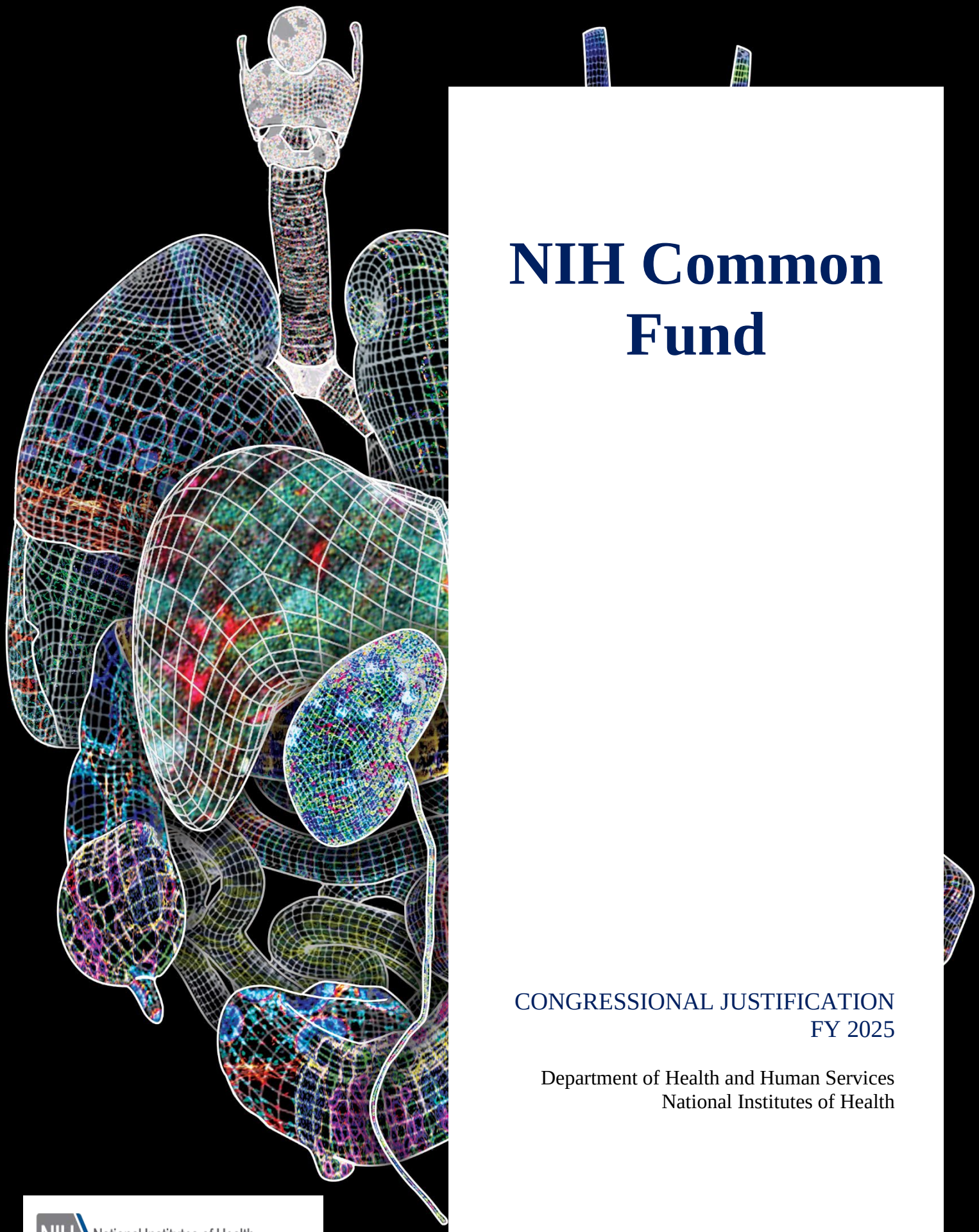

NIH Common Fund

CONGRESSIONAL JUSTIFICATION
FY 2025

Department of Health and Human Services
National Institutes of Health

NIH 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

FY 2025 Budget Table of Contents

General Notes

1. FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
2. Detail in this document may not sum to the subtotals and totals due to rounding.

Cover Page

Nature cover image depicting progress made by the Human BioMolecular Atlas Program (HuBMAP) in mapping how cell types are arranged in the human body. The program is both developing and then deploying the necessary technology to create maps of organs at single-cell resolution. Image credit: Heidi Schlehlein

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Director's Overview

Douglas Sheeley, Sc.D., Acting Director, Office of Strategic Coordination

The NIH Common Fund (CF) is a unique and exciting component of NIH, specifically designed to address challenges and opportunities that are high priority for the agency as a whole.[1] In order to enhance the basic and applied research that has been a hallmark of the American innovation enterprise and the envy of the world, 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; and are designed to achieve specific, high-impact goals and milestones within a 5- to 10-year timeframe. Many Common Fund programs are strategically designed to produce specific deliverables, such as data sets, tools, technologies, or fundamental scientific paradigms, that fill a significant need across multiple fields of biomedical and behavioral research. We intend for these deliverables to spur subsequent scientific advances that would not be possible without our catalytic investment. The Common Fund provides an avenue for NIH to experiment with funding processes to better achieve its R&D mission by designing, trying, and assessing new approaches, such as engaging new R&D performers, exploring new R&D methods, and forging new partnerships. The Common Fund is managed by the Office of Strategic Coordination (OSC) in the NIH Office of the Director, in partnership with NIH Institutes, Centers, and Offices.

Since Common Fund programs are designed with clearly defined goals and milestones, it is important to rigorously monitor ongoing progress to ensure programs are on track, and to adjust if needed. Additionally, as Common Fund programs are intended to produce valuable resources and knowledge to spur subsequent research advances, it is also important to assess the impact of each program and its deliverables on the broad biomedical research landscape. We thoroughly evaluate Common Fund programs during their lifetime, and outcomes are assessed as programs end. Continuous, ongoing 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.

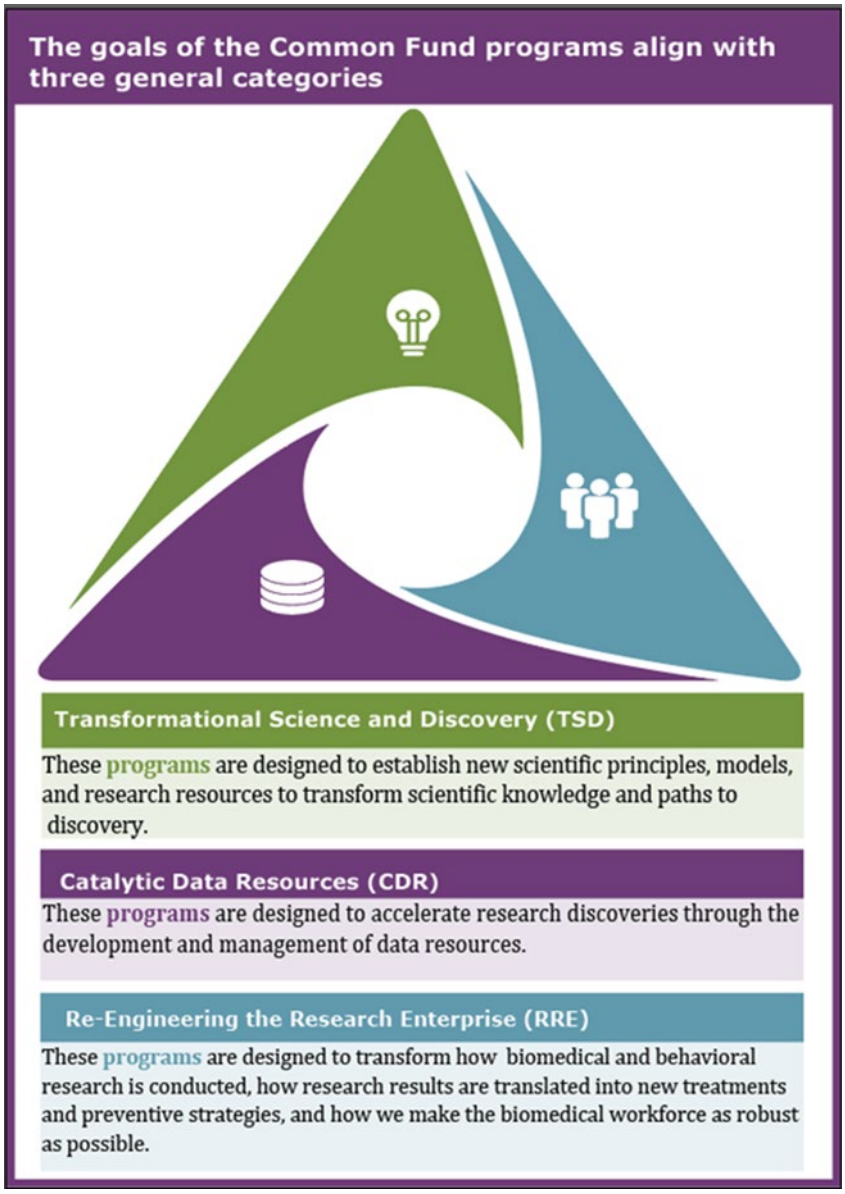
The responsive nature of Common Fund programs has enabled a highly strategic approach to leveraging budget increases over the past several fiscal years. High priority activities have been rapidly identified and implemented, including an accelerated launch of the Human Virome Project in FY 2024, support for additional clinical studies and data analysis to explore the molecular pathways underlying the benefits of physical activity, enhancement of activities to

[1] commonfund.nih.gov/

support use of Common Fund data resources, and support for additional early-stage investigators through the New Innovator Awards.

Common Fund programs are broad-reaching and span the entire NIH mission. As a general framework, they can be grouped into three categories:

- **Transformational Science and Discovery**: programs designed to establish new scientific principles, models, and research resources to transform scientific knowledge and paths to discovery.
- **Catalytic Data Resources**: programs designed to accelerate research discoveries through the development and management of data resources.
- **Re-Engineering the Research Enterprise**: programs designed to transform how biomedical and behavioral research is conducted, how research results are translated into new treatments and preventive strategies, and how we make the biomedical workforce as robust as possible.



The Common Fund: Past, Present, and Future

The Common Fund has its roots in the NIH Roadmap for Medical Research, initiated in 2004. The goal of the Roadmap was to transform biomedical research by identifying and addressing significant opportunities and challenges that no single or small group of NIH Institutes and Centers (ICs) could or should take on alone, but that the NIH as a whole must address.

In 2006, the NIH Reform Act provided continued support for Roadmap programs through a new entity called the NIH Common Fund. The Common Fund has continued to support innovative, high-impact programs that advance research across many biomedical and behavioral research fields. Although support for programs within the Common Fund is time-limited, the far-reaching impact of many programs often lasts beyond their Common Fund lifespan, exemplifying the catalytic nature of these programs to spur subsequent discovery that would not be possible without Common Fund investment. Notable examples include:

- **Large datasets developed by programs such as the Genotype-Tissue Expression (GTEx) program.**[2] GTEx data transformed our understanding of how genetic variants influence gene expression across multiple tissues and across individuals. GTEx data remains available to the biomedical research community and has recently been used to elucidate mechanisms of genetic susceptibility to COVID-19-related severe lung disease, identify genetic risk factors and gene expression patterns in migraines, and identify expression patterns for genetic variants associated with tobacco and alcohol use.[3,4,5]
- **New paradigms for how clinical research information is collected, used, and reported.** The Patient-Reported Outcomes Measurement Information System (PROMIS) program developed a rigorously tested measurement tool to quantify patient outcomes that have major impacts on quality of life, such as pain, fatigue, and emotional distress. PROMIS measures continue to be expanded and utilized in clinical research and practice and are integrated into the HealthMeasures suite of measurement tools along with other NIH-supported clinical measurement systems.[6,7]
- **Novel technologies that enable additional research discoveries**. Development of novel technologies is a hallmark of many Common Fund programs, and the High-Risk, High-Reward (HRHR) program has been particularly fruitful in generating groundbreaking new tools.[8] For example, HRHR awardees developed optogenetics, a technique used to precisely control the activity of genetically selected cells using light. This technique has become widespread in biomedical research, with over 8,000 scientific publications, 300 awarded patents, and 8 clinical trials related to optogenetics.[9]
- **Expanded research capacity around the globe.** Through programs like Human Health and Heredity in Africa (H3Africa), the Common Fund has expanded research capacity to enable scientists in more African regions to contribute to innovative discoveries.[10,11] H3Africa generated rich data resources on hereditary and environmental contributions to health and disease that remain available for future studies, as well as providing robust

[2] commonfund.nih.gov/GTEx
[3] ncbi.nlm.nih.gov/pmc/articles/PMC9259496/
[4] ncbi.nlm.nih.gov/pmc/articles/PMC8837554/
[5] ncbi.nlm.nih.gov/pmc/articles/PMC9771818/
[6] healthmeasures.net/index.php
[7] healthmeasures.net/explore-measurement-systems/promis
[8] commonfund.nih.gov/highrisk
[9] iSearch query for publications with the MeSH term "optogenetics"; USPTO patent public search for keyword "optogenetic"; iSearch query for clinical trials with keyword "optogenetic". All queries conducted Sept/Oct 2023.
[10] commonfund.nih.gov/global-health
[11] h3africa.org/

training experiences to build informatics capacity for African scientists who are now pursuing additional research projects.

Current Common Fund programs span the NIH mission, encompassing basic, translational, clinical, and behavioral research. These programs improve health and save lives through development of fundamental knowledge and resources that lead to new understanding of the basic biological processes that influence human health and disease, establishment of innovative approaches to translate novel therapeutics into the clinic, testing and evaluation of novel models to support the biomedical research workforce, and clinical research to improve health for diverse populations.

Several Common Fund programs are addressing urgent challenges that have a substantial impact on the health and well-being of our nation in order to ameliorate inequities and create opportunity in ways that strengthen our values. The Community Partnerships to Advance Science for Society (ComPASS) program is developing and testing multi-level structural interventions to reduce health disparities and advance health equity, so that all populations can achieve optimal health.[12] These interventions include innovative projects to support access to healthy food in underserved rural areas, explore whether early childcare improves mental health for children and parents, and create culturally appropriate and inclusive health resources for older adults from sexual and gender minority populations. The Acute to Chronic Pain Signatures (A2CPS) program is addressing the issue of chronic pain, which has contributed, in part, to the current opioid epidemic.[13] A2CPS is developing a set of objective biomarkers that provide "signatures" to predict if pain is likely to resolve or become chronic after an incident of acute pain, potentially leading to new pain therapies and prevention strategies.

Common Fund programs also leverage cutting-edge technologies to speed novel therapies to the clinic. The first stage of the Somatic Cell Genome Editing (SCGE) program developed novel genome editing tools with improved efficacy and specificity, enabling researchers to precisely target disease-causing genes even in tissues that have traditionally been difficult to reach, such as the brain, ear, heart, and lung. In the second phase, the program is now accelerating the translation of genome editing therapies into the clinic by developing and disseminating resources to enable genome editing clinical trials. These include technologies and assays for safety and efficacy studies, optimizing therapeutic leads to support advancement toward clinical trials, and supporting novel genome editing clinical trials for more than one disease.

The Common Fund is well-poised to address emerging scientific opportunities and research challenges of the future. As programs end, funds are available to address new challenges and opportunities. Through a robust strategic planning process involving broad input and prioritization by NIH senior leadership, the Common Fund identifies new program concepts that are high priority across NIH.

Upcoming programs include the Human Virome Program (launching in FY 2024) and Complement Animal Research in Experimentation (Complement-ARIE, potentially launching in FY 2025). The Human Virome program will explore the largely understudied collection of

[12] commonfund.nih.gov/compass
[13] commonfund.nih.gov/pain

viruses that live in the human body without causing obvious clinical disease.[14] Complement-ARIE will leverage new and emerging technologies to catalyze the development, standardization, validation, and use of human-based new approach methodologies (NAMs) to better model human biology, complementing, or in some cases possibly replacing, traditional model studies. Another exciting activity on the horizon is the development of a new Common Fund Venture Program to support high-risk, short-term initiatives, introducing additional flexibility and a more nimble approach to tackle a wider variety of research topics.

[14] commonfund.nih.gov/humanvirome

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The Common Fund

Bold science, catalyzing discoveries

The NIH Common Fund provides a dedicated source of support for scientific programs that are high-priority for NIH as a whole

SUPPORTING multi-disciplinary research efforts

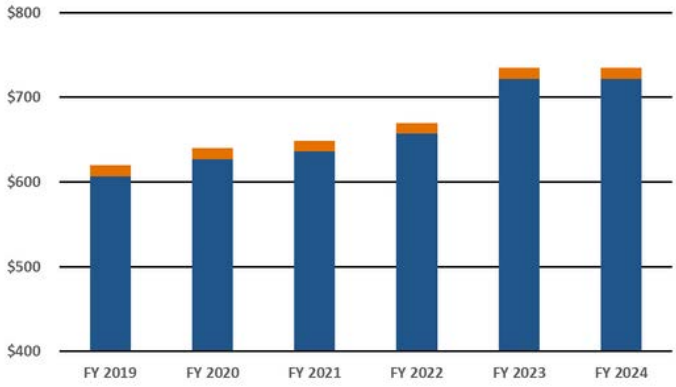
INVESTING in time-limited, goal-driven programs

ACCELERATING emerging science

REMOVING research roadblocks

FUNDING HISTORY

Dollars in millions



The FY 2025 President's Budget request is $722.4 million.

Blue = Common Fund base appropriation
*Orange = Gabriella Miller Kids First Pediatric Research**
**FY 2025 request does not include Gabrilla Miller funding due to transfer of program out of Common Fund*

FACTS AND FIGURES

23 Scientific Programs in FY 2023

544 Principal Investigators (PIs)*

188 High-Risk, High-Reward (HRHR) PIs*

102 Early-Career HRHR PIs*

142 Competing Research Project Grants*

23 NIH Institutes, Centers, and Offices Co-Leading Programs in FY 2023

**yearly averages FY 2019 - FY 2023*

COMMON FUND LEADERSHIP

Douglas Sheeley, Sc.D.

Dr. Sheeley became the Deputy Director of the Office of Strategic Coordination (OSC) in 2022 and the Acting Director of OSC in 2023.

COMMON FUND VENTURE PROGRAM

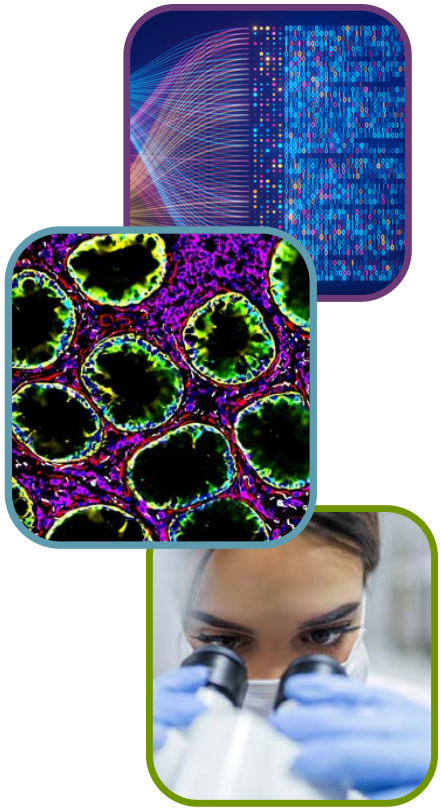
Amazing Things with Modest Funding

The new Common Fund Venture Program will support high-risk, short-term initiatives with potential to have a major impact in biomedical and behavioral research.

Venture projects will be:

- Highly innovative
- Responsive to the shared interests of NIH Institutes, Centers, and Offices
- Goal-driven and focused on a specific outcome

RESEARCH ACCOMPLISHMENTS



Common Fund Data Ecosystem (CFDE)

CFDE is supporting collaborative projects to develop resources and tools to enable discoveries across multiple CF data sets. As an example, researchers have developed a tool to map potential connections between parental exposure to drugs and birth defects, leveraging data from four CF programs.

Human BioMolecular Atlas Program (HuBMAP)

HuBMAP has published a collection of articles bringing together data on RNA, proteins, and metabolites in human organs at single-cell resolution to generate an open-access data platform for researchers to study the inner workings of the cells and how they affect health.

Transformative High-Resolution Cryoelectron Microscopy (CryoEM)

The CryoEM program has broadened access to cutting-edge microscopy techniques, leading to new discoveries such as the structure of tau fibrils bound to RNA (implicated in Alzheimer's disease) and the interactions between Substance P and neurokinin 1 receptor (implicated in conditions such as pain, inflammation, and mood disorders).

CURRENT ACTIVITIES

Community Partnerships to Advance Science for Society (ComPASS)

ComPASS is advancing health equity research by supporting community-driven, structural intervention research projects in areas such as health care access and quality, nutrition and access to healthy food, and neighborhood characteristics.

Human Virome Program

New in FY 2024, the Human Virome Program aims to transform our understanding of viruses that live in the human body and their impact on human health by identifying and characterizing a broad range of viruses and developing novel technologies.

Nutrition for Precision Health (NPH)

NPH is developing algorithms that predict individual responses to food and dietary patterns, leveraging the size and diversity of the NIH's All of Us Research cohort. Enrollment for this unprecedented study launched in FY 2023.

PLANNING FOR THE FUTURE

An NIH-wide strategic planning process led to the identification of a potential new program concept for FY 2025.

Complement Animal Research in Experimentation (Complement-ARIE)

This potential program would catalyze the development, standardization, validation, and use of human-based new approach methodologies (NAMs) to transform the way we do basic, translational, and clinical sciences by complementing, or in some cases possibly replacing, traditional models.

Major Changes in the Budget Request

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note there may be some overlap between budget mechanisms and activity detail, and these highlights will not sum to the total for the FY 2025 President's Budget request for the Common Fund, which is $722.4 million, a decrease of $12.6 million or 1.7 percent compared with the FY 2023 Final level.

Research Project Grants (RPGs) (+$27.1 million; total $354.2 million): The Common Fund expects to support a total of 352 RPG awards in FY 2025, 23 RPGs less than in FY 2023. Estimated awards for FY 2025 include 254 Noncompeting RPGs and 98 Competing RPGs.

Research Centers (-$21.5 million; total $136.4 million): The Common Fund expects to support a total of 61 Research Centers in FY 2025, 12 awards less than in FY 2023. This decrease reflects the planned completion of support for Clinical Research Centers within the Enhancing the Diversity of the NIH-Funded Workforce program, Biotechnology Centers within the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program, and Comparative Medicine Centers within the Somatic Cell Genome Editing program.

Other Research (-$7.4 million; total $197.0 million): The Common Fund expects to support a total of 109 Other Research awards in FY 2025, 5 awards less than in FY 2023. Within this category, the Common Fund will continue to prioritize Other Transaction (OT) awards in several programs. Several new or expanded activities, including Venture Program and Complement Animal Research in Experimentation (Complement-ARIE) will support OT awards in FY 2025.

Research Training (-$3.7 million; total $0.6 million): The Common Fund expects to support a total of eight full time training positions (FTTPs) as new Research Training Individual Awards within the Common Fund Data Ecosystem. The decrease in support for Research Training overall reflects the planned completion of Research Training Institutional Awards within the Enhancing the Diversity of the NIH-Funded Workforce program.

Budget Mechanism Table*

Mechanism	FY 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Research Projects:								
Noncompeting	209	$155,874	277	$256,338	254	$252,341	45	$96,467
Administrative Supplements	*(39)*	$8,004	*(29)*	$5,988	*(25)*	$5,194	*-(14)*	-$2,810
Competing:								
Renewal	17	$18,684	0	$0	0	$0	-17	-$18,684
New	149	$144,546	99	$97,322	98	$96,669	-51	-$47,877
Supplements	0	$0	0	$0	0	$0	0	$0
Subtotal, Competing	**166**	**$163,230**	**99**	**$97,322**	**98**	**$96,669**	**-68**	**-$66,561**
Subtotal, RPGs	375	$327,108	376	$359,648	352	$354,204	-23	$27,096
SBIR/STTR	0	$0	0	$0	0	$0	0	$0
Research Project Grants	375	$327,108	376	$359,648	352	$354,204	-23	$27,096
Research Centers								
Specialized/Comprehensive	59	$131,825	74	$166,039	61	$136,417	2	$4,592
Clinical Research	10	$12,540	0	$0	0	$0	-10	-$12,540
Biotechnology	2	$9,094	3	$12,487	0	$0	-2	-$9,094
Comparative Medicine	2	$4,422	0	$0	0	$0	-2	-$4,422
Research Centers in Minority Institutions	0	$0	0	$0	0	$0	0	$0
Research Centers	**73**	**$157,882**	**77**	**$178,526**	**61**	**$136,417**	**-12**	**-$21,465**
Other Research:								
Research Careers	0	$100	0	$0	0	$0	0	-$100
Cancer Education	0	$0	0	$0	0	$0	0	$0
Cooperative Clinical Research	6	$14,455	6	$15,226	6	$15,027	0	$572
Biomedical Research Support	0	$0	0	$0	0	$0	0	$0
Minority Biomedical Research Support	0	$0	0	$0	0	$0	0	$0
Other	108	$189,877	76	$133,642	103	$181,961	-5	-$7,916
Other Research	**114**	**$204,432**	**82**	**$148,868**	**109**	**$196,988**	**-5**	**-$7,444**
Total Research Grants	562	$689,422	535	$687,042	522	$687,609	-40	-$1,813
Ruth L Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	8	$600	8	$600
Institutional Awards	156	$4,329	0	$0	0	$0	-156	-$4,329
Total Research Training	**156**	**$4,329**	**0**	**$0**	**8**	**$600**	**-148**	**-$3,729**
Research & Develop. Contracts	3	$8,168	5	$15,008	1	$1,026	-2	-$7,142
SBIR/STTR (non-add)	*(0)*	*($0)*	*(0)*	*($0)*	*(0)*	*($0)*	*(0)*	*($0)*
Intramural Research	0	$690	0	$383	0	$383	0	-$307
Res. Management & Support	0	$32,392	0	$32,568	0	$32,783	0	$391
SBIR Admin. (non-add)		*($0)*		*($0)*		*($0)*		*($0)*
Construction		$0		$0		$0		$0
Buildings and Facilities		$0		$0		$0		$0
Total, Common Fund	**0**	**$735,001**	**0**	**$735,001**	**0**	**$722,401**	**0**	**-$12,600**

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

Common Fund Budget by Initiative

Common Fund Program (Dollars in Thousands)	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
4D Nucleome	$27,931	$28,378	$245
Acute to Chronic Pain Signatures	1,281	3,338	3,138
Bridge to Artificial Intelligence (Bridge2AI)	35,391	20,589	32,394
Cellular Senescence Network (SenNET)	42,833	43,850	38,850
Common Fund Data Ecosystem	4,757	18,900	22,750
Community Partnerships to Advance Science for Society (ComPASS) Program	32,731	17,707	52,674
Enhancing the Diversity of the NIH-Funded Workforce	36,718	120	0
Extracellular RNA Communication	313	113	0
Faculty Institutional Recruitment for Sustainable Transformation (FIRST)	53,025	72,688	50,295
Gabriella Miller Kids First Pediatric Research	13,070	12,983	0
Global Health	90	0	0
Harnessing Data Science for Health Discovery and Innovation in Africa (DSI-Africa)	16,434	16,418	16,748
High-Risk Research	171,157	198,958	193,300
NIH Director's Pioneer Award	*44,607*	*42,515*	*39,413*
NIH Director's New Innovator Award Program	*58,401*	*88,551*	*86,790*
Transformative Research Award	*44,452*	*42,932*	*41,124*
NIH Director's Early Independence Award Program	*23,697*	*24,961*	*25,973*
Human BioMolecular Atlas Project (HuBMAP)	44,211	34,586	18,275
Human Virome Program (HVP)	0	42,259	46,357
Illuminating the Druggable Genome	7,168	390	0
Molecular Transducers of Physical Activity	19,019	15,783	8,420
Nutrition for Precision Health	42,399	42,404	46,955
Somatic Cell Genome Editing	47,445	46,254	47,501
Somatic Mosaicism across Human Tissues (SMaHT)	22,852	25,913	30,927
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	32,100	39,277	463
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	25,907	4,255	4,055
Transformative Research to Address Health Disparities	16,239	17,540	17,440
Undiagnosed Diseases Network	11,493	0	0
Venture Program	0	10,000	25,000
Strategic Planning, Evaluation, and Infrastructure	30,436	22,300	22,300
Subtotal Common Fund	735,001	735,001	678,086
New Initiatives in Common Fund	0	0	44,315
Total Common Fund	$735,001	$735,001	$722,401

NIH Common Fund

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

Budget Authority (BA):

	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget	FY 2025 +/- FY 2023
BA	$735,001,000	$735,001,000	$722,401,000	-$12,600,000
FTE	0	0	0	0

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

Overall Budget Policy: The FY 2025 President's Budget request for the Common Fund is $722.4 million, a decrease of $12.6 million or 1.7 percent compared with the FY 2023 Final level. This decrease reflects the planned transfer of the Gabriella Miller Kids First Pediatric Research program from the Common Fund to the Division of Program Coordination, Planning, and Strategic Initiative within the NIH Office of the Director, in accordance with long-standing policy that Common Fund programs are supported for a maximum of 10 years. This funding level will support high priority activities within existing program and support the launch of exciting new activities, as described below.

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 that can be achieved 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. New scientific challenges and opportunities will be addressed in FY 2025 from funds made available as current programs end, move to other sources of support, or require decreased support as indicated by evaluative data.

Several CF programs will receive their last year of support in FY 2024; funds are therefore not requested in FY 2025 for these programs. These include Enhancing the Diversity of the NIH-Funded Workforce, Extracellular RNA Communication, Gabriella Miller Kids First Pediatric

Research, and Illuminating the Druggable Genome. [15,16,17,18] In accordance with long-standing policy that Common Fund programs are supported for a maximum of 10 years, funds for the Gabriella Miller Kids First Pediatric Research program are requested within the NIH Office of the Director, rather than the Common Fund, starting in FY 2025. Additionally, the Global Health and Undiagnosed Diseases Network programs received their last year of support in FY 2023; funds are therefore not requested in FY 2024 or FY 2025.[19,20] Information on these programs and their accomplishments can be found on the program websites.

Highlighted below are programs that exemplify the high priority science to be supported in FY 2025, and/or which are undergoing significant programmatic changes in FY 2025.

4D Nucleome

The 4D Nucleome program aims to develop a fundamentally new understanding of how genetic material is organized in the cell in space and time, and how this organization influences human development, health, and disease.[21] Each human cell contains approximately 6.5 feet of DNA within the cell's microscopic nucleus. The arrangement of DNA in the nucleus is not random – it is carefully organized and packaged, and this arrangement dynamically changes to modulate which genes are turned on and off. However, the process of nuclear arrangement and re-arrangement is not well-understood. The 4D Nucleome program is producing tools and resources for the research community to explore the health effects of nuclear organization, including identification of new targets for human diseases that are caused by abnormal nuclear organization. To date, the 4D Nucleome program has developed and made available nearly 2,000 data sets, 52 software packages, and 23 protocols and reagents.

Budget Policy: The FY 2025 President's Budget request is $0.2 million, a decrease of $27.7 million or 99.1 percent compared with the FY 2023 Final level. The budget reflects the planned completion of the program, having achieved its goals of developing new datasets, tools, and technologies to enable to study of genetic organization over space and time. Requested funds will be used to support the final closing out of program activities.

Bridge to Artificial Intelligence (Bridge2AI)

Bridge2AI aims to set the stage for widespread adoption of AI that addresses complex biomedical challenges beyond human intuition.[22] A key deliverable for this program is the generation of new "flagship" data sets and best practices for machine learning (ML) analysis. These flagship data sets include voice and other data to identify abnormal changes in the body, data to make connections between genetic pathways and changes in cell shape and function, data to improve decision-making in critical care settings, and data to uncover biological processes underlying recovery from illness. Bridge2AI will also produce tools, software, and standards to accelerate the creation of AI/ML-ready data sets and design training materials and

[15] commonfund.nih.gov/diversity
[16] commonfund.nih.gov/Exrna
[17] commonfund.nih.gov/KidsFirst
[18] commonfund.nih.gov/IDG
[19] commonfund.nih.gov/globalhealth
[20] commonfund.nih.gov/Diseases
[21] commonfund.nih.gov/4Dnucleome
[22] commonfund.nih.gov/bridge2ai

activities for skills and workforce development. Additionally, Bridge2AI will foster a culture change for the community to embrace data preparation for AI/ML analysis and expand the interdisciplinary community between AI and biomedical and behavioral research.

Budget Policy: The FY 2025 President's Budget request is $32.4 million, a decrease of $3.0 million or 8.5 percent compared with the FY 2023 Final level. Funds in FY 2025 will continue to support generation of flagship data sets, tools, software, and standards, along with coordination and integration activities. Bridge2AI will leverage the flexibility of the Other Transactions funding mechanism to shift funds from FY 2024 to FY 2025, to optimally align with the scientific and budgetary needs of these highly dynamic projects and resulting in a temporarily lower level of funding for FY 2024.

Cellular Senescence Network (SenNet)

As we age, tissues throughout the body accumulate small numbers of specialized cells that no longer divide, yet they remain active and develop specialized characteristics that are different from other non-dividing cells. These specialized cells are called senescent cells. There are many unanswered questions about how, when, why, and where senescent cells form and what impact they have on human health and disease. 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.[23] SenNet researchers are mapping senescent cells in 18 human tissues and additional body fluids across the lifespan, in addition to 19 tissues from multiple mouse strains.

Budget Policy: The FY 2025 President's Budget request is $38.9 million, a decrease of $4.0 million or 9.3 percent compared with the FY 2023 Final level. The FY 2025 request reflects a planned decrease in technology application and development projects, while maintaining support for tissue mapping centers and a data coordination and organization center.

Common Fund Data Ecosystem

As data-intensive strategies are increasingly undertaken to achieve the goals of Common Fund programs, infrastructure to address challenges facing all data management centers has become necessary. This infrastructure, referred to as the Common Fund Data Ecosystem (CFDE), is enabling researchers to query across and use multiple Common Fund data sets, 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 Common Fund programs by enabling researchers to interrogate multiple disparate data sets, and thereby make new kinds of scientific discoveries that were not possible before. Prior to FY 2023, support for the CFDE was included within the Strategic Planning, Evaluation, and Infrastructure budget line. With the launch of a new stage in FY 2023, support for the new CFDE activities appears as a stand-alone line in the budget by initiative table. Ongoing FY 2023 activities from the first stage remain within the Strategic Planning, Evaluation, and Infrastructure item.

Budget Policy: The FY 2054 President's Budget request is $22.8 million, an increase of $3.1 million or 16.0 percent compared with the FY 2023 Final level (consisting of total support of

[23] commonfund.nih.gov/senescence

$4.8 million from the FY 2023 CFDE budget line as well as the FY 2023 amount for CFDE of $14.9 million within Strategic Planning, Evaluation, and Infrastructure). The new stage of CFDE will continue to engage with many Common Fund data generating programs and coordinate across the entire data ecosystem, enhancing the findability and accessibility of data and increasing emphasis on training and outreach to develop a diverse user base for Common Fund data resources.

Community Partnerships to Advance Science for Society (ComPASS)

The ComPASS program aims to accelerate the science of health disparities and advance health equity research. [24] The goals of ComPASS are to: 1) develop, share, and evaluate community-driven structural health equity interventions that leverage partnerships across multiple sectors to reduce health disparities; and 2) develop a new health equity research model for community-led, multisectoral structural intervention research across NIH and other federal agencies. These interventions will include ambitious projects to address underlying conditions and environments that influence health outcomes, such as economic development, social and community context, neighborhood characteristics, health care access and quality, and nutrition and access to healthy food.

Budget Policy: The FY 2025 President's Budget request is $52.7 million, an increase of $19.9 million or 60.9 percent compared with the FY 2023 Final level. The budget will support the scaling up of this program as it moves from development to implementation of health equity structural intervention research projects and coordinates cross-program activities.

Faculty Institutional Recruitment for Sustainable Transformation (FIRST)

While progress has been made to increase participation of historically underrepresented groups in biomedical research training stages, members of these groups are still less likely to be hired in positions as independently funded faculty researchers. 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.[25] Based on early successes of other cohort-based recruitment programs, FIRST employs 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.

Budget Policy: The FY 2025 President's Budget request is $50.3 million, a decrease of $2.7 million or 5.2 percent compared with the FY 2023 Final level. The budget reflects the planned decrease in support for the first faculty cohort as they transition to other funding sources, while continuing to support the second and third faculty cohorts, launched in FY 2022 and FY 2023, respectively, as well as program-wide coordination and evaluation efforts.

High-Risk, High-Reward Research (HRHR)

The HRHR program supports exceptionally creative scientists proposing innovative and transformative research with the potential for broad impact in any scientific area within the NIH

[24] commonfund.nih.gov/compass
[25] commonfund.nih.gov/first

mission.[26] This program supports four complementary initiatives: the Pioneer Award, New Innovator Award, Transformative Research Award, and Early Independence Award. These awards are intended to support research that is designed for unusual impact, but may be inherently difficult and scientifically risky, often because the project is exceptionally novel or is in an early stage of development. However, investment in high-risk research is an important approach to accelerate the pace of scientific discovery and advance human health.

Budget Policy: The FY 2025 President's Budget request is $193.3 million, an increase of $22.1 million or 12.9 percent compared with the FY 2023 Final level. Funds requested in FY 2025 will be used to support additional innovative projects with the potential for extraordinary impact.

Human BioMolecular Atlas Program (HuBMAP)

HuBMAP 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.[27] In complex, multicellular organisms like humans, the proper functioning of organs and tissues is dependent on the organization, specialization, and interaction of individual cells. However, determining the functions of and relationships between the estimated 37 trillion cells in the human body is a monumental undertaking. HuBMAP is developing an open and global platform to map healthy cells in the human body, generating foundational tissue maps, and developing tools, technologies, and resources for broad dissemination to the entire biomedical research community. To date, HuBMAP has generated over 2,000 datasets representing 31 human organs. HuBMAP researchers are also developing sophisticated ways to visualize this rich spatial and biomolecular information, including through development of a user-friendly virtual reality platform that enables researchers to explore HuBMAP data in a three-dimensional space.

Budget Policy: The FY 2025 President's Budget request is $18.3 million, a decrease of $25.9 million or 58.7 percent compared with the FY 2023 Final level. This funding level reflects the planned reduction in the final year of the program.

Molecular Transducers of Physical Activity in Humans (MoTrPAC)

Physical activity promotes health in a wide variety of ways, and lack of physical activity is a contributing factor to many common chronic health problems. However, we have a limited understanding of the molecular mechanisms that underlie how physical activity provides health benefits. 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. MoTrPAC is cataloging the biological molecules affected by physical activity in humans, identifying some of the key molecules that underlie the systemic effects of physical activity and characterizing their function.[28] Initial results from MoTrPAC's complementary animal studies are revealing exciting new insights into the effects of physical activity, including strong effects on biological pathways

[26] commonfund.nih.gov/highrisk
[27] commonfund.nih.gov/HuBMAP
[28] commonfund.nih.gov/MolecularTransducers

related to metabolism and the new discovery that a significant number of responses demonstrate sex-specific differences. Human studies and subsequent analyses are currently ongoing.

Budget Policy: The FY 2025 President's Budget request is $8.4 million, a decrease of $10.6 million or 55.7 percent compared with the FY 2023 Final level. The budget reflects the planned winding down of human clinical studies and associated coordination activities, while continuing support for sample analysis, animal studies, and data management.

Human Virome Program

The viruses that exist in the human body are large in number and very diverse, but research has predominantly focused on the relatively small number of viruses that cause obvious clinical disease. The vast majority of the human virome is not well-studied, and the impact of these viruses on human health is unknown. However, there is growing evidence that these viruses may play underappreciated roles in human health, including influencing the immune system, altering susceptibility to some diseases, or affecting metabolic processes. For example, recent research has shown that changes in components of the gut virome are linked to obesity and metabolic syndrome in children. Launching in FY 2024, the Human Virome Program aims to characterize the many viruses that reside inside humans and to improve our understanding of how these viruses impact human health.[1] This program will characterize the "healthy" human virome in diverse cohorts across the lifespan, remove technological roadblocks to studying these viruses, and define the virome's role in health and disease. Funds requested in FY 2025 will support these activities.

[1] commonfund.nih.gov/humanvirome

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 perfect, "one size fits all" diet. The goal of NPH is to describe and understand variations in how different people respond to diet, with the aim of developing algorithms that predict individual responses to food and dietary patterns.[29] 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. NPH will leverage the *All of Us* infrastructure and recent advances in biomedical science, such as artificial intelligence (AI) and microbiome research, to provide unprecedented opportunities to examine associations between nutrition and a variety of long-term outcomes.[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. NPH achieved an exciting milestone in spring 2023, opening enrollment for clinical nutrition studies at 14 sites nationwide.

Budget Policy: The FY 2025 President's Budget request is $47.0 million, an increase of $4.6 million or 10.7 percent compared with the FY 2023 Final level. Increased funds requested in FY 2025 will support increases in data and study coordination and biobanking, while supporting ongoing clinical nutrition studies, data generation, and AI and data modeling.

[29] commonfund.nih.gov/nutritionforprecisionhealth
[30] allofus.nih.gov/

Somatic Mosaicism across Human Tissues (SMaHT)

Over time, different cells within the body accumulate changes to the inherited DNA sequence, resulting in genetically distinct cells within an individual. There is mounting evidence that this genetic variation, called somatic mosaicism, plays important roles in biological processes such as development, aging, and disease. However, technical challenges in detecting rare somatic variations mean this phenomenon is understudied. The SMaHT program aims to transform our understanding of how somatic mosaicism influences biology and disease.[31] SMaHT will catalog somatic variants in 10-15 sets of tissues from diverse human donors at different life stages, develop innovative sequencing tools and analysis methods, and create a workbench to integrate analysis of somatic variation with the human genome.

Budget Policy: The FY 2025 President's Budget request is $30.9 million, an increase of $8.1 million or 35.3 percent compared with the FY 2023 Final level. Increased funds requested in FY 2025 will be used to support planned increases in support for generation of somatic variant catalogs, development of tools and methods, and creation of an integrative data workbench..

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

The SPARC program is accelerating the development of novel neuromodulatory therapeutic devices to advance bioelectronic medicine through provision of foundational data and tools.[32] SPARC is addressing this need by generating maps and tools to precisely 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 2 diabetes, inflammatory disorders, and more. The first stage of the SPARC program developed new tools and technologies, mapped connections among a variety of different nerves and organ systems and created a public resource providing data and tools for advancing bioelectronic medicine. Now in its second stage, SPARC is investigating the anatomy and functional connectivity of the human vagus nerve, developing open-source neural engineering technologies, and supporting prize competitions for innovators to demonstrate proof of principle neuromodulation therapeutic benefits.

Budget Policy: The FY 2025 President's Budget request is $0.5 million, a decrease of $31.6 million or 98.6 percent compared with the FY 2023 Final level. Decreased funds requested in FY 2025 reflect the planned closing out of the program.

Transformative High-Resolution Cryoelectron Microscopy (CryoEM)

The CryoEM program is enabling novel discoveries in structural biology by broadening access to cutting-edge cryoelectron microscopy and cryoelectron tomography techniques and training.[33] These approaches enable researchers to determine the structure of biological molecules with unprecedented detail and accuracy. However, the high cost of required equipment and a lack of training mean that many researchers cannot leverage these critical approaches, and therefore opportunities for novel discoveries are missed. By providing increased access, the CryoEM program is anticipated to catalyze fundamental biological discoveries, as well as accelerate

[31] commonfund.nih.gov/smaht/
[32] commonfund.nih.gov/sparc
[33] commonfund.nih.gov/CryoEM

development of vaccines and therapeutics. Projects supported through the CryoEM program have made new discoveries about proteins that play roles in neurodegenerative and neuropsychiatric diseases, COVID-19, and antibiotic resistance.

Budget Policy: The FY 2025 President's Budget request is $4.1 million, a decrease of $21.9 million or 84.4 percent compared with the FY 2023 Final level. The funding level reflects the planned completion of support for cryoelectron microscopy efforts, while supporting the final year of the cryoelectron tomography network.

Venture Program

The Venture Program is a new approach within the Common Fund to support high-risk, short-term initiatives with the potential for high impact. These cross-cutting initiatives will be highly responsive to the shared interests of the NIH Institutes, Centers, and Offices, and will explore flexible ways of supporting innovative research projects that can be implemented quickly in response to emerging opportunities. Venture initiatives will have clear goals focused on a specific outcome, in the form of new knowledge, methods, or technologies. Similar to the HRHR program, Venture is anticipated to be an ongoing investment, in which new science is continually being supported through a series of short-term investments. Venture will launch as a pilot in FY 2024 with a small number of initial projects and will expand in FY 2025 to support additional innovative initiatives identified through an NIH-wide planning process.

Strategic Planning, Evaluation, and Infrastructure

CF management requires that certain activities be undertaken for the stewardship of the CF as a whole. These include activities related to strategic planning, evaluation, and infrastructure.

Strategic planning is undertaken every year to identify new scientific challenges and opportunities that may be ready for dedicated investment via a CF program. CF strategic planning first identifies broad scientific areas that are priorities for NIH as a whole and then establishes a focused strategy for investments that will catalyze research progress in those areas. The initial idea (or concept) gathering phase of strategic planning often involves input from interested parties with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. The strategy development phase of 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 biomedical 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 adopt 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 2025 Common Fund programs leveraged the wide-ranging expertise of NIH's senior leadership and scientific staff, combined with public input through a Request for Information. Planning efforts led to the identification of one potential program idea for active exploration and further development, **Complement Animal Research in Experimentation (Complement-ARIE**). The purpose of this potential program is to catalyze the development, standardization, validation, and use of human-based new approach methodologies (NAMs) that will transform the way the biomedical research community conducts basic, translational, and clinical research by complementing, or in some cases possibly replacing, traditional models. This program is anticipated to lead to a new understanding of health and disease across diverse populations, support standardization and regulatory use of NAMs, and make all research more efficient and effective by adding validated new approaches for researchers to leverage. Planning for this program will leverage an innovative ideation challenge and robust listening sessions to gather input from the broad biomedical community, supported in FY 2024 via funds reserved for strategic planning activities. These planning activities will help to determine whether to proceed with the potential program, as well as define its possible scope and direction. Additionally, NIH is exploring potential opportunities to support a new approach for support of clinical research across a range of sites that will engage primary care providers to reach underserved communities. Plans for this activity are in very early stages of development but may leverage Common Fund support.