

NIH Common Fund

Congressional Justification FY 2023

Department of Health and Human Services National Institutes of Health

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES NATIONAL INSTITUTES OF HEALTH

NIH Common Fund

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Director's Overview

The 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.¹ We support 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 are designed to achieve specific, high-impact goals and milestones within a 5- to 10year timeframe. These bold scientific programs often accelerate emerging science, enhance the biomedical research workforce, remove research roadblocks, or support high-risk, high-reward science. 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.



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

Bold Science, Catalyzing Discoveries Supporting intovation and science Supporting intovation and science Supporting Suppo

The NIH Common Fund

¹ commonfund.nih.gov/

CF programs are broad-reaching and span the entire NIH mission. As a general framework, however, they can be grouped into four categories, with some programs relevant to more than one category: Transformational Discoveries and Tools, Catalytic Data Resources, Reengineering Clinical and Translational Research Processes, and Innovative Approaches to Workforce Development.

Transformational Discoveries and Tools

Many CF programs have a primary objective to enable discovery, often through the development of novel and broadly useful tools, data, and methods. For example, the Molecular Transducers of Physical Activity² program is investigating the molecular responses to exercise and, where possible, associating individual signatures with specific physiologic outcomes, allowing for the development of more targeted exercise interventions and physical activity prescriptions. The Transformative High Resolution Cryo-Electron Microscopy³ program is providing nationwide access to high resolution cryo-electron microscopy and tomography for biomedical researchers by creating national service centers, technological improvements, and development of an expert workforce. The High-Risk, High-Reward⁴ program supports several initiatives that foster innovation and scientific discovery across all areas of the NIH mission through support of exceptionally creative scientists and projects that may carry high levels of risk, but which hold the promise of exceptional impact.

Catalytic Data Resources

Several CF programs have an overarching goal of establishing new data resources or new methods for managing data. Also included in this category are efforts to enhance the utility of CF data sets. The Human BioMolecular Atlas Program (HuBMAP)⁵ is catalyzing development of an open, global data framework for comprehensively mapping the human body at cellular resolution through data generation and by interoperating with other single cell mapping efforts. Bridge to Artificial Intelligence (Bridge2AI)⁶ is generating flagship data sets and best practices for the collection and preparation of data sets amenable to AI and machine learning approaches to address biomedical and behavioral grand challenges.

Re-engineering Clinical and Translational Research Processes

Several CF programs are establishing new models for translational and clinical research. The Somatic Cell Genome Editing⁷ program is developing a translational pipeline for somatic cell genome editing therapies through improved, Investigational New Device (IND)– enabling technologies. The Transformative Research to Address Health Disparities and Advance Health Equity⁸ initiative is supporting innovative research projects that aim to have a major impact in developing, disseminating, or implementing novel and effective interventions that prevent, reduce, or eliminate health disparities and health inequities.

² <u>commonfund.nih.gov/MolecularTransducers</u>

³ <u>commonfund.nih.gov/CryoEM</u>

⁴ <u>commonfund.nih.gov/highrisk</u>

⁵ <u>commonfund.nih.gov/HuBMAP</u>

⁶ commonfund.nih.gov/bridge2ai

⁷ <u>commonfund.nih.gov/editing</u>

⁸ commonfund.nih.gov/healthdisparitiestransformation

Innovative Approaches to Workforce Development

The most valuable resource for the biomedical research enterprise is the energy, creativity, and innovation of its workforce. Several CF programs aim to establish new models for training, workforce development, and research capacity building. The Faculty Institutional Recruitment for Sustainable Transformation (FIRST)⁹ program aims to establish a more inclusive and diverse biomedical research workforce through support of cluster hiring and institutional culture change efforts. The Enhancing the Diversity of the NIH-Funded Workforce¹⁰ program is developing, implementing, assessing, and disseminating innovative approaches to engaging, training, and mentoring students; enhancing faculty development; and strengthening institutional research and training infrastructure to enhance participation and persistence of individuals from underrepresented backgrounds in biomedical research careers.

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 emerging priorities and research opportunities that have recently arisen or come to the forefront of the Nation's attention during the past several years of rapid change.

In response to the COVID-19 pandemic, CF is supporting research to prevent, prepare for, and respond to SARS-CoV-2. With support from the Coronavirus Aid, Relief, and Economic Security (CARES) Act,¹¹ CF supported emergency competitive revisions to existing grants and cooperative agreements to conduct innovative research on COVID-19/coronavirus in FY 2020.¹² Research supported by these supplements includes investigation of the causes of inequities in COVID-19 severity, with the aim of developing more targeted interventions; screening thousands of well-characterized drugs for their ability to block SARS-CoV-2 infection for rapid translation into the clinic; exploring the use of a robotic lung ultrasound to standardize diagnosis, lower costs, and keep medical staff safer in resource-limited settings; and using telemedicine to make advance care decisions and improve end-of-life choices for COVID-19 patients. In FY 2021, CF issued five Transformative Research Awards to bring new, innovative perspectives to COVID-19/coronavirus research. These awards, part of the High-Risk, High-Reward program, support highly innovative research that is expected to have exceptional impact. These awards are addressing the impact of SARS-CoV-2 on multiple organ systems, using deep machine learning to predict therapeutic antibody structures for future viral pandemics, determining the disease mechanism of the virus in the brain, developing a handheld rapid sensing system to detect and monitor SARS-CoV-2 in air, and engineering therapeutic molecular antivirals that can co-adapt along with SARS-CoV-2 in infected hosts.¹³

Recent events, including health inequities highlighted by the COVID pandemic and growing attention to social justice issues, have elevated the urgent need for additional research to address

⁹ commonfund.nih.gov/first

¹⁰ commonfund.nih.gov/diversity

¹¹ congress.gov/116/plaws/publ136/PLAW-116publ136.pdf

¹² commonfund.nih.gov/covid19/fundedresearch

¹³ commonfund.nih.gov/TRA/fundedresearch

health disparities. Through a new initiative called UNITE,¹⁴ NIH has begun to identify shortterm 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 negatively impacted by racism. Launched in FY 2021, the Transformative Research to Address Health Disparities and Advance Health Equity initiative originated with the UNITE initiative and is now being implemented as a Common Fund program. This initiative is funding bold projects aiming to develop, disseminate, and/or implement innovative and effective interventions that prevent, reduce, or eliminate health disparities and health inequities. Additionally, this initiative is expected to increase the competitiveness of investigators and expand the research base dedicated to health disparities research at minority serving institutions. Projects funded in FY 2021 include community-based research collaborations that develop and test financial interventions addressing structural racism, spiritual healing and stress reduction interventions for youth from racial and ethnic minority communities to prevent chronic disease outcomes, technology-enhanced approaches to advance cancer health equity among diverse deaf, deafblind, and hard-of-hearing populations, and school-based, telehealth-driven care to prevent health disparities in underserved rural and socioeconomically disadvantaged children.¹⁵

The CF has undertaken a robust, community-informed planning process to develop a comprehensive, coordinated program in FY 2023 to address health disparities. The Community Partnerships to Advance Science for Society (ComPASS) program will support interventions that target the upstream structural targets contributing to health disparities, such as transportation development, housing policies, early childhood screening, education programs, and more.¹⁶ These structural intervention targets span many sectors and require innovative approaches to advance health equity. Importantly, ComPASS will support community-driven structural interventions, ensuring that communities are engaged as partners in research, interventions address the most important issues for the community, and successful interventions are sustainable. It will support workforce development in academic and community-based organizations to establish research and community engagement expertise that will lead to sustainable health equity partnerships. Once expertise is established within partner organizations, research opportunity announcements will be issued in future years to demonstrate the capacity of these networks to engage communities in research that addresses health issues of importance to those communities and that address pervasive and harmful health disparities and health inequities.

The CF fulfills a unique role at NIH, supporting research that is often broad-reaching across scientific disciplines and provides catalytic data, tools, and resources with the potential to advance many different research areas. Planning for CF programs involves identifying areas of extraordinary opportunity and pressing need for biomedical research as a whole. Therefore, although several CF activities were rapidly launched to address critical needs highlighted by recent events, continued investment in CF programs to provide foundational support for the biomedical research enterprise remains crucially important. These activities are essential to continue even in times of major upheavals and rapid change, helping to ensure the biomedical

¹⁴ <u>nih.gov/ending-structural-racism</u>

¹⁵ commonfund.nih.gov/healthdisparitiestransformation/fundedresearch

¹⁶ <u>https://dpcpsi.nih.gov/sites/default/files/2.10PM-Cf-Concept-COMPASS-Zenk-Gordon-FINAL-508.pdf</u>

research community is well-poised to respond nimbly to new and unpredictable issues that emerge in the future.

CF has accelerated the launch of several exciting initiatives. The Cellular Senescence Network,¹⁷ originally planned to launch in FY 2022, was instead launched in FY 2021. This accelerated launch jumpstarted the development of critical resources, tools, and technologies that will help researchers investigate the role of senescent (non-dividing) cells in health and disease, across multiple tissues, and across the lifespan. Originally planned to launch in FY 2021, a second stage of the 4D Nucleome¹⁸ program was launched in FY 2020 to develop data and tools to catalyze research on how the spatial arrangement of DNA in the cell influences health and disease over time. Additional funding also allowed support of increased numbers of promising early career researchers through the New Innovator award¹⁹ initiative.

Since CF programs are designed with clearly defined goals and milestones, it is critically important to rigorously monitor ongoing progress to ensure programs are on track, and to adjust if needed. Additionally, as CF programs are intended to produce valuable resources and knowledge to spur subsequent research advances, it is also important to assess the impact of the program and its deliverables on the broad biomedical research landscape. We make significant efforts to evaluate CF 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. New challenges and opportunities will be addressed in FY 2023 from funds made available as programs end, move to other sources of support, or require decreased support as indicated by evaluative data.

¹⁷ <u>commonfund.nih.gov/senescence</u>

¹⁸ commonfund.nih.gov/4Dnucleome

¹⁹ commonfund.nih.gov/newinnovator

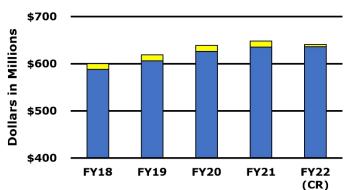
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Bold Science, Catalyzing Discoveries

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, highreward 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.



FUNDING HISTORY

Elizabeth Wilder, Ph.D., has been the Director of the Office of Strategic Coordination since 2010.

FACTS AND FIGURES

- 21 Scientific Programs in FY 2021
- 544 Principal Investigators (PIs)*

 181 High-Risk, High-Reward PIs*
 - 104 Early career High-Risk, High Reward PIs*
- 136 competing Research Project Grants*
- 24 NIH Institutes, Centers, and Offices co-leading programs in FY 2021

*Data represent yearly averages from FY 2017 – FY 2021

The FY 2023 President's Budget request is \$658.5 million. Blue = base appropriation Yellow = Pediatric Research Initiative Fund

COMMON FUND RESEARCH ACCOMPLISHMENTS



The **Extracellular RNA Communication** program has cataloged extracellular RNA molecules found in human biofluids like plasma, saliva, and urine from over 2,000 donors. This program has identified potential extracellular RNA biomarkers for nearly 30 diseases and conditions, including cardiovascular disease, pregnancy complications, glaucoma, diabetes, and multiple types of cancer.

The **Gabriella Miller Kids First Research** program has performed genetic sequencing on over 40 childhood cancer and structural birth defects patient cohorts, representing over 16,000 patients and 40,000 genomes. Kids First data has led to new discoveries about genetic causes of childhood neuroblastoma, congenital heart defects, disorders of sex development, Ewing sarcoma, orofacial cleft, and syndromic cranial dysinnervation.





Common Fund programs generate a wide array of broadly useful tools and technologies. These include a combination of small molecules that could enhance the therapeutic potential of induced pluripotent stem cells, an approach to comprehensively map neurons within various organs in 3D, a new method to image the arrangement of small regions of DNA in the nucleus, and a web application that allows researchers to map their own data onto reference maps of 8 organs.



Bold Science, Catalyzing Discoveries

SELECTED CURRENT ACTIVITIES

- The Nutrition for Precision Health program is leveraging the large, diverse participant pool in the All of Us Research Program to develop algorithms to predict personalized responses to food and dietary patterns.
- Faculty Institutional Recruitment for Sustainable Transformation (FIRST) is establishing a more inclusive and diverse biomedical research workforce through support of cluster hiring and institutional culture change efforts.
- The Cellular Senescence Network is comprehensively identifying and characterizing senescent (no longer dividing) cells across the body, across various states of health, and across the lifespan.



LOOKING TO THE FUTURE



- The Somatic Mosaicism Across Human Tissues program, launching in FY 2023, aims to expand our understanding of the causes and effects of genetically distinct cells within an individual, known as mosaicism.
- The **Somatic Cell Genome Editing** program is planning a second phase to facilitate the transfer of genome editing approaches into the clinic.
- The Community Partnerships to Advance Science for Society (ComPASS) program will develop and evaluate community-driven structural interventions to address health disparities.

SPOTLIGHT ON.....

COMMON FUND DATA

Common Fund programs generate a significant number of large-scale, diverse data sets for the biomedical research community. These data sets are highly valuable on their own but hold the potential to enable entirely new kinds of discoveries if researchers can interrogate multiple disparate data sets in combination. The **Common Fund Data Ecosystem** is building infrastructure to enable researchers to query across and use multiple Common Fund data sets, provide training for users to operate on the data in a cloud environment, and ensure that Common Fund data continue to be available after individual programs are completed.

SUPPORTING THE BIOMEDICAL WORKFORCE

All biomedical research breakthroughs rely on the creativity and skill of a robust and diverse scientific workforce. The Common Fund supports several programs that aim to develop and assess novel approaches to support researchers from diverse backgrounds at different career stages. These programs include efforts to support highly creative early career researchers, researchers seeking to explore new directions or "out of the box" ideas, novel training and mentoring approaches to engage and retain researchers from diverse backgrounds, and faculty cluster hiring approaches to establish cultures of inclusive excellence at research institutions.

https://commonfund.nih.gov/

MAJOR CHANGES IN THE BUDGET REQUEST

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 2023 President's Budget request for the Common Fund, which is \$18.3 million more than the FY 2022 CR level, for a total of \$658.5 million.

Research Project Grants (-\$8.4 million; total \$301.4 million): The Common Fund expects to support a total of 355 Research Project Grant (RPG) awards in FY 2023, down from 362 in FY 2022. Estimated awards for FY 2023 include 206 Noncompeting RPGs and 149 Competing RPGs. The decrease in RPGs reflects the planned ramping down of several programs.

Research Centers (+\$23.3 million; total \$153.5 million): The Common Fund expects to support a total of 121 Research Centers in FY 2023, up from 104 in FY 2022. This change reflects increased support for Specialized/Comprehensive Centers within the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program.

Other Research (+\$10.3 million; total \$155.6 million): The Common Fund expects to support 6 Cooperative Clinical Research awards and 89 Other Research (Other) awards. The increase in the Other Research mechanism reflects increased support for Cooperative Clinical Research activities within the Precision for Nutrition Health program.

Research Training (-\$2.1 million; total \$8.5 million): The Common Fund expects to support 396 full-time training positions (FTTPs) through Institutional Training Awards. This decrease reflects the planned winding down of the Building Infrastructure Leading to Diversity (BUILD) initiative within the Enhancing the Diversity of the NIH-Funded Workforce program.

Intramural Research (-\$7.2 million; total \$0.3 million): The decrease in support for intramural research reflects the planned completion of the Undiagnosed Diseases Network, the Common Fund program with the most substantial intramural component.

BUDGET MECHANISM TABLE isands) (Doll , in Th

(Dol	lars in	Thousand	ls)
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(Donars in Thousands) FY 2023 FY 2023								
MECHANISM	FY 20)21 Final	FY 2	022 CR		sident's	ГТ	+/-
			I FI 2022 CK		Bı	ıdget	FY 2022 CR	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	272							
Administrative Supplements	(25)	3,863	(49)	7,544	(4)	600	(-45)	-6,944
Competing:								
Renewal	0	-	-	0	-	-	-	-
New	140	· · ·		· · ·		,		· · ·
Supplements	0	-	-		-	-	-	-
Subtotal, Competing	140	+ - / -				. ,		\$37,421
Subtotal, RPGs	412	\$345,598		\$309,814		-		
SBIR/STTR	0	-	-	-		-	-	-
Research Project Grants	412	\$345,598	362	\$309,814	355	\$301,449	-7	-\$8,365
Research Centers:								
Specialized/Comprehensive	48	\$57,035	89	\$105,504	106	\$126,481	17	\$20,977
Clinical Research	10	16,244	7	10,762	8	12,477	1	1,715
Biotechnology	0	0	5	7,500	5	10,000	0	2,500
Comparative Medicine	4	7,271	3	6,344	2	4,500	-1	-1,844
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	62	\$80,550	104	\$130,110	121	\$153,458	17	\$23,348
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	6	5,761	6	14,684	0	8,923
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	117	184,290	89	139,485	89	140,908	0	1,423
Other Research	117	\$184,290	95	\$145,246	95	\$155,592	0	\$10,346
Total Research Grants	591	\$610,438	561	\$585,170	571	\$610,499	10	\$25,329
Ruth L Kirschstein Training Awards:	FTTPs		<u>FTTPs</u>		FTTPs		<u>FTTPs</u>	
Individual Awards	0							• •
Institutional Awards	380			10,631	396	,		, -
Total Research Training	380	\$8,048	495	\$10,631	396	\$8,505	-99	-\$2,126
Research & Develop. Contracts	0	\$258	0	\$7,974	0	\$8,000	0	\$26
(SBIR/STTR) (non-add)	(0)	,5238 (0)		\$7,974 (0)	(0)	\$8,000 (0)		(<i>0</i>)
(SBIRSTIK) (non-uuu)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Intramural Research	0	7,927	0	7,460	0	307	0	-7,153
Res. Management & Support	0							· ·
SBIR Admin. (non-add)	(0)	(0)		(0)	(0)	(0)		(0)
Construction		0		0		0		C
Buildings and Facilities		0		0		0		C
Total, Common Fund	0	\$648,539	0	\$640,230	0	\$658,539	0	\$18,309

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

BUDGET BY PROGRAM (Dollars in Thousands)

Common Fund Program			FY 2023 President's
č	FY 2021 Final	FY 2022 CR	Budget
4D Nucleome	28,148	28,378	28,394
Acute to Chronic Pain Signatures	16,350	6,432	125
Bridge to Artificial Intelligence (Bridge2AI)	170	32,556	32,406
Cellular Senescence Network (SenNET)	24,997	40,350	41,850
Enhancing the Diversity of the NIH-Funded Workforce	48,941	44,222	39,478
Extracellular RNA Communication	11,509	10,841	102
Faculty Institutional Recruitment for Sustainable Transformation (FIRST)	4,237	31,062	52,886
Gabriella Miller Kids First Pediatric Research	12,960	4,754	13,080
Global Health	10,063	844	85
Glycoscience	5,331	320	0
Harnessing Data Science for Health Discovery and Innovation in Africa (DSI-Africa)	12,485	12,455	16,418
Health Care Systems Research Collaboratory	1,750	225	0
High-Risk Research	202,465	171,249	177,314
NIH Director's Pioneer Award	46,216	47,278	43,759
NIH Director's New Innovator Award Program	65,389	48,301	49,459
Transformative Research Award	44,057	47,323	42,815
NIH Director's Early Independence Award Program	22,962	23,329	23,894
Transformative Health Disparities Research	23,841	5,019	17,387
Human BioMolecular Atlas Project (HuBMAP)	28,416	36,676	42,636
Illuminating the Druggable Genome	14,763	13,390	6,400
Knockout Mouse Phenotyping Program	423	0	0
Metabolomics	11,942	106	0
Molecular Transducers of Physical Activity	43,886	40,493	13,489
Nutrition for Precision Health	0	20,691	37,105
Somatic Cell Genome Editing	39,901	50,433	47,572
Somatic Mosaicism across Human Tissues (SMaHT)	0	0	11,453
S.P.A.R.C Stimulating Peripheral Activity to Relieve Conditions	42,702	30,932	35,677
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	37,478	19,890	19,508
Undiagnosed Diseases Network	22,199	16,400	0
Strategic Planning, Evaluation, and Infrastructure	27,424	27,532	28,986
Subtotal Common Fund	648,539	640,230	644,962
New Initiatives in Common Fund	0	0	13,577
Total Common Fund	648,539	640,230	658,539

JUSTIFICATION OF BUDGET REQUEST

NIH Common Fund

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

Budget Authority (BA)

		FY 2023	
FY 2021	FY 2022	President's	FY 2023 +/-
Final	Enacted	Budget	FY 2022
\$648,539,000	\$640,229,600	\$658,539,000	\$18,309,400
0	0	0	0
	Final	Final Enacted	FY 2021FY 2022President'sFinalEnactedBudget

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

<u>Overall Budget Policy</u>. The FY 2023 President's Budget request for the CF is \$658.5 million, an increase of \$18.3 million or 2.9 percent compared with the FY 2022 CR level. This level of funding will support high priority activities within existing programs and support the launch of the new Somatic Mosaicism across Human Tissues (SMaHT)and Community Partnerships to Advance Science for Society (ComPASS) programs, as described below.

PROGRAM DESCRIPTIONS

The CF supports approximately 25 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 5 to 10 years. Planned activities and budgets for CF programs are strategically developed, with clear milestones defined throughout the lifetime of the program to enable measurement of progress towards pre-defined goals. Therefore, CF programs often undergo planned budget shifts driven by the needs and activities for each program.

Several CF programs will receive their last year of support in FY 2022; funds are therefore not requested in FY 2023. These include Glycoscience,²⁰ Health Care Systems Research Collaboratory,²¹ Metabolomics,²² and Undiagnosed Diseases Network.²³ Information on these programs and their accomplishments can be found on the program websites. Additionally, the Global Health program will receive a small amount of additional Research Management Support

²⁰ <u>https://commonfund.nih.gov/Glycoscience</u>

²¹ commonfund.nih.gov/hcscollaboratory

²² commonfund.nih.gov/metabolomics

²³ commonfund.nih.gov/Diseases

(RMS) funds in FY 2023 to enable active management for awards in no-cost extensions that have remaining balances due to delays related to the COVID-19 pandemic.

Highlighted below are programs that exemplify the science to be supported in FY 2023, and/or which are undergoing significant programmatic changes in FY 2023.

Acute to Chronic Pain Signatures (A2CPS)

A2CPS²⁴ aims to improve understanding of the transition from acute to chronic pain following injury. Currently, 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 high prevalence of chronic pain has contributed to the current opioid epidemic, and a signature to predict susceptibility to transition from acute to chronic pain could help accelerate therapy development and ultimately guide pain prevention strategies. A2CPS enhances the objectives of the NIH Helping to End Addiction Long-termSM (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. Decreased funds requested in FY 2023 reflect the planned completion of clinical studies and data generation, while providing appropriate levels of support for continuing data integration efforts.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$0.1 million, a decrease of \$6.3 million or 98.1 percent compared with the FY 2022 CR level. These funds will allow the A2CPS program to continue to support data integration after completion of the clinical studies.

Enhancing the Diversity of the NIH-Funded Workforce

The Enhancing the Diversity of the NIH-Funded Workforce program, also known as the Diversity Program Consortium, is addressing the persistent disparities that exist in the biomedical workforce, despite years of investment by NIH and others to increase diversity. This program is developing, implementing, assessing, and disseminating innovative and effective training and mentoring approaches to enhance participation and persistence of individuals from underrepresented backgrounds in biomedical research careers, so that future programs may be more effective at recruiting and retaining a diverse workforce. Additionally, this program is supporting efforts to increase the productivity of sponsored program activities in institutions of higher learning, thereby enhancing capacity for biomedical research and/or research training. Decreased funding requested in FY 2023 reflects the planned ramping down of the program, as effective training and mentoring approaches piloted through this program are disseminated for widespread adoption.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$39.5 million, a decrease of \$4.7 million or 10.7 percent compared with the FY 2022 CR level. This decrease reflects a planned ramping down of program activities, with the expectation that successful training and mentoring approaches will be taken up by research institutions for widespread impact.

²⁴ <u>commonfund.nih.gov/pain</u>

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 Communication²⁵ program seeks to understand new paradigms of cellular information exchange based on these extracellular RNAs. This program has established data standards, developed a data portal, and made tools and reagents widely available to the scientific community. Additionally, it has cataloged extracellular RNA molecules from over 2,000 donors and identified potential extracellular RNA biomarkers for over 30 diseases, such as cardiovascular disease, pregnancy complications, glaucoma, diabetes, and multiple types of cancer. Decreased funding in FY 2023 reflects the planned ramping down in the program's final year, as the tools, resources, and new paradigms established through the Extracellular RNA Communication program continue to enable this growing area of research.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$0.1 million, a decrease of \$10.7 million or 99.1 percent compared with the FY 2022 CR level. This decrease reflects the planned ramping down of this program, which has catalyzed the field of extracellular RNA research.

Faculty Institutional Recruitment for Sustainable Transformation (FIRST)

The FIRST program aims to establish a more inclusive and diverse biomedical research workforce through support of cluster hiring and institutional culture change efforts. Based on early results from other cohort-based recruitment programs, FIRST will 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. The NIH expects its efforts to lead to the recruitment of talented researchers from all groups, to improve the quality of the training environment, to balance and broaden the perspective in setting research priorities, and to positively impact scientific discovery. Increased funds requested in FY 2023 will support awards to launch the third and final planned faculty cohort.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$52.9 million, an increase of \$21.8 million or 70.3 percent compared with the FY 2022 CR level. This increase will be supporting the launch of the third faculty cohort of promising researchers with demonstrated commitment to inclusive excellence.

Gabriella Miller Kids First Pediatric Research (Kids First)

The Kids First²⁶ 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. Through FY 2021, the Kids First program selected 44 cohorts for whole genome sequencing, representing

²⁵ commonfund.nih.gov/exrna

²⁶ commonfund.nih.gov/KidsFirst

20,000 patients and 48,000 genomes. Kids First has developed one of the largest pediatric data resources of its kind and has fostered new biological insights into genetic causes of conditions such as childhood neuroblastoma, congenital heart defects, disorders of sex development, Ewing sarcoma, orofacial cleft, and syndromic cranial dysinnervation. Funds requested in FY 2023 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 the statutory level set by this legislation. These 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 Kids First data. A small amount to support program management activities is requested from the general CF appropriation.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$13.1 million, an increase of \$8.3 million or 175.2 percent compared with the FY 2022 CR level. The FY 2022 CR level provided a reduced amount for the Kids First program due to depletion of funds in the Pediatric Research Initiative Fund. The FY 2022 CR level was used to support the Kids First data resource. Transfer of additional funds into the Pediatric Research Initiative Fund in FY 2023 restores the budget to historical levels and allows for additional data generation. In the FY 2023 President's Budget request, 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.

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

The DS-I Africa²⁷ 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. Although many enabling factors, such as extensive mobile phone coverage, are already in place in Africa, data science applications to improve health are largely undeveloped. This represents an opportunity for strategic investment in data science with the potential for transformative impact on health outcomes in Africa and around the world, including in the United States. The program aims to promote sustainability of the African health research enterprise by encouraging innovative partnerships, and will also consider ethical, legal, and social issues (ELSI) for data science research and its applications to public health in Africa. Research supported through this program is leveraging data science to address some of the most pressing health needs not just in Africa, but in the world. These include tracking SARS-CoV-2 and HIV pandemic spread to inform potential interventions and enhance pandemic preparedness, improving maternal and child health, mitigating health impacts of climate change, and combating antimicrobial resistance. Increased funds requested in FY 2023 will be used to expand efforts to develop industry partnerships, as well as launch new short-term training activities and training for early-stage investigators.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$16.4 million, an increase of \$4.0 million or 31.8 percent compared with the FY 2022 CR level. This increase will support expansion of industry partnerships and new training activities.

²⁷ commonfund.nih.gov/AfricaData

TRANSFORMATIVE RESEARCH TO ADDRESS HEALTH DISPARITIES AND ADVANCE HEALTH EQUITY

NIH's UNITE initiative is an agency-wide effort to address structural racism and promote racial equity and inclusion at the NIH and within the larger biomedical research enterprise. One component of UNITE focuses on addressing long-standing health disparities and promoting health equity, ensuring that all populations benefit from the lifesaving and health promoting research supported by NIH. As a rapid response from the NIH Office of the Director that emerged from UNITE, the CF launched the Transformative Research to Address Health Disparities and Advance Health Equity initiative in FY 2021. This initiative is a bold approach to fund unusually innovative research projects with the potential to have a major impact on inequalities in health outcomes through development, dissemination, and/or implementation of innovative and effective interventions that address health disparities and advance health equity. Additionally, through dedicated support for researchers at under-resourced institutions that educate significant numbers of students from underrepresented backgrounds, this initiative also aims to expand the research base dedicated to health disparities research at minority-serving institutions. A second round of awards targeted toward minority serving institutions is being supported in FY 2022.

High-Risk, High-Reward Research (HRHR)

The HRHR program supports exceptionally creative scientists proposing innovative and transformative research in any scientific area within the NIH mission through four complementary initiatives: 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 risky, but necessary to accelerate the pace of scientific discovery and advance human health. Additionally, in FY 2021, the CF 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 health inequities. 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. To improve financial stewardship, starting in FY 2021, the New Innovator awards provide support for years one through three of the projects 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. Funds requested in FY 2023 will be used to support additional innovative projects with the potential for extraordinary impact.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$177.3 million, an increase of \$6.1 million or 3.5 percent compared with the FY 2022 CR level. These funds will continue to support highly creative, high-impact projects.

Illuminating the Druggable Genome (IDG)

Three protein families – G-protein coupled receptors, ion channels, and protein kinases – are well-established "druggable" protein families that have potential to be targets of pharmaceuticals. However, only a small number of proteins within each of these families are well-studied, representing an opportunity to greatly expand the druggable genome by catalyzing research into these understudied proteins. Additionally, these well-studied proteins are often present in many cells throughout the body, and drugs that target these proteins might therefore cause widespread adverse effects. In contrast, the lesser-known members of these protein

families may be present in fewer tissues, and thus have potential as specific drug targets that lead to fewer side effects. IDG is developing data, tools, and technologies to enable investigation of understudied proteins within these three protein families, expanding the repertoire of potential drug targets that may have high potential to impact human health. Having largely completed the goals of developing these resources for the biomedical research community, IDG will undergo a planned ramping down of the Data and Resource Generation Centers in FY 2023.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$6.4 million, a decrease of \$7.0 million or 52.2 percent compared with the FY 2022 CR level. This decrease reflects a planned ramping down of data and resource generation efforts, while continuing to support data analysis.

Molecular Transducers of Physical Activity in Humans

Physical activity has been demonstrated to contribute to health via a wide variety of measures, and lack of physical activity is at the root of many common chronic health problems. Despite this, we have a poor understanding of the molecular mechanisms by which the benefits of 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 in Humans Consortium (MoTrPAC) will improve our understanding of the molecular mechanisms by which physical activity in people, identifying some of the key molecules that underlie the systemic effects of physical activity, and characterizing the function of these key molecules. Decreased funds requested in FY 2023 reflect the planned ramping down of human and animal physical activity studies and associated molecular analyses of samples.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$13.5 million, a decrease of \$27.0 million or 66.7 percent compared with the FY 2022 CR level. This decreased reflects the completion of human and animal physical activity studies, with continued support to explore the mechanisms of action of the molecules that underlie the benefits of physical activity.

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 program²⁸ is to develop algorithms that predict individual responses to food and dietary patterns. NPH will leverage the *All of Us²⁹* infrastructure and recent advances in biomedical science, such as artificial intelligence and microbiome research, to provide unprecedented opportunities to examine associations between nutrition and a variety of long-term outcomes. This program addresses some of the important scientific opportunities identified in the first Strategic Plan for NIH Nutrition Research.³⁰ Additionally, this program is closely coordinated with activities of the Office of Nutrition Research, to ensure NIH-wide nutrition efforts are complementary, not duplicative. Ultimately, the predictive algorithms developed through NPH are anticipated to enable tailored dietary recommendations to be provided by physicians, as well as development of

²⁸ <u>commonfund.nih.gov/nutritionforprecisionhealth</u>

²⁹ <u>allofus.nih.gov/</u>

³⁰ <u>niddk.nih.gov/about-niddk/strategic-plans-reports/strategic-plan-nih-nutrition-research</u>

tools to allow individuals to make more informed decisions about healthy food choices. Increased funds requested in FY 2023 will support ramping up of this program, particularly for the clinical and data generation centers.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$37.1 million, an increase of \$16.4 million or 79.3 percent compared with the FY 2022 CR level. This increase supports the ramping up of clinical studies and data generation efforts.

Somatic Cell Genome Editing (SCGE)

The SCGE 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. 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. The first stage of the SCGE program winds down in FY 2023, and a second stage of support is planned for FY 2023 to address new and ongoing opportunities in facilitating the transfer of genome editing

SOMATIC MOSAICISM ACROSS HUMAN TISSUES (SMaHT)

An individual's personal genome is composed of the DNA sequence inherited from their parents and changes in DNA sequence that occur over the lifetime. The changes that occur over the lifetime result in genetically distinct cells within an individual, or somatic mosaicism. There is mounting evidence that somatic mosaicism plays important roles in biological processes such as fetal development, aging, and disease. However, technical challenges in detecting rare somatic variations means that this phenomenon is grossly understudied. The goal of the SMaHT program is to deepen understanding of how much variation there is within personal genomes, what causes this variation, and how this variation affects human health and disease. Launching in FY 2023, SMaHT will catalog somatic variants in select tissues from diverse human donors, develop innovative sequencing tools and analysis methods, and create a workbench to integrate analysis of somatic variation with the human genome. These resources, which will be widely available to the research community, are anticipated to catalyze an entirely new framework for understanding and probing the complexity of the human genome.

approaches into the clinic. This second stage will aim to optimize and validate broadly applicable assays for preclinical studies, support Investigational New Device (IND)enabling studies targeting multiple diseases in the same tissue or cell type, and identify and disseminate successful, streamlined strategies for initiating clinical trials for genome editing therapies.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$47.6 million, a decrease of \$2.9 million or 5.7 percent compared with the FY 2022 CR level. This decrease reflects the net effect of the winding down of the first stage of the program and the launch of a planned second stage to facilitate the transfer to genome editing approaches into the clinic.

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

The SPARC³¹ program is accelerating the development of novel neuromodulatory therapeutic devices to advance bioelectronic medicine through provision of foundational data and tools. Modulation of nerve function

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

³¹ <u>commonfund.nih.gov/sparc</u>

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. Increased funds requested in FY 2023 will support expansion of efforts to develop open-source neural engineering technologies and prizes for the research community to demonstrate proof of principle for neuromodulation therapeutic benefits.

<u>Budget Policy</u>. The FY 2023 President's Budget request is \$35.7 million, an increase of \$4.7 million or 15.3 percent compared with the FY 2022 CR level. This increase will support development of neuroengineering technologies and prizes, as described above.

Strategic Planning, Evaluation, and Infrastructure

Management of the CF requires that certain activities be undertaken for the benefit of the CF as a whole. These activities include strategic planning, evaluation, and support of infrastructure to support data-intensive CF programs. This infrastructure, referred to as the Common Fund Data Ecosystem (CFDE), is enabling researchers to query across and use multiple CF data sets, providing training for users to operate on the data in a cloud environment, and ensuring that CF 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.

Strategic planning is undertaken every year to identify new scientific challenges and opportunities. CF strategic planning involves the identification of broadly relevant scientific challenges and opportunities for strategic investments and the subsequent articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic. The initial activities for strategic planning often involve gathering broad input from stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Subsequent refinement activities often involve 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 2023 CF programs leveraged the wide-ranging expertise of NIH's senior leaders and scientific staff. One new FY 2023 program, Somatic Mosaicism Across Human Tissues, described above, has already undergone extensive planning to develop a robust scientific strategy for program implementation. Funds for this program are therefore included within the overall CF budget.

With additional resources, CF would support the Community Partnerships to Advance Science for Society (ComPASS) program to develop and test structural interventions addressing a broad range of upstream drivers of persistent health disparities. These partnerships may be funded as Other Transaction Awards to organizations not traditionally involved with research but with deep reach into communities that are underserved by traditional research. These partnerships may include community health storefronts, that have extensive coverage in rural as well as urban America and that are willing to partner with academic organizations to engage local communities across the country in research. Partnerships will also include local community-based organizations and/or Tribal Health organizations that are interested in forming a network so that their local communities can work together for large scale clinical studies. This program will support workforce development in these academic and community-based organizations to establish research and community engagement expertise that leads to sustainable health equity partnerships. Once expertise is established within partner organizations, research opportunity announcements will be established in future years to demonstrate the capacity of these networks to engage communities in research that addresses health issues of importance to those communities and that addresses the pervasive and devastating health disparities and health inequities that plague the Nation.

In addition, one current CF program, Somatic Cell Genome Editing, is planning for a potential second stage to launch in FY 2023. As described above, the second stage would focus on facilitating IND-enabling studies, establishing pathways to regulatory approval for genome editing approaches, and disseminating successful strategies for initiating first in human clinical trials. Funds for the second stage are included within the overall CF budget.