prior to FY 2021, New Innovator awards provided all five years of funding in the first fiscal year; thus, this change in funding approach results in a temporary decline in funding levels while maintaining similar numbers of expected awards.

Human BioMolecular Atlas Program (HuBMAP)

HuBMAP[21] is developing a framework for mapping the human body at single cell resolution to provide a new foundation for understanding human health and diagnosing, monitoring, and treating disease. Since the cell is the fundamental unit of the human body, an understanding of normal and disease processes at this level is anticipated to lead to more specific and effective therapies, and lead to new insights into human health, growth, development, and aging. In recent years, technologies that enable the analysis of single cells within the context of tissues have made mapping the human body at the level of single cells feasible. However, this is an enormous challenge, given that there are approximately 37 trillion cells in the body. HuBMAP will address this challenge through a globally coordinated effort to develop an open and global platform to map healthy cells in the human body, generate foundational tissue maps, and develop tools, technologies, and resources for broad dissemination to the entire biomedical research community. Increased funds requested in FY 2022 will support additional efforts in tissue mapping, technology development, and data coordination, integration, and analysis.

[19] commonfund.nih.gov/healthdisparitiestransformation
[20] www.nih.gov/ending-structural-racism
[21] commonfund.nih.gov/HuBMAP

Budget Policy. The FY 2022 President's Budget request is $44.7 million, an increase of $16.0 million or 55.9 percent from the FY 2021 Enacted level. This increased level of funding will support the additional efforts described above.

Illuminating the Druggable Genome (IDG)

Most drugs target proteins within four families – G-protein coupled receptors, nuclear receptors, ion channels, and protein kinases. However, only a small number of proteins within each of these families are well-studied, and these are typically proteins that are present in many cells throughout the body. Therefore, drugs that target these proteins may cause widespread adverse effects in cells and tissues that are not affected by disease. In contrast, the lesser known members of these protein families may be present in fewer tissues, and thus have potential as specific drug targets leading to fewer side effects. IDG, originally launched as a pilot in FY 2014, initially aimed to compile data about the uncharacterized proteins within the four protein classes that are most frequently targeted by drugs. An integral part of this effort was the development of publicly available resources integrating information about understudied proteins so that researchers everywhere can leverage this information to catalyze their own research. In the second, or implementation, stage, IDG is capitalizing on the information gathered and technologies developed in the pilot to further elucidate the function of uncharacterized proteins within three of the families that are least characterized – G-protein-coupled receptors, ion channels, and protein kinases. IDG is also expanding the informatics tools developed in the pilot stage and disseminating the IDG-generated resources to the biomedical research community. Funds requested in FY 2022 will continue these efforts.

Budget Policy. The FY 2022 President's Budget request is $13.4 million, a decrease of $1.4 million or 9.3 percent from the FY 2021 Enacted level. IDG will continue efforts initiated in the implementation stage, providing information, tools, and resources to the broad biomedical research community on uncharacterized proteins within three protein families of interest for drug development.

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, researchers 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 Molecular Transducers of Physical Activity Consortium (MoTrPAC) will improve understanding of the molecular mechanisms by which physical activity improves health by extensively cataloguing the biological molecules affected by physical activity in people and in animals, identifying some of the key molecules that underlie the systemic effects of physical activity, and characterizing the function of these key molecules. Support requested in FY 2022 will continue to support clinical and animal studies, analysis of biological samples, and coordination and data management.

Budget Policy. The FY 2022 President's Budget request is $40.5 million, a decrease of $3.5 million or 8.0 percent from the FY 2021 Enacted level. This funding level will continue to support data collection, analysis, and coordination.

Nutrition for Precision Health, powered by the *All of Us* Research Program (NPH)

Nutrition plays an integral role in human development and in the prevention and treatment of disease. However, there is no such thing as a perfect, one-size-fits-all diet. The goal of the **NPH program**[22] is to develop algorithms that predict individual responses to food and dietary patterns. The NPH program will build on recent advances in biomedical science, including artificial intelligence (AI) and microbiome research, as well as the infrastructure and large, diverse participant group of the *All of Us* Research Program. These advances provide unprecedented opportunities to generate new data to provide insight into personalized, or precision, nutrition. Designed to implement aspects of the Strategic Plan for NIH Nutrition Research,[23] the NPH program will conduct a study nested in the *All of Us* Research Program to explore how individuals respond to different diets. Ultimately, the predictive algorithms developed through NPH are anticipated to enable 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.

Budget Policy. The FY 2022 President's Budget request is $22.5 million, an increase of $22.5 million from the FY 2021 Enacted level. The first year of funding for this program will support clinical centers; data generation centers; an AI, data modeling, and bioinformatics center; a biobank; data and study coordination; and oversight and coordination.

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

The SPARC[24] program is accelerating the development of novel therapeutic devices that modulate electrical activity in nerves to improve organ function. Foundational data and tools from SPARC are allowing researchers to design more effective and specific devices. Modulation of nerve activity has the potential to treat a variety of diseases and conditions, but there is an urgent need to better understand the precise pattern of connections between nerves and their end organs, so that the nerves can be precisely and specifically stimulated. SPARC is addressing this need by generating maps and tools to identify and influence therapeutic targets within the neural circuitry of a wide range of organs and tissues. Ultimately, this therapeutic strategy could offer new treatment options for diverse diseases and conditions such as hypertension, heart failure, gastrointestinal disorders, type II diabetes, inflammatory disorders, and more. The first stage of the SPARC program ends in FY 2021, and a second stage beginning in FY 2022 plans to engage industry to help catalyze development of next-generation bioelectronic medicines by providing access to therapeutic targets and devices, high-value datasets, and computational science resources.

[22] commonfund.nih.gov/nutritionforprecisionhealth
[23] niddk.nih.gov/about-niddk/strategic-plans-reports/strategic-plan-nih-nutrition-research
[24] commonfund.nih.gov/sparc

Budget Policy. The FY 2022 President's Budget request is $25.0 million, a decrease of $17.6 million or 41.4 percent from the FY 2021 Enacted level. This level of funding will support the second stage of the SPARC program, which will build on the capabilities and resources of the first stage to accelerate bioelectronic medicines.

Transformative High Resolution Cryo-Electron Microscopy (CryoEM)

The CryoEM[25] program is enabling novel discoveries in structural biology by broadening access to cutting-edge cryo-electron microscopy techniques and training. 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. By providing greater access, the CryoEM program is anticipated to catalyze fundamental biological discoveries, as well as accelerate development of vaccines and therapeutics. In FY 2022, there is a planned decrease in support as the centers for cryo-electron microscopy and cryo-electron tomography, a related technology, have completed their purchase of high-end equipment and are focused on processing samples to enable the biomedical research community and accelerate development of drugs and vaccines to combat many diseases and conditions.

Budget Policy. The FY 2022 President's Budget request is $19.9 million, a decrease of $17.6 million or 47.0 percent from the FY 2021 Enacted level. This decrease in funding reflects the completion of high-end equipment purchases and will support processing samples for the biomedical research community.

Undiagnosed Diseases Network (UDN)

The UDN[26] is fostering a nationwide network of clinicians and laboratory scientists to improve diagnosis of rare and undiagnosed diseases. Based on the success of the NIH Clinical Center's Undiagnosed Diseases Program, the UDN expanded this approach to academic health centers across the county, working through challenges associated with implementation in different clinical settings and economic models. UDN promotes the use of state-of-the-art genomic sequencing technologies in disease diagnosis and engages basic researchers to uncover underlying disease mechanisms so that treatments may be identified. In the first 20 months of operation, UDN accepted 601 participants undiagnosed by traditional medical practices. Of those who completed their UDN evaluation during this time, 35 percent were given a diagnosis. Many of these diagnoses were rare genetic diseases, including 31 previously unknown syndromes. Now in its second stage, UDN is focusing on forming a sustainable national resource to diagnose both rare and new diseases, advancing laboratory and clinical research, enhancing global coordination and collaboration among laboratory and clinical researchers, and sharing resulting data and approaches throughout the scientific and clinical communities. As part of the planned effort to build a sustainable, long-term national model for the use of genomic

[25] commonfund.nih.gov/CryoEM
[26] commonfund.nih.gov/Diseases

data in disease diagnosis, the program will begin to transition to other sources of support in FY 2022.

Budget Policy. The FY 2022 President's Budget request is $16.4 million, a decrease of $6.0 million or 26.8 percent from the FY 2021 Enacted level. This decrease in support reflects the planned transition of UDN centers to sustainable sources of support as the program ramps down, thereby enabling a national, long-term approach for diagnosing patients with rare and undiagnosed diseases.

Strategic Planning, Evaluation, and Infrastructure

Management of the Common Fund requires that certain activities be undertaken for the benefit of the Common Fund as a whole. In addition to long-standing investments in strategic planning and evaluation, described below, the Common Fund has more recently expanded investments in infrastructure to address challenges facing programs that are increasingly employing data-intensive strategies to achieve their goals. This infrastructure, referred to as the Common Fund Data Ecosystem (CFDE),[27] is helping to ensure that all Common Fund data sets are Findable, Accessible, Interoperable, and Reusable (FAIR), providing training for users to operate on the data in a cloud environment, and ensuring that Common Fund data continue to be available after individual programs are completed. The CFDE will amplify the impact of many CF programs by enabling researchers to interrogate multiple disparate data sets, and thereby make new kinds of scientific discoveries that were not possible before. The CFDE is also being designed in parallel with NIH IC data platforms to enable crosstalk between Common Fund and IC data sets and to address NIH-wide data management objectives described in the NIH Strategic Plan for Data Science.

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 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 Common Fund 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

[27] commonfund.nih.gov/dataecosystem

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 2022 programs involved gathering ideas from across the NIH community, leveraging the wide-ranging expertise of the NIH's scientific staff and senior leaders. From this process, two promising ideas emerged. One, the Cellular Senescence Network, was able to be launched on an accelerated timeframe in FY 2021. Another idea, Somatic Mosaicism across Human Tissues (SMaHT) is currently undergoing planning for a potential launch in FY 2022. SMaHT will investigate the causes and effects of genetically distinct cells within a single individual (mosaicism).