

Common Fund Update

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National Institutes of Health

Office of Strategic Coordination – The Common Fund

Outline

- Introduction to the Common Fund
- Science Highlights
- Enhancements on the Horizon

Common Fund Historical Perspective



2004: NIH Roadmap is launched

2006: NIH Reauthorization establishes within the NIH Office of the Director:

- Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)
 - Common Fund
 - Dedicated source of funding for *trans*-NIH research
 - FY23 Enacted budget: **\$735M**

The Common Fund Moves the NIH Mission Forward – Faster

Bold programs that **catalyze discovery** across biomedical and behavioral research

Advances research areas important to the missions of **multiple NIH Institutes, Centers, and Offices**

Spurs subsequent advances not possible without an **initial strategic investment**



Features of Common Fund Programs and How They Catalyze Biomedical Discovery

Programs designed to change the trajectory of biomedical research

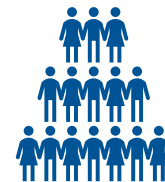
- Substantial investments (~\$10-50M/year)
- Time-limited (10 years or less)
- Goal-driven (milestones, active management)



Accelerate
emerging
science



Remove
research
roadblocks



Enhance the
research
workforce



Support high-risk, high-
reward science

Common Fund Science and Management are Collaborative



Scientists from diverse disciplines provide input as we plan new programs.



Researchers participate in interdisciplinary consortia to tackle shared goals.



Leadership and staff from Institutes, Centers, and the Office of the Director work together to design funding opportunities and oversee the projects.

The Breadth of Common Fund Programs

24 Programs in 3 Broad Categories

Transformational Science and Discovery

New scientific principles, models, and research resources

MoTrPAC

ExRNA

HRHR

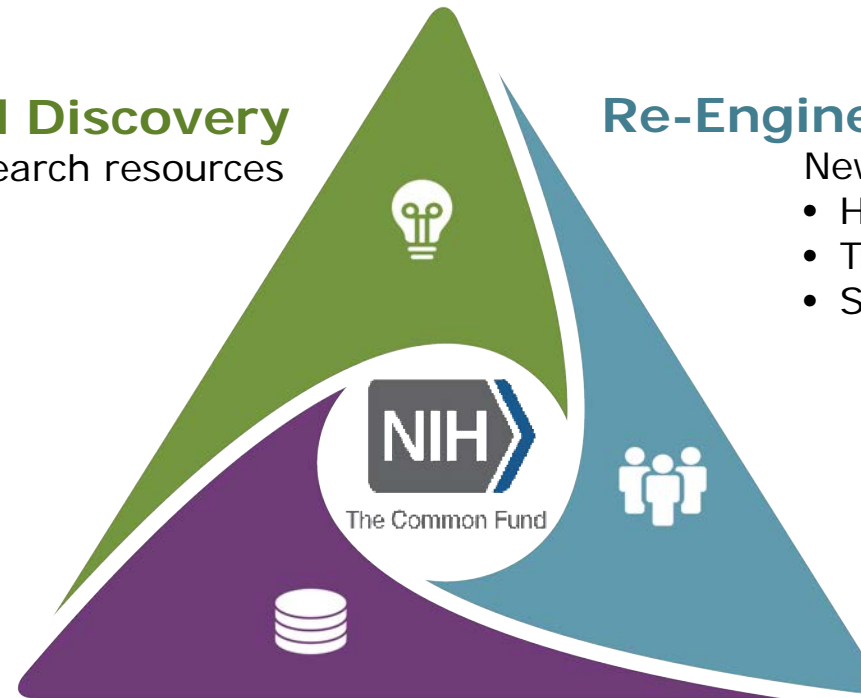
Re-Engineering the Research Enterprise

New approaches to:

- How we do research
- Translating research into interventions
- Supporting a robust workforce

ComPASS

UDN



Catalytic Data Resources

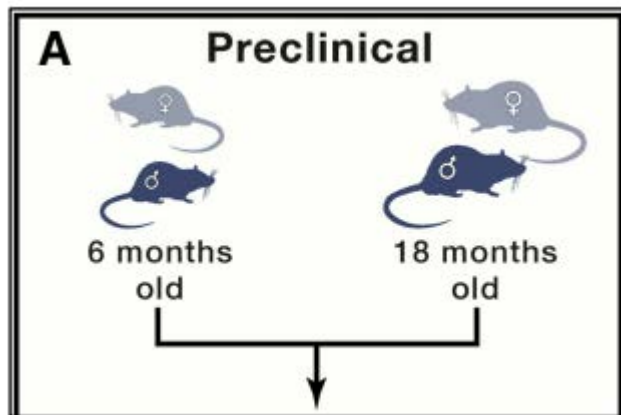
Data resources to accelerate discovery

CFDE Kids First

Science Highlights

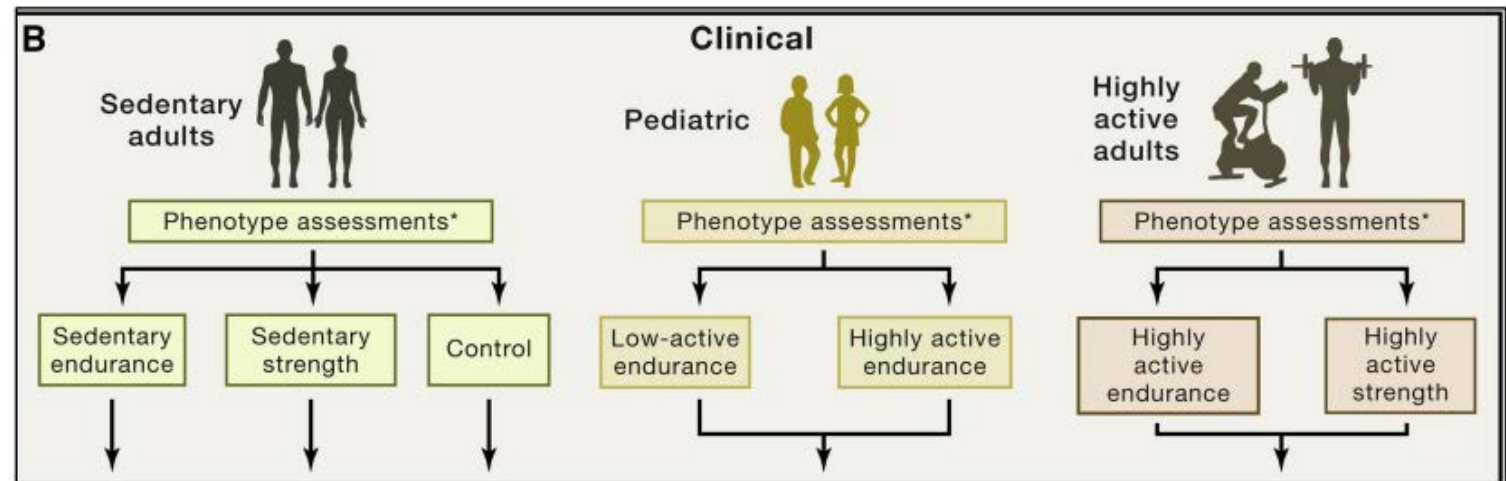
Molecular Transducers of Physical Activity Consortium (MoTrPAC)

Assembling a comprehensive map of molecular changes that occur in response to exercise and, when possible, relate these changes to the benefits of physical activity



Molecular profiles:

- Before/after single bout of endurance exercise?
- Before/after training?

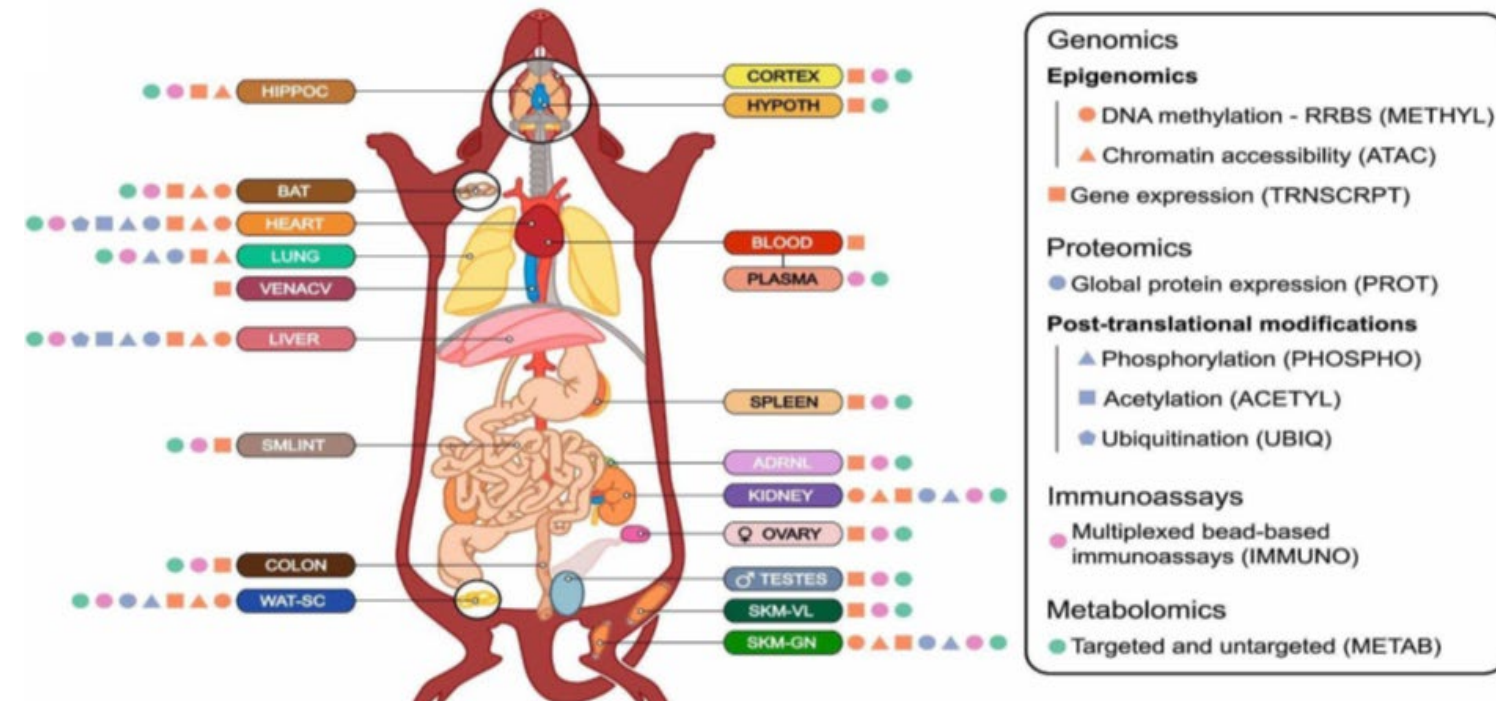


Molecular profiles:

- Of people who exercise regularly?
- Before/after 12 weeks of exercise training (for non-exercisers)?
- Of low-active/highly-active children?

Cell 2020 Jun 25; 181(7):1464-1474

MoTrPAC Pre-clinical Study



Preliminary Analyses:

- Over 40,000 analytes regulated over the training time course
- Multiomics clustering identified several major molecular trajectories over time course
- Top 10 most enriched pathways related to metabolism
- Strong sex-specific response – half of the multiomics clusters have different trajectories in males and females

Data available at <https://motrpac-data.org/>

Extracellular RNA Communication (ExRNA)

Established a new understanding of how RNA can be exported from cells (extracellular RNA) and play a role in cell-to-cell communication

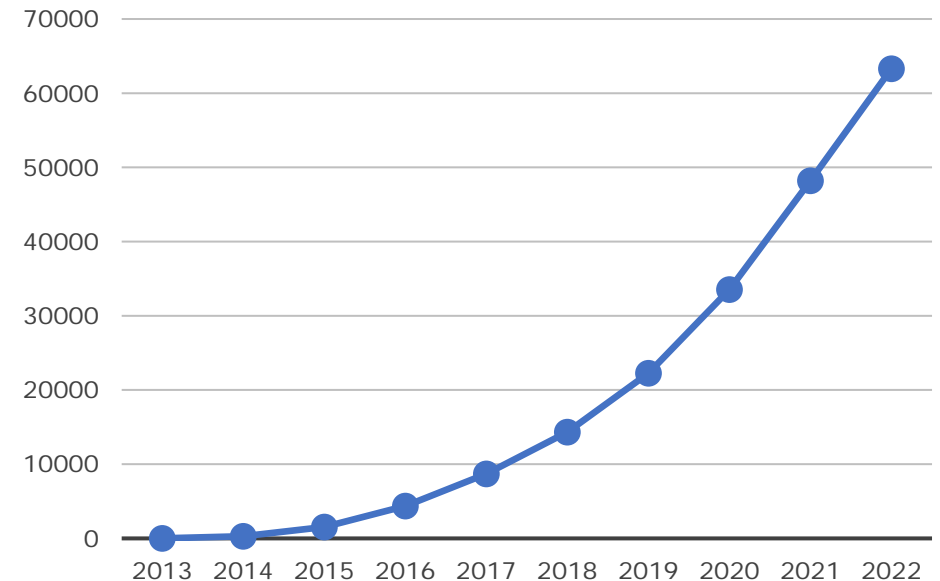
Phase 1

- Established data standards, a data portal, and tools/reagents
- Catalogued exRNA in human biofluids from over 2000 donors
- Identified potential exRNA biomarkers for over 30 diseases (cancer, diabetes, glaucoma, and more)

Phase 2

- Developing technologies to better separate and study different types of exRNA carrier vesicles

Citations



ExRNA Tool Predicts Response to Immunotherapy in Lung Cancer Patients

- Tool to diagnose non-small cell lung cancer (NSCLC) and predict response to immunotherapy
- With just a blood sample, the tool allows measurement of exRNA and proteins from individual extracellular vesicles
- Predicted NSCLC with 93.2% accuracy and immunotherapy response with 72.2% accuracy (invasive tissue biopsies correctly predict only 20-40% of responders)
- Potential to expand to other diseases and conditions



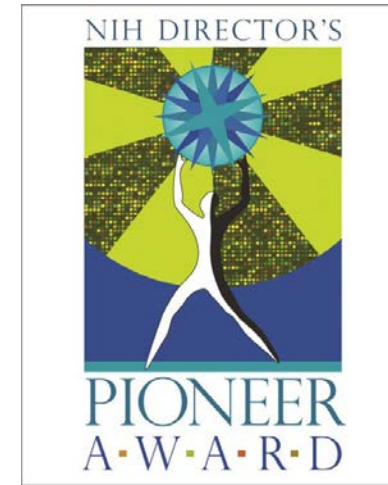
Animation by XVIVO Scientific Animation, Wethersfield, CT

Nguyen et al. 2022, J Extracell Vesicles.
<https://directorsblog.nih.gov/tag/extracellular-rna/>

High-Risk, High-Reward Research Program

Four NIH Director's Awards support exceptionally innovative research from scientists at all career stages

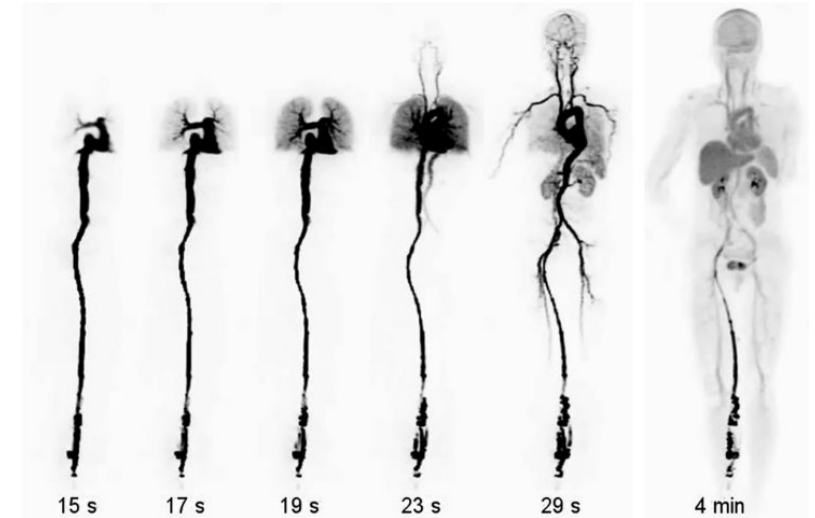
- Annual funding opportunities
- High-risk, high-impact ideas
- No preliminary data needed
- Any topic relevant to the NIH mission
- Independent evaluations show high levels of innovation and impact (Pioneer and New Innovator)



High-Risk, High-Reward Research Program: Examples

HRHR awards across the NIH mission, supporting diverse, groundbreaking science

- A 3D, full-body imaging device that can create videos of changes over time
- A new approach to accurately identify emerging COVID-19 hotspots
- A novel technology to create nanoscale 3D objects
- 3D printed components of the human heart
- Finding neural structures mosquitoes use to target human odor



Time lapse images via EXPLORER total-body PET scanner show movement of a marker from the heart to the lungs and to the rest of the body.

[J Nucl Med. 2019 Mar; 60\(3\):299-303. doi: 10.2967/jnumed.119.226498. Epub 2019 Feb 7.](#)

Gabriella Miller Kids First Pediatric Research Program



Kids First is building a large-scale data resource to bring together **genetic and clinical data** to enable new discoveries about the biology of **childhood cancer** and **structural birth defects**, including discovery of shared genetic pathways between these disorders



Gabriella Miller

Kids First Data and Data Resource Portal

ABOUT THE DATA



22
Birth defect
cohorts



15
Cancer
cohorts



32,000+
Study
participants



192,000+
Data files
available

ABOUT THE PORTAL



50
Unique
countries
represented by
portal users



500+
Approved access
requests for
secondary data
use



3,389+
Total portal
users



6,500+
Total portal
logins in
2022

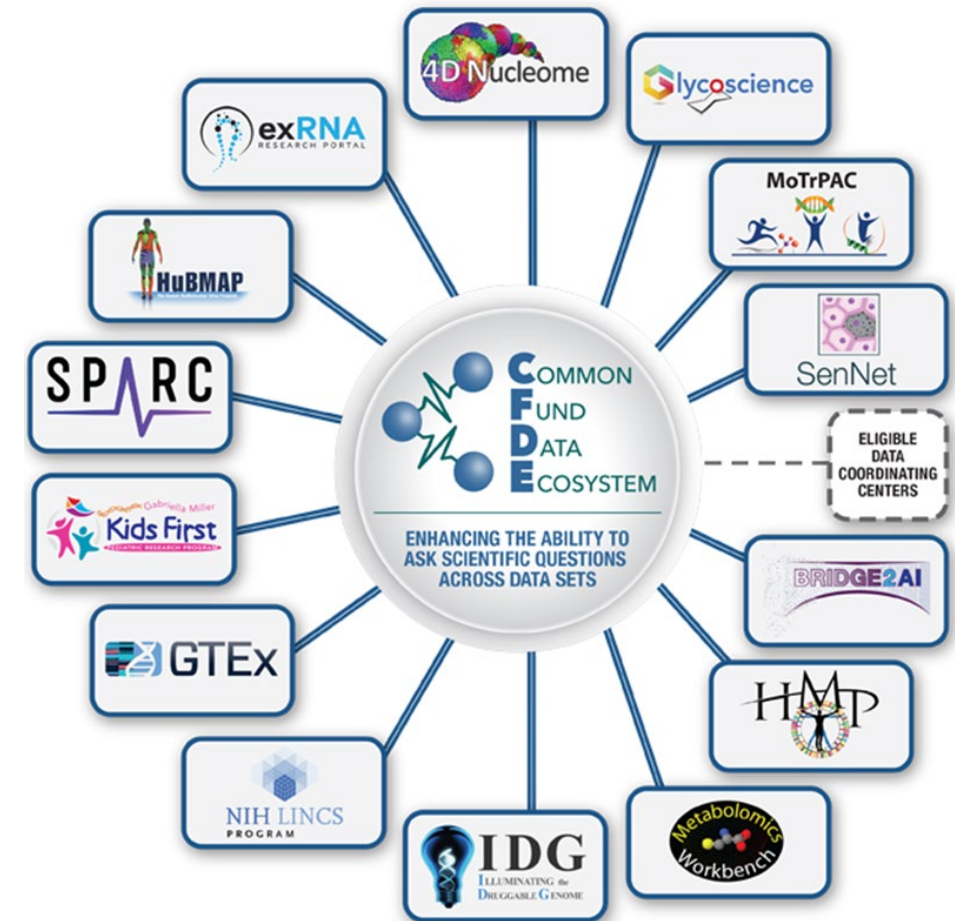
Common Fund Data Ecosystem (CFDE)

Goal: create a functioning ecosystem that makes Common Fund data sets more impactful by enabling easier data access and use

FY23/24: Phase II funding for data and knowledge portals, training center, and coordinating center.

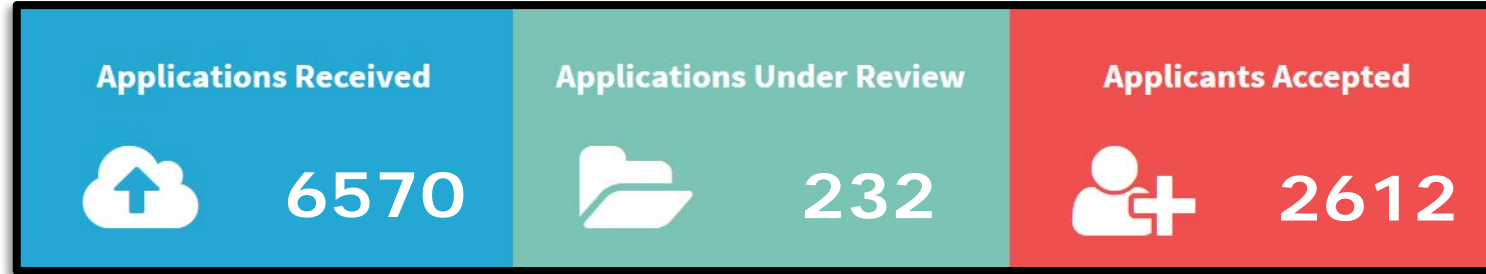
CFDE aims to:

1. Enable users to **query across & use** multiple Common Fund data sets
2. **Sustain** Common Fund data and tools
3. **Training and outreach** to bring people to Common Fund data
4. Coordinate and integrate infrastructure and activities into a **cohesive ecosystem**



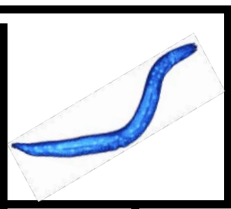
Undiagnosed Diseases Network (UDN)

<https://undiagnosed.hms.harvard.edu/about-us/facts-and-figures/> July 2023 data



Participants evaluated
2220

Sequences completed
2199 exomes or genomes



Model Organisms
465 variants analyzed

Metabolomics
328 cases analyzed



Working Together 676 Diagnosed

UDN – Patient Perspective

How the Undiagnosed Diseases Network helped solve my daughter's medical mystery

December 1, 2017



When [Avery] was just a few months old, we noticed she was not moving as much as our other children had at that age...

Over the next few years, *we consulted an army of doctors who conducted innumerable tests on Avery*, but they could not find the exact cause of her developmental delays. *This was a very difficult time for us, and left us feeling frustrated and helpless...*

Life was moving along, until one day, one of our friends [told] us about a new initiative...the *Undiagnosed Diseases Network*...

Using a combination of exome sequencing of Avery's DNA, and *extensive experiments conducted in fruit flies*, a team of [UDN] researchers...concluded *Avery carried a new type of mutation*, a toxic gain-of-function, in a calcium channel gene, CACNA1A...

This unexpected discovery helped Avery's doctors to switch her medication regimen to a drug that blocks the calcium channel...

Despite her condition, Avery has a very fulfilling life. She continues to amaze all of us, especially the doctors, with steady progress in her motor skills.



- Program duration: 10 years
- Planned budget: ~ \$153M over a 5-year period

Community-led health equity **structural interventions** that leverage partnerships to reduce health disparities

A new health equity research model for community-led, multisectoral structural intervention research across NIH and other federal agencies



Community-Led, Health Equity Structural Interventions (CHESIs)



Health Equity Research Hubs (Hubs)



ComPASS Coordination Center (CCC)

Community-Led, Health Equity Structural Interventions (CHESIs) Initiative: Three-Phased Approach

1

PLANNING (Year 1-2)

- Plan, develop, pilot (as appropriate) structural interventions
- Capacity and partnership building
- Develop local Health Equity Research Assembly (HERA)

2

IMPLEMENTATION (Year 3-8)

- Implement community-led, health equity structural interventions, with local HERAs
- Interventions will influence health outcomes across multiple health conditions and diseases

3

DISSEMINATION (Year 9-10)

- Assess health impacts of structural intervention research findings
- Develop dissemination and sustainability plan for structural interventions

CF Enhancements on the Horizon

Engagement with NIH ICO Directors

OSC has been working with NIH Institute and Center Directors to enhance and improve CF policies and processes

- Small group conversations with IC Directors
- Discussion with all IC Directors at a “Common Fund Retreat”
- Improved strategic planning process for FY26

KEY TAKEAWAY: ICO Directors are enthusiastic to increase engagement with Common Fund



Common Fund Process and Policy Outcomes

Reaffirmed Common Fund program criteria

New Approach to Short-term High-risk Investment – “Venture” Space

Re-emphasized flexibility in program design

- Length of investment, program configuration

Improved ICO Director engagement

- Improved information on impact of CF programs on ICO mission areas
- Developing new analytic approaches with DPCPSI’s Office of Portfolio Analysis

Clearer, simpler program management tools

- Program milestones and reporting simplified and strengthened
- More active, longer-term planning for program sunset

Common Fund FY 2026 Strategic Planning

Approach:

Idea funnel leading to ICO Directors' recommendations and NIH Director decision

Jun-Jul '23	Aug '23	Sep-Dec '23	Dec '23	Jan '24
RFI open	OSC analysis	ICO idea development	Selection for retreat by ICODs	Retreat and selection for full development

Goals:

- A regular, predictable pattern of soliciting ideas
 - Annual
 - Focused on the CF criteria
- Outreach to the extramural community
- Inclusion of the NIH community

NEW – Venture Space

“Amazing things with modest funding”

The Venture Space will make CF support available for **high-risk, short-term** initiatives.

Prioritized by ICOD Venture Board, with final approval by NIH Director

Criteria:

- Emphasis on **innovation** and **speed**
- Projects should be **high-risk** with **potential for major impact**

Features of Venture Space projects:

- Brief funding, probably no more than **3 years**
- Clearly defined goals with **go/no-go milestones**
- **Flexible approach** to funding mechanisms and project timelines
- **Nimble, streamlined** management
- **Smaller scale** cross-cutting initiatives

Discussion



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National Institutes of Health

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