Department of Health and Human Services
National Institutes of Health

Common Fund Strategic Planning Report 2013

2013

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

About the NIH Common Fund

Initiated in 2004 as the National Institutes of Health (NIH) Roadmap for Medical Research and re-named in the NIH Reform Act of 2006, the Common Fund supports research in areas of emerging scientific opportunities, rising public health challenges, and knowledge gaps that deserve special emphasis or would otherwise benefit from strategic planning and coordination.

Common Fund programs represent strategic investments in which 5- to 10-year initiatives can have a transformative impact. Common Fund programs are expected to address science that is too large in scope, too complex, or sometimes too basic to be funded by individual NIH Institutes and Centers (ICs) or other entities but which will synergistically promote and advance individual missions of NIH ICs.

Common Fund programs do not focus on a specific disease, condition, or target population. They are intended to catalyze research across a broad spectrum of biomedical disciplines by supporting the development of catalytic tools, technologies, databases, models of research and funding, and other resources.

The Office of Strategic Coordination (OSC) within the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) is responsible for managing and coordinating activities for the NIH Common Fund. Programs supported through the Common Fund are administered by the NIH ICs.

Our Vision

The intent of Common Fund programs is to provide a strategic and nimble approach to address key *roadblocks* in biomedical research that impede scientific discovery and its translation into improved human health. In addition, these programs capitalize on *emerging scientific opportunities* to catalyze the rate of progress across multiple biomedical fields.

Common Fund Programs are intended to be:

Transformative: Must have high potential to dramatically affect biomedical and/or behavioral research over the next decade.

Catalytic: Must achieve a defined set of high impact goals within a 5- to 10-year time frame.

Synergistic: Outcomes must cooperatively promote and advance individual missions of NIH Institutes and Centers to benefit health.

Cross-cutting: Program areas must cut across missions of multiple diseases or conditions, and be sufficiently complex to require a coordinated, trans-NIH approach.

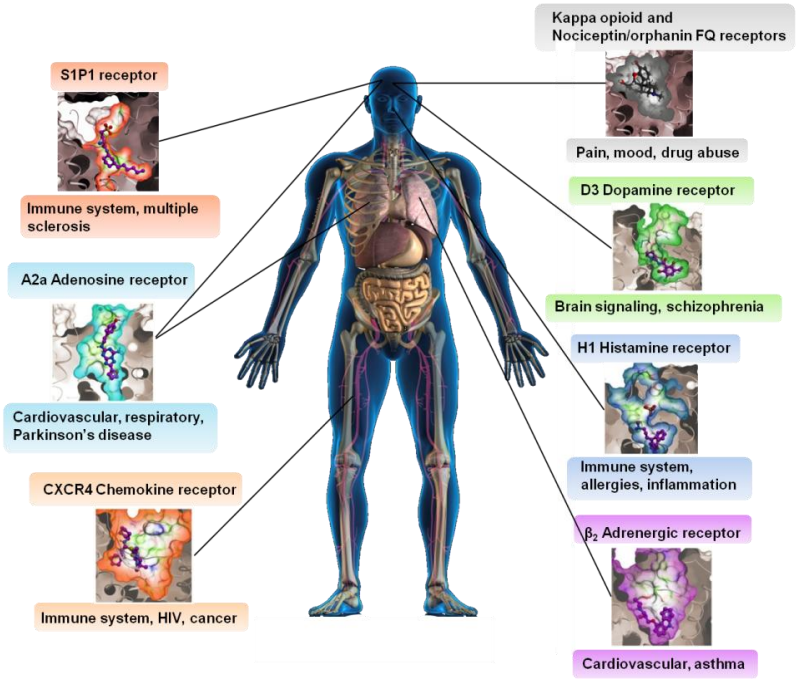
Unique: Must be something no other entity is likely or able to do.

About the Strategic Plan

The Public Health Service Act requires the Director of the NIH to submit a report to Congress containing a strategic plan for funding research that "…represents important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from conducting or supporting additional research that involves collaboration between two or more national research institutes or national centers, or would otherwise benefit from strategic coordination and planning" (42 U.S.C. §§ 282(b)(7)(A), 283(a)(3)).

This report describes:

- **The Lifecycle of Common Fund programs**
- **Common Fund strategic planning goals and process**
- **Plans for future strategic planning efforts for the Common Fund**
- **Implementation and status of Common Fund programs designed to meet needs articulated through strategic planning**
- **Evaluation of Common Fund programs to assess progress towards strategic goals**

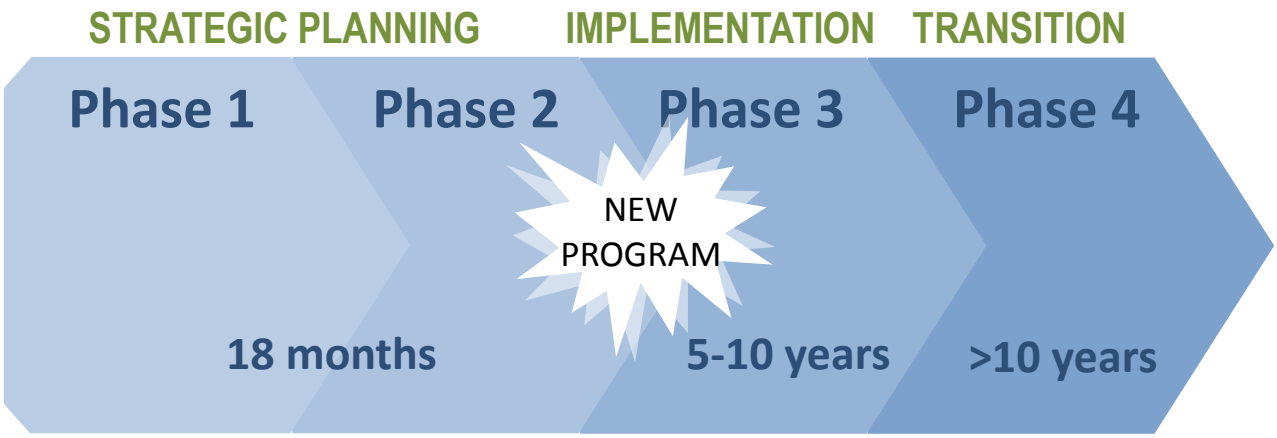


The Common Fund's **Structural Biology** program is addressing critical roadblocks in the purification and characterization of membrane-bound proteins, which represent a large class of targets for drug development. Novel techniques pioneered by the Structural Biology program have led to a rapid acceleration in researchers' ability to determine the structure of G-protein coupled receptors (GPCRs), including GPCRs implicated in multiple sclerosis, HIV, cancer, neurological disorders, asthma, allergies, and drug addiction.

Common Fund Program Lifecycle

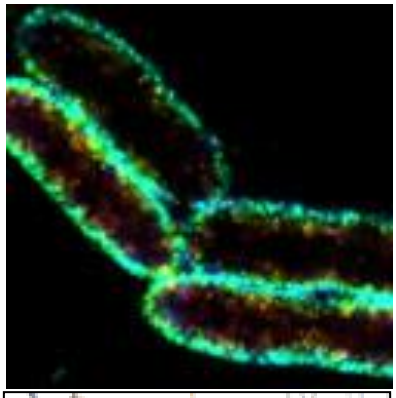
Common Fund programs are a limited-term, strategic investment in which a set of well-defined goals are expected to be achieved in a 5- to 10-year period. Common Fund programs are identified through an extensive strategic planning process, designed to include input from various stakeholders to ensure that programs will have maximum utility to the broad biomedical community and address major obstacles to research progress. Each program is administered and guided by multiple NIH ICs. At the completion of each program, the tools, technologies, and data produced by the program are taken up and used by the community at large, and/or the infrastructure that the Common Fund has built transitions to other sources of support for management.

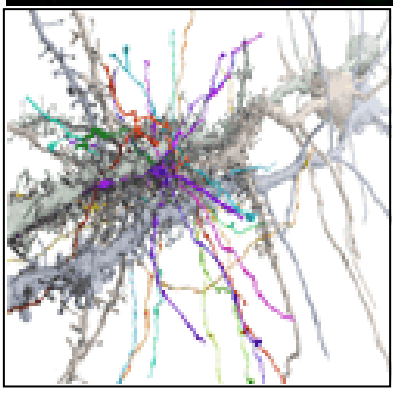
The lifecycle of Common Fund programs can be envisioned as evolving through several different stages, including strategic planning (**Phases 1 and 2**, culminating in the official start of selected programs), program implementation (**Phase 3**), and transition of mature programs to other sources of support or use within the scientific community (**Phase 4**).

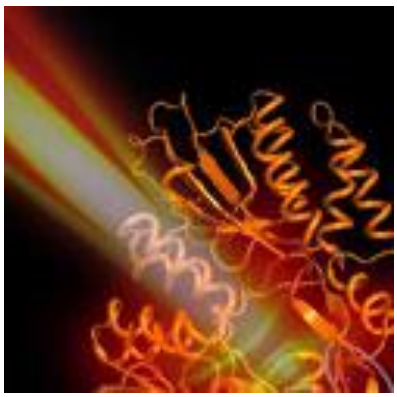


Although Phases 3 and 4 begin after the conclusion of the official strategic planning phases, approaches to program implementation and transition are considered during strategic planning. The early consideration of implementation and transition ensure that program goals and milestones address the needs identified during strategic planning and provide a sustainable model for continued use by the scientific community once Common Fund support for a program has ended.

Common Fund Strategic Planning







Images courtesy of NIH Director Transformative Research Award recipients Drs. Xiawei Zhuang and Xiaoliang Xie; Drs. Jeff Lichtman, Markus Meister, Joshua Sanes, and Sebastian Seung; and Drs. Paola Arlotta, J. Keith Joung, and Feng Zhang.

Goals of Strategic Planning

Strategic planning is used to identify research areas that are not currently well supported by the ICs but which would enable and synergize with IC-funded research and would best be pursued via limited-term Common Fund investment. The strategic planning process for the Common Fund varies from year to year to accommodate changing opportunities and needs of the scientific community and the available level of research funds. Although the yearly process varies, core principles and activities underlie all the planning activities. These include:

- Input is sought from people representing the perspectives of all ICs. This may include input gathered directly from NIH staff and IC Directors and/or provided by external scientists who represent trans-NIH research interests. Common Fund planning engages people from a wide range of disciplines and career stages.

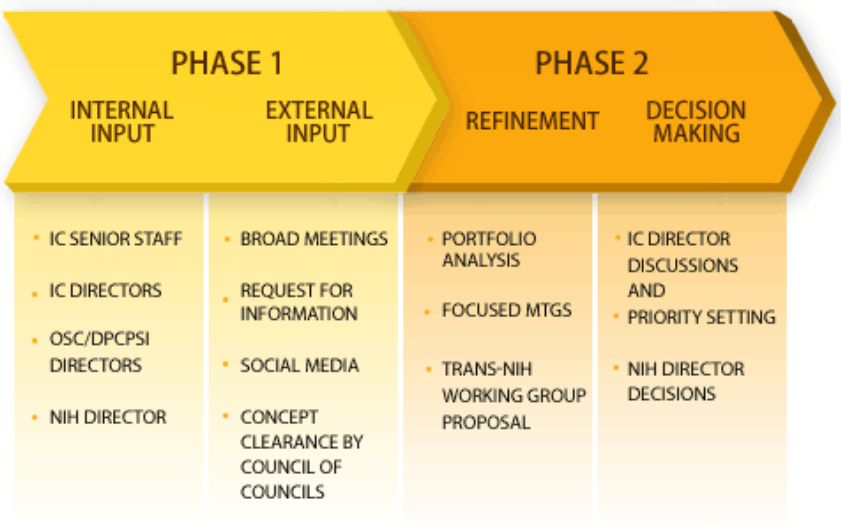
- Input is gathered systematically and transparently rather than through *ad hoc* submission of individual unsolicited ideas. The process for soliciting ideas for new Common Fund programs must be balanced in its inclusion of representatives from across the NIH mission and must involve the review of many ideas together, so that competition among many ideas will result in the most compelling programs.

- The trans-NIH research portfolio is reviewed to assess the current level of support for the concepts that are identified by internal or external stakeholders. Review of the scientific portfolio is an iterative process that helps in the selection of broad program areas as well as the development of specific initiatives within these broad areas so that the program is designed to make a unique contribution of high impact.

- The leadership across NIH is engaged early in the selection of new program areas to ensure that program development is focused on areas for which there is the greatest enthusiasm and broadest potential impact.

Strategic Planning Process

Strategic planning involves the identification of broad program areas representing trans-NIH challenges and opportunities that could best be addressed through short-term, goal-driven programs within the Common Fund. These broad program areas are then refined into a series of well-defined initiatives.



Phase 1 of the strategic planning process identifies broad scientific needs and opportunities through meetings with external scientific experts, solicitation of ideas from NIH ICs, discussions with NIH Leadership and Advisory Committees, and/or engagement with the public through requests for information or through social media. The Council of Councils for DPCPSI acts as an external advisory panel to the DPCPSI and NIH Directors for consideration of Phase 1 concepts. Concepts cleared by the Council of Councils are prioritized by the DPCPSI and NIH Directors to identify concepts that should move to Phase 2 planning.

Phase 2 of the strategic planning process refines the broad concepts identified in Phase 1 into specific, well-defined initiatives. The refinement process may include external and internal meetings and workshops; analysis of the NIH and external scientific research portfolios; trans-NIH Working Group proposals; and priority setting by IC, DPCPSI, and NIH Directors.

Phase 2 planning produces a unique strategic implementation plan for each program, including well-defined goals and milestones. Each Common Fund program includes a plan for active program management for the duration of Common Fund support to ensure goals and milestones are being met and to allow flexibility to adjust to the changing needs of the community and the current state of the science. The implementation plan for each program is reviewed and adjusted annually through program reviews conducted in partnership by the administering ICs and DPCPSI/OSC.

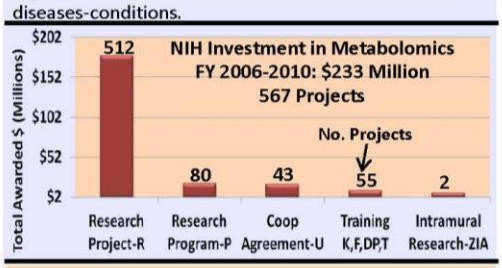
Portfolio Analysis: Moving from Phase 1 to Phase 2

Portfolio analysis is in an integral part of strategic planning, providing critical information about ongoing efforts in areas being considered as potential Common Fund programs to identify specific niches where strategic investment by the Common Fund could support unique and potentially transformative research. An example of how portfolio analysis is used to refine ideas moving from Phase 1 into Phase 2 is illustrated by the portfolio analysis conducted for the Metabolomics program. The findings from this report, highlighted in the "Major Opportunities to Spur Metabolomics" section below, helped shape the current Metabolomics program initiatives focused on increasing metabolomics capacity, training in metabolomics, technology development, and synthesis of reference standards.

Metabolomics Portfolio Analysis Overview:

NIH RESEARCH

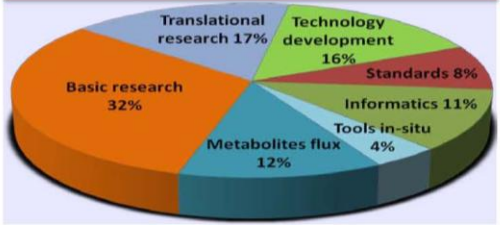
The NIH Metabolomics portfolio was evaluated by the trans-NIH working group to determine NIH investment in scientific areas including limitations, strengths and research opportunities. Focus areas include: technology development, translational research, standards and measurement protocols, databases-informatics-algorithms, metabolites flux, *in-situ* measurement and diseases-conditions.



SUMMARY

- Limited large-scale coordinated efforts for standards development
- Limited emphasis in translational research (17%), technology development (16%) and training in Metabolomics (4%)
- One previous Common Fund initiative in Metabolomics Technology Development and standards
- Diverse disease portfolio. Major areas include: diabetes, cancer, heart disease, digestive diseases and brain disorders
- There are 38 Centers in the US with some Metabolomics expertise, only a few of which have significant throughput for community use. Further expansion of Metabolomics capacity is needed
- Multiple public Metabolomics databases available in the US

SCIENTIFIC AREAS



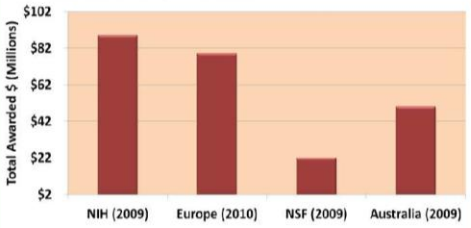
NATIONAL & INTERNATIONAL

NATIONAL – NSF RSEARCH

- NSF funding mostly in plant sciences and technology
- NSF awarded 59 projects ($54 million) during FY 2005-present
  - Arabidopsis 2010 Metabolomics: $1 million

INTERNATIONAL

- Australia Metabolomics Bioplatforms: $208 million
- Netherlands Metabolomics Center: $67 million
- BBSRC, UK Plant and Microbial Metabolomics: $10.4 million
- Canadian Human Metabolome Database: $8.1 million
- Global investment in Metabolomics for FY 2010 is Estimated to be $ 225 million*



* Current trends in the Metabolomics sector within Europe. http://www.frost.com/prod/servlet/market-insight-top.pag?docid=128394679

- International Metabolomics Centers : Australia, Canada, Japan Netherlands, UK, Spain, Finland
- There are coordinated metabolomics efforts within and among international research agencies to develop standards, comprehensive data repository and technology

MAJOR OPPORTUNITIES TO SPUR METABOLOMICS

1. Support generation of more metabolite standards through coordinated collaborative approach
2. Train more scientists in Metabolomics
3. Increase the capacity in Metabolomics through establishing more centers
4. Support Metabolomics technology development

Geetha Senthil. Ph.D.. OPA. DPCPSI. NIH.

Strategic Planning Activities since 2011

The Common Fund Strategic Planning Report for 2011 described strategic planning activities and the current status of programs emerging from those activities up to early 2011. Two programs, Metabolomics and Single Cell Analysis, were undergoing Phase 2 strategic planning at the time of the 2011 Report and were launched as new Common Fund programs in fiscal year 2012. New rounds of strategic planning started in 2011 and 2012, leading to new programs being implemented in fiscal year 2013 and planned for fiscal year 2014 and beyond, pending availability of funds.

Innovation Brainstorm: Transforming Discovery into Impact

Strategic Planning for the Common Fund in 2011

On May 4-6, 2011, the NIH hosted the "Innovation Brainstorm: Transforming Discovery into Impact" to identify areas where strategic investments by the NIH might accelerate the development of a nascent scientific field or capitalize on a recent groundbreaking discovery. Invited participants from a wide range of scientific disciplines were selected based on their records of interaction, innovation, and broad thinking. Participants were asked to identify the most exciting research paper in any field within the past year that illustrates an emerging area of science with high potential to be transformative, describe the importance of the paper, and outline possible ways that strategic investment could reduce the time needed for the impact to be realized. At the meeting, participants discussed these papers and produced recommendations for potential Common Fund investments in these areas.

The ideas emerging from the Innovation Brainstorm meeting were combined with idea nominations from the NIH ICs. These ideas were then posted on an interactive social media website, where the public was encouraged to comment on how to refine these broad program areas into specific initiatives, and how these initiatives could be implemented as a Common Fund program. In total, the social media website received more than 290 comments, over 60 percent of which provided concrete recommendations about how to refine or implement the proposed ideas (http://commonfund.nih.gov/planningactivities/socialmedia_summary.aspx). An additional idea on how to systematically study currently Undiagnosed Diseases emerged from meetings with NIH IC Directors and was also considered during the strategic planning process.

Two ideas were selected to move through Phase 2 planning and are being implemented as Common Fund programs in fiscal year 2013, pending availability of funds:

- Extracellular RNA Communication
- Undiagnosed Diseases Program

Forward Focus Workshop: Strategic Planning for the NIH Common Fund

Strategic Planning for the Common Fund in 2012

In May 2012, the NIH hosted a series of three meetings called "Forward Focus: Strategic Planning for the NIH Common Fund." One meeting, which took place in Potomac, Maryland, included invited participants recognized as leaders and innovators in a range of biomedical research areas. Two other meetings, taking place in San Francisco and Chicago, were open to the public and included 60-100 attendees from academia, industry, government, and the general public. At the Forward Focus meetings, participants presented broad concepts for initial discussion and voted for the most promising ideas. Small breakout groups then refined and merged these ideas to create a list of recommended programs along with rough draft implementation plans.

As in 2011, ideas were also gathered from the NIH ICs. In addition, the Advisory Committee to the NIH Director presented recommendations in the areas of Biomedical Workforce, Diversity in the Biomedical Workforce, and Data and Informatics, which were considered as potential Common Fund programs.

From this process, four ideas were selected to move on to Phase 2 strategic planning for implementation as Common Fund programs in fiscal years 2013 and 2014, pending availability of funds:

- Big Data to Knowledge (BD2K)
- Increasing the Diversity of the NIH-Funded Workforce
- Strengthening the Biomedical Research Workforce
- Illuminating the Druggable Genome *(potential launch in fiscal year 2014*)

As part of the Phase 2 refinement process, unique strategic plans were developed for each program to articulate a set of goals that, if achieved, will transform the way research is conducted across a variety of biomedical fields. Table 1 describes the strategic goals of Common Fund programs launched since 2011, and Appendix B provides a more detailed description of these programs. Budget information for the Common Fund as a whole is provided in Appendix A.

Table 1: Strategic Goals of New Common Fund Programs since 2011 (see Appendix B for additional details)

Common Fund Program	Strategic Goals
Metabolomics	• To create Comprehensive Metabolomics Resource Cores, in order to facilitate collaborative large-scale metabolomics projects • To provide interdisciplinary training in metabolomics research • To develop novel technologies and methods to enable metabolomics research • To develop high-quality metabolite standards • To maximize the exchange of best practices, data, technical advances, and training programs
Single Cell Analysis	• To define general principles regarding the extent to which seemingly identical cells are actually heterogeneous, and to discover the functional consequences of this heterogeneity • To develop exceptionally innovative tools and technologies to enable single cell analysis • To extend current single cell analysis technologies for use in living tissues and in the clinic • To foster communication between scientists working in single cell analysis, and to disseminate technologies and data
Extracellular RNA Communication	• To establish fundamental biological principles of extracellular ("outside the cell") RNA, or exRNA, secretion, delivery, and impact on target cells • To create a catalogue of exRNAs present in human body fluids • To test the clinical utility of exRNAs as biomarkers of disease or as therapeutic molecules • To provide a data/resource repository for the scientific community
Undiagnosed Diseases Program	• To test whether the cross-disciplinary approach to disease diagnosis pioneered by the NIH intramural program in Undiagnosed Diseases is feasible to implement in academic medical centers around the U.S. • To develop a robust process for collaboration between clinicians and basic scientists so that mechanisms underlying rare diseases can be rapidly elucidated and information fed back to the clinic to inform patient

Common Fund Program	Strategic Goals
	care • To train clinicians in the use of contemporary genomic approaches so that genomic methods can be increasingly brought to bear on a myriad of diseases • To engage basic researchers to elucidate the mechanisms underlying diseases so that treatments may be identified • To catalyze the field of rare disease research in order to help patients and make discoveries
Big Data to Knowledge (BD2K)	• To facilitate broad use of biomedical big data • To develop and disseminate analysis methods and software • To enhance training for disciplines relevant for large-scale data analysis • To establish centers of excellence for biomedical big data
Increasing the Diversity of the NIH-Funded Workforce	• To increase the number of underrepresented minority scientists pursuing biomedical, behavioral, clinical, and social science research and essential research-related occupations • To strengthen the infrastructure of comparatively under-resourced institutions that have a demonstrated commitment to diverse student groups • To develop a nation-wide mentoring consortium to develop standards for good mentorship and provide training opportunities for students and mentors • To assess efficacy of a coordinated, network approach to training and mentoring diverse groups
Strengthening the Biomedical Research Workforce	• To expand training opportunities for early career scientists to prepare them for entry into the dynamic biomedical workforce landscape • To support the development of innovate approaches to complement traditional research training in the biomedical sciences • To assess the impact of innovative training approaches developed through this program, and to disseminate proven approaches

Strategic Planning for Fiscal Year 2015 and Beyond

A new round of Phase 1 strategic planning aimed at generating ideas for potential new Common Fund programs began in early 2013. This round of strategic planning will continue to explore innovative approaches to generate creative and transformative ideas suitable for Common Fund support.

As in previous years, strategic planning efforts will focus on identifying the ***greatest challenges*** to research discovery and translation and the most promising ***emerging opportunities*** to catalyze research across a variety of scientific disciplines and disease conditions.

Phase 1 strategic planning will involve the nomination of ideas from NIH ICs. Through their extensive and continuous interactions with external scientists, the ICs are well positioned to develop ideas that reflect the needs of both the broad scientific community as well as within NIH.

- ***Idea nominations from NIH Institutes and Centers***: Each NIH IC is invited to submit up to two idea nominations for concepts they recommend as being relevant, not only for the IC-specific mission, but relevant across the NIH as a whole. To effectively evaluate the responsiveness of the proposed idea to Common Fund criteria, as well as the potential impact of the program, NIH ICs are asked to address the following questions in their nomination:

    - ***What is the major obstacle/challenge/opportunity that the Common Fund should address?***
    - ***What would the goals of the program be?***
    - ***Why is a trans-NIH strategy needed to achieve these goals?***
    - ***What initiatives might form the strategic plan for this topic?***
    - ***If a Common Fund program on this topic achieved its objectives, what would be the impact?***

Concepts emerging from the Phase 1 strategic planning activities will be reviewed by the Council of Councils in the spring of 2013. Cleared concepts will then be refined in Phase 2 strategic planning, and approved programs will potentially receive funding in fiscal year 2015 and beyond.

Common Fund Program Implementation

Each Common Fund program has a unique implementation plan, specifically designed to overcome the most pressing needs and capitalize on the most exciting emerging opportunities identified within each program's realm of science. Each program must develop well-defined strategic goals and milestones, and programs are monitored for progress towards these goals and milestones on a continuous basis.

Some Common Fund programs aim to generate a data resource for the scientific community, such as the Human Microbiome Project's reference set of genetic information from virtually all microbes living in or on healthy humans at 18 different body sites. Many Common Fund programs also generate new tools or technologies that are widely disseminated. For example, the Single Cell Analysis program aims to develop "quantum leap" improvements in technologies to examine the behavior and function of single cells within tissues, with high levels of spatial and temporal specificity, and to extend technologies that work in the laboratory so they can be used in the clinic. Still other Common Fund programs seek to bring about a change in the culture of scientific research, such as the High Risk-High Reward program initiatives focusing on fostering exceptional innovation, creativity, and intellectual risk-taking for researchers at all career stages. Common Fund programs span the spectrum from basic to translational science, with many programs containing a mix of initiatives focused on basic and clinically driven goals.

Appendix C gives an overview of the major features of all current Common Fund programs.

Fostering Transformative Innovation: The High Risk-High Reward program

The Common Fund's High Risk-High Reward program aims to support researchers who demonstrate exceptional innovation and creativity and who propose ground-breaking, transformative research ideas. The High Risk-High Reward program consists of four initiatives:

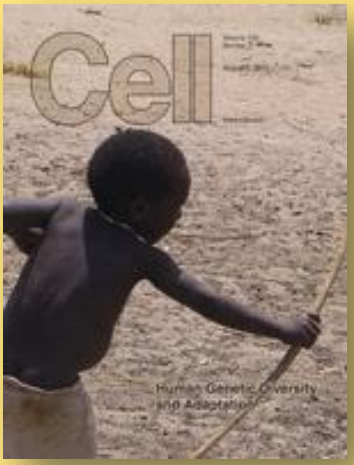
- NIH Director's Pioneer Award
- NIH Director's New Innovator Award
- NIH Director's Transformative Research Award
- NIH Director's Early Independence Award

NIH Director's New Innovator Award recipient Dr. Edward Boyden and **NIH Director's Pioneer** and **Transformative Research Award** recipient Dr. Karl Deisseroth share the 2013 Brain Prize, along with four other researchers, for their ground-breaking research in developing and refining a technique called optogenetics. Optogenetics allows select groups of neurons to be turned on or off with light, allowing researchers to explore brain circuitry in both healthy and diseased brains. Additionally, optogenetics may one day be used as a new approach to treat brain disorders by modulating the abnormal activity of neurons that underlies some diseases.

Read more about the Brain Prize winners: http://www.thebrainprize.org/files/4/uk_pr_final_05_03_13_ext.pdf

Top picture: Edward Boyden; Bottom picture: Karl Deisseroth

Dr. Sarah Tishkoff, **NIH Director's Pioneer Award** recipient, earned a spot on the cover of *Cell* journal for her groundbreaking studies of human genetics (Vol 150, Issue 3, Aug 2012). Dr. Tishkoff's research team sequenced the whole genomes of five individuals in three different hunter-gatherer populations: Pygmies from Cameroon and Khoesan-speaking Hadza and Sandawe from Tanzania. The genetic sequences allowed them to identify targets of natural selection that affect immunity, reproduction, metabolism, and height in these diverse hunter-gatherer populations. Studies such as these provide insight into human evolutionary history and the origin of traits that make each of us unique.



One example of a current Common Fund program that is capitalizing on emerging opportunities and overcoming barriers to research is the Epigenomics program, which is exploring how chemical modifications to DNA resulting from environmental chemicals, pharmaceuticals, diet, aging, and normal developmental process can influence human health and disease.

Epigenomics: Capitalizing on Novel Technologies to Explore New Frontiers in Human Health and Disease Research

Genes encoded by DNA are the blueprint for life, containing instructions for development, health, and disease. But genes alone don't tell the whole story. Chemical modifications to DNA or DNA-associated proteins can regulate when and where genes are switched on and off, greatly affecting the behavior and function of cells. These modifications occur "on top of" the genome and are referred to as epigenomic modifications. Similar to genes, epigenomic modifications can be inherited and may explain why environmental exposures experienced by one generation can exert an influence on subsequent generations. Epigenomic modifications can influence normal development as well as a wide variety of diseases, but the exact mechanism for how they do this, or when and why epigenomic modifications occur, is not well understood.

The Common Fund's ***Epigenomics*** program aims to generate new research tools, technologies, and resources to enable scientists to understand how epigenomic modifications regulate both normal development and disease. Epigenomics researchers are creating maps of all modifications across the genome of many different human cell types, including cells from the blood, brain, lung, heart, and stomach. These maps, 61 to date, can be used by scientists as a reference to compare against samples of diseased tissues to pinpoint epigenomic modifications that are specifically associated with disease. Epigenomics researchers are also developing novel techniques for detecting epigenomic changes with extreme precision or in very small samples, which will enable a more comprehensive understanding of the epigenome than ever before.

In 2012, researchers supported in part by the Epigenomics program uncovered an important breakthrough in our understanding of the relationship between genetic and epigenetic factors contributing to disease. Dr. John Stamatoyannopoulos at the University of Washington, along with his colleagues, discovered that genetic variants associated with many common diseases are frequently located in regions of DNA that play a role in gene regulation, and that these regions are marked by specific epigenomic changes. Interestingly, many genetic variants associated with adult-onset diseases were found in regions of DNA active during fetal development. This finding may help explain why environmental exposures in utero or during early childhood are known to increase risk of diseases that produce symptoms years or even decades later.

Common Fund Program Transition

Common Fund programs are designed to achieve a set of high-impact goals within a 5- to 10-year timeframe. At the conclusion of each program, how deliverables will be disseminated, how established resources will be maintained, and how to find suitable support for new research stimulated by the program must be considered. Transition plans are considered early in the lifecycle of a Common Fund program, and are reconsidered throughout the lifecycle to ensure the transition accommodates the changing needs of both the program and the external scientific community. To date, two Common Fund programs have undergone successful transitions, including:

- Interdisciplinary Research program: This program raised awareness of the importance of interdisciplinary approaches to complex problems within the biomedical research community. It helped to stimulate the softening of departmental boundaries within academic institutions, making it easier for investigators to collaborate. Interdisciplinary training curricula were developed that are still in use. Administrative mechanisms, such as multi-principal investigator (multi-PI) leadership of individual projects and the Interdisciplinary Research Consortia mechanism, are permanently available to NIH ICs when interdisciplinary research is required. Science areas addressed by the Common Fund's Interdisciplinary Research program are now ongoing via investigator-initiated research at the NIH ICs.

- Clinical and Translational Science Awards (CTSAs): Support of the CTSAs, which originated as a Common Fund program, has now transitioned to the National Center for Advancing Translational Sciences (NCATS) within NIH. The CTSAs continue to improve the way clinical and translational research is conducted, to accelerate the translation of laboratory discoveries into treatments for patients, to engage local communities in clinical research efforts, and to train a new generation of clinical and translational researchers.

Evaluation of Common Fund Activities

Common Fund programs are routinely evaluated throughout their lifecycle to ensure programs are meeting goals and milestones, and that the resources, technologies, tools, and data developed through the program are useful for the scientific community. Annual progress reports for each program are reviewed by OSC/DPCPSI for advancement towards goals and milestones, with program adjustments made to reflect emerging needs and opportunities. Many Common

Fund programs also undergo regular reviews by external scientific panels to assess progress and provide feedback on future directions. Additionally, programs must assess their progress at the end of the first 4 to 6 years of funding to determine whether a second phase of funding (up to a limit of 10 years total) is necessary to reap maximum benefit from the program. This assessment may take the form of a Mid-Course Review or may be collected via regular assessments of the program by external scientific panels. At the conclusion of mature Common Fund programs, outcomes are assessed via formal or informal evaluations. For a list of evaluations and reviews conducted to date, see Appendix D.

Lessons learned from program evaluations are critical to the ongoing management of the Common Fund and provide valuable information during the strategic planning process. Identification of effective program implementation and transition plans can help inform the development and design of new Common Fund programs, to ensure that each program is designed to be of high value to the scientific community. Thus, the information learned from evaluation of ongoing and transitioning programs is used to strengthen the planning activities for the next round of new programs, continuing the Common Fund program lifecycle.

In addition to program evaluations, the strategic planning process itself is evaluated to assess which approaches to planning are most effective. Evaluations of the two public Forward Focus meetings (Chicago and San Francisco) revealed a high level of participant satisfaction, with 100 percent of meeting participants indicating they would be willing to provide input in a future NIH Common Fund strategic planning effort. For each meeting, between 93 and 100 percent of participants indicated that the meeting encouraged an open exchange of ideas and provided the opportunity for meaningful input. Participants were also enthusiastic about the idea nomination process and group discussion used to develop ideas (86-100 percent agreeing these approaches were effective). The Common Fund will continue to evaluate future strategic planning efforts, retaining those approaches that prove most useful.

As the Common Fund grows, the NIH will continue to evaluate and enhance its strategic planning process to ensure that new programs are responsive to the most pressing needs of the biomedical community.

Appendix A: Common Fund Budget Data

Dollars in Millions	FY 2008 Actual B.A.	FY 2009 Actual B.A.	FY 2010 Actual B.A.	FY 2011 Actual B.A.	FY 2012 Actual B.A.	FY 2013 PB
Roadmap/ Common Fund	$498.24	$541.13	$544.03	$543.02	$544.93	$544.93
Roadmap/ Common Fund Percent of NIH Labor/HHS Budget Authority[1]	1.71%	1.80%	1.77%	1.77%	1.77%	1.77%

[1]Adjusted to exclude mandatory funding for the Type 1 Diabetes Research program; funding appropriated to NIH for the Global Fund for HIV/AIDS, Tuberculosis, Malaria prior to FY 2012; funding appropriated through the Interior, Environment, and Related Agencies Appropriations Bill for the NIEHS Superfund Research and Worker Training Program; and the PHS Evaluation fund assessments appropriated to the NLM.

Appendix B: Common Fund Programs since 2011

Metabolomics

Metabolites are small molecules that are produced or consumed in the chemical reactions that take place in the body to sustain life. The sum of all metabolites at any given moment—the metabolome—is a form of "chemical read out" of the state of health of the cell or system and provides a wealth of information about nutrition, environmental insult, infection, health, and disease status. Recent advances in technology have enabled metabolomic analysis to be conducted in basic and clinical research settings, resulting in the discovery of new diagnostic tools and yielding important clues about disease mechanisms that suggest new treatment strategies. However, the use of these technologies is limited by the number of research centers that have the necessary equipment and expertise to conduct the studies and the lack of uniform standards for identifying unknown metabolites.

The Common Fund's Metabolomics program is intended to establish the needed resources, training, technology development, and standards to catalyze the field of metabolomics to advance scientific discovery and clinical practice. It also facilitates the dissemination of data through an informatics component and through the establishment of an international consortium. This consortium will ensure that Common Fund investments are leveraged against investments made in other countries, resulting in increased data sharing, reduced redundancy of effort, and faster translation toward improvements in health.

Single Cell Analysis

Cells are the basic unit of life, yet individual cells are difficult to study in their natural environments. Although most analyses of intact tissues are performed on groups of cells, individual cells within the same population may differ dramatically, and these differences can have important consequences for the health and function of the entire population. New approaches to single cell analyses are needed to uncover fundamental biological principles and ultimately improve the detection and treatment of disease.

The Single Cell Analysis program seeks to overcome the scientific and technological hurdles to understanding how cells vary normally and how they respond to their microenvironment within populations of tissues. The program addresses significant challenges that currently exist with regard to systematically describing the given "state" of a cell, defining normal cell-to-cell variation, measuring the impact of environmental perturbations, understanding cellular responses in the larger context of tissues and networks, and overcoming limitations in measurement approaches. The Single Cell Analysis program is planning to undertake several new initiatives—including support for development of methods for the spatiotemporal tracking, characterization, and analysis of live cells in situ—and will consider the use of a prize mechanism, compliant with the COMPETES Act, to address highly specific challenges that face the single cell analysis community.

Extracellular RNA Communication

Ribonucleic acid (RNA) was once thought to exist in a stable form only inside cells, where it served as an intermediate in the translation of proteins from genes. However, it has recently been discovered that RNA can be exported from cells in extracellular vesicles or bound to lipids or proteins to circulate through the body and affect cells at a great distance. These extracellular RNAs, or "exRNAs," may also be absorbed from food, the microbes that live in our bodies, or the environment, potentially eliciting a variety of biological responses. The impact of these exRNAs is currently unknown. To capitalize on the opportunity to understand entirely new paradigms of information exchange based on the release, transport, uptake, and regulatory role of exRNAs, the Common Fund launched the Extracellular RNA Communication Program. This program aims to define fundamental principles of exRNA generation, distribution, uptake, and function; to develop a catalogue of exRNAs in normal human body fluids; and to investigate the potential for using exRNAs as therapeutic molecules or biomarkers of disease.

Undiagnosed Diseases Program

To aid individuals with rare and difficult-to-diagnose diseases, and to also make progress in uncovering, understanding, and treating these disorders, the NIH established in 2008 a group within its intramural research program focused specifically on diagnosing these rare and elusive disorders. Building on the success of this program in diagnosing both known and new diseases, the Common Fund launched the Undiagnosed Diseases Program to test whether this type of cross-disciplinary approach to disease diagnosis is feasible to implement in academic medical centers around the United States. The goals of this program are to establish a network of Centers, bringing specialized expertise to diagnosis of an expanded number of patients, and to move quickly from the bedside of these patients to the bench so that the mechanism of disease may be determined. Inter-Center collaborations will be established to bring the appropriate expertise to each patient and to ensure that the bench results are brought rapidly back to the patient. This is a pilot program, intended to resolve logistical issues pertaining to the conduct of this type of program in an extramural environment. It will assist patients with unknown disorders in reaching an accurate diagnosis, and it will discover new diseases that provide insight into human physiology and genetics. The program will also provide training in next-generation genomic sequencing analysis for rare disease diagnostics.

Big Data to Knowledge (BD2K)

As biomedical tools and technologies rapidly improve, researchers are producing and analyzing an ever-expanding amount of complex biological data. New analytics tools are needed to extract critical knowledge from this vast amount of data, and new policies must be developed to encourage data and software sharing to maximize the value of the data for all researchers across the spectrum of biomedical research. In addition, data and metadata standards to ensure data

quality and uniformity must be developed, with broad input from the scientific community to ensure that these standards will have maximum utility and value.

In response to the needs articulated by the Advisory Committee to the Director, NIH, Working Group on Data and Informatics (http://acd.od.nih.gov/Data%20and%20Informatics%20Working%20Group%20Report.pdf), the NIH is undertaking several initiatives to address the challenges and opportunities associated with big data. As one component of the NIH-wide strategy, the Common Fund is supporting the Big Data to Knowledge (BD2K) program, which aims to facilitate broad use of biomedical big data, develop and disseminate analysis methods and software, enhance training for disciplines relevant for large-scale data analysis, and establish centers of excellence for biomedical big data.

Increasing the Diversity of the NIH-Funded Workforce

The NIH recognizes a unique and compelling need to promote diversity in the biomedical, behavioral, clinical, and social sciences research workforce. The NIH expects efforts to diversify the workforce to lead to the recruitment of the most talented researchers from all groups; to improve the quality of the educational and training environment; to balance and broaden the perspective in setting research priorities; to improve the ability to recruit subjects from diverse backgrounds into clinical research protocols; and to improve the nation's capacity to address and eliminate health disparities.

In 2012, the NIH Advisory Committee to the Director, NIH, Working Group on Diversity in the Biomedical Research Workforce provided concrete recommendations toward improving the recruitment and retention of underrepresented minorities, people with disabilities, and people from disadvantaged backgrounds (collectively referred to as Under-Represented Groups, or URGs) across the lifespan of a biomedical research career from graduate study to acquisition of tenure in an academic position or the equivalent in a non-academic setting (http://acd.od.nih.gov/Diversity%20in%20the%20Biomedical%20Research%20Workforce%20Report.pdf). Influenced by these recommendations, the NIH is undertaking a variety of activities both internally and in its support of extramural institutions. One component of this comprehensive response to the Committee's recommendations is the establishment of the Increasing the Diversity of the NIH-Funded Workforce program. This program is intended to unify and strengthen institutions and faculty dedicated to the recruitment and retention of diverse scientists.

The program, to be launched and piloted through the NIH Common Fund, will build on the many existing programs that currently support students, faculty, and institutions. It is intended to create an integrated consortium of institutions and organizations working together to establish a community of diverse scientists, strengthening ties between mentors and mentees at all career stages, and building

effective collaborative networks. The program will consist of a series of coordinated initiatives:

- NIH Building Infrastructure Leading to Diversity (BUILD): This initiative aims to strengthen the infrastructure of comparatively under-resourced institutions that have demonstrated a commitment and ability to train diverse student groups by providing both student and faculty support, with the goal of increasing the number of underrepresented minority scientists pursuing biomedical, behavioral, clinical, and social science research and essential research-related occupations. BUILD will establish and solidify collaborative relationships between comparatively under-resourced institutions, pipeline institutions such as community colleges, and research-intensive partnering sites to complement strengths and participate in a nationwide BUILD consortium. It will build on, and integrate with, existing diversity-building programs that have similar aims and which are funded by ICs or other entities.

- National Research Mentoring Network (NRMN): NRMN will build a network of qualified mentors from all biomedical and behavioral disciplines into a nation-wide consortium that will mentor students and junior faculty from diverse groups. It will establish effective mentoring practices and tools for face-to-face and virtual mentoring. It will also develop standards for good mentorship and provide training opportunities for both mentors and mentees.

- Coordinating and Evaluation Center: To enhance career development, networking opportunities, and resource sharing between BUILD, NRMN, and other diversity-building programs, a Coordinating and Evaluation Center will develop and maintain a database available to participants within both programs, with information on demographics, productivity measures, and outcome measures. The Center will also conduct an annual meeting to facilitate the sharing of best practices with all participants.

Strengthening the Biomedical Research Workforce

NIH shares concern with the broader biomedical community that the long training time and the declining percentage of Ph.D. graduates that obtain independent academic research positions are making biomedical research a less attractive career. Additionally, although many graduates are moving into essential research-related occupations rather than research-intensive positions, the current training programs do little to prepare trainees for these other career options. The NIH is committed to supporting a sustainable and robust workforce equipped to address the greatest challenges and opportunities in biomedical research, recognizing that traditional research-intensive positions are not the only means by which Ph.D. graduates can meaningfully contribute to the biomedical research enterprise.

Based on recommendations from the Advisory Committee to the Director, NIH, Working Group on Biomedical Workforce (http://acd.od.nih.gov/Biomedical_research_wgreport.pdf), the Common Fund is

launching the Strengthening the Biomedical Research Workforce program to expand the training opportunities for early career scientists to prepare them for entry into the dynamic biomedical workforce landscape. This program supports the NIH Director's Workforce Innovation Award to Enhance Biomedical Research Training, also called the Broadening Experiences in Scientific Training (BEST) awards. These five-year awards provide support for institutions to develop innovative approaches to complement traditional research training in biomedical sciences. Institutions are encouraged to partner with industry or other entities to provide a wealth of diverse training opportunities for their trainees, and the awardees will form a network to share experiences and determine best practices. Novel training approaches will be rigorously analyzed to assess impact, and proven approaches will be widely disseminated throughout the community.

Appendix C: Features of Common Fund Programs

Current Program	Tools/Tech/ Data	Basic Science	Translational Science	Innovation
Big Data to Knowledge (BD2K)	+			+
Bioinformatics and Computational Biology	+	+	+	+
Bridging Interventional Development Gaps (BrIDGs)	+		+	+
Building Blocks, Biological Pathways, and Networks	+	+		+
Epigenomics	+	+		+
Extracellular RNA Communication	+	+	+	+
Genotype-Tissue Expression (GTEx)	+	+	+	+
Global Health	+	+	+	+
Gulf Oil Spill			+	+
HCS Research Collaboratory	+		+	+
Health Economics	+		+	+
High-Risk Research (Pioneer, New Innovator, Transformative Research, and Early Independence Awards)	+	+	+	+

Current Program	Tools/Tech/ Data	Basic Science	Translational Science	Innovation
Human Microbiome Project	+	+		+
Increasing the Diversity of the NIH-Funded Workforce				+
Knockout Mouse Phenotyping Project	+	+		+
Library of Integrated Network-based Cellular Signatures (LINCS)	+	+	+	+
Metabolomics	+	+		+
Molecular Libraries and Imaging	+	+	+	+
Nanomedicine	+	+	+	+
NIH Center for Regenerative Medicine (NIH CRM)	+		+	+
NIH Medical Research Scholars Program			+	+
PROMIS: Patient-Reported Outcomes Measurement Information System	+		+	+
Protein Capture Reagents	+			+
Regulatory Science	+		+	+
Science of Behavior Change	+		+	+
Single Cell Analysis	+	+	+	+

Current Program	Tools/Tech/ Data	Basic Science	Translational Science	Innovation
Strengthening the Biomedical Research Workforce				+
Structural Biology	+	+		+
Undiagnosed Diseases	+		+	+

Appendix D: Common Fund Program Evaluations

Common Fund programs that have been evaluated or formally reviewed by an external panel to date include:

Epigenomics – A process evaluation was undertaken to inform and assist the NIH program managers in their administration of the Epigenomics Program. The results indicate that the program is meeting or exceeding the planned targets for the funded projects, demonstrating synergy, and achieving the catalyzing effects of large-scale funding (http://commonfund.nih.gov/epigenomics/summary.aspx). The Epigenomics program is also assessed at least annually by an external scientific panel. The input from this panel provides guidance about how to make the program as useful to the scientific community as possible and is used for internal decision-making within the Epigenomics Working Group and DPCPSI/OSC.

Human Microbiome Project – In 2012, an External Panel convened to assess the HMP progress in the first five years of support as well as concepts under review for potential new initiatives. The Panel agreed that the HMP had met its original goals, catalyzed the nascent field of human microbiome research, and brought together a diverse community of scientists. The Panel also agreed that the trans-NIH Common Fund mechanism used to support the HMP was important to the successes of the program. They found that other scientists were leveraging the datasets, tools, and standard operating procedures created by the HMP in their own research (http://commonfund.nih.gov/hmp/meeting022012/index.aspx).

Interdisciplinary Research program – An evaluation of the Interdisciplinary Research Consortia (2009-2010) documented numerous measures of interdisciplinary activities, behaviors, and outcomes for researchers and trainees within this program. These measures included frequent meetings with investigators from multiple disciplines, increased scholarly activity and scientific productivity in new disciplines, interdisciplinary training/mentoring, and sharing of resources (http://commonfund.nih.gov/Interdisciplinary/evaluation.aspx). An informal assessment of the Interdisciplinary Training initiative found that trainees from the Interdisciplinary Research program were as successful as non-Interdisciplinary Research trainees in overall grant and R01 success rates but were more successful in obtaining career and individual training (F32) awards. They were also more likely to be in an academic research or teaching career track compared to the general Ph.D. Biomedical Workforce.

Molecular Libraries – The mid-course review meeting was held in 2006, consisting of external reviewers who were not receiving funding from the Common Fund. The review provided a set of recommendations for the Molecular Libraries program, which included focusing on difficult or unique problems to drive innovation and differentiation from drug discovery screening efforts in industry, as well as to maintain the Molecular Libraries program as a diversified portfolio of initiatives (http://commonfund.nih.gov/molecularlibraries/midcoursereview/summary2006.aspx). In addition, an evaluation was conducted in 2010 to evaluate the need for

molecular screening centers and other aspects of the program. The outcome of this evaluation was used to design the transition of the programs component out of the Common Fund (http://commonfund.nih.gov/pdf/Executive_Summary_ML_Needs_Assessment.pdf).

National Centers for Biomedical Computing (NCBC) – The mid-course review of the NCBC was conducted in 2007 by an external review panel. The panel concurred that a long-term investment in biomedical computing is critically important in addressing the health care needs of the country and recommended several actions, including the continued support of biomedical computing, developing a process to sustain and expand this effort, and focusing on educating the next generation of computational scientists (http://commonfund.nih.gov/pdf/NCBC_Mid-course_Report.pdf). As this program transitions from the Common Fund to other mechanisms of support, plans to assess program outcomes are under way. This outcomes assessment will examine the tools generated by the NCBCs, including their utility to the scientific community.

Nanomedicine – In 2009, the Nanomedicine program underwent a mid-course review. The review panel agreed that the Nanomedicine program is a transformational program that is meeting its goal of synergizing multiple disciplines to focus on a specific biomolecular pathway or question in each of the eight Nanomedicine Centers. However, the panel stated that although good science was being done in all of the Centers, some Centers had evolved in directions that were not aligned with the goals of the Nanomedicine program as a whole. As a result, the panel recommended phasing out Centers that were not meeting key goals of the program in order to fully fund activities of the Centers that were more successful. As a result, the number of Nanomedicine Centers was reduced from eight to four (http://commonfund.nih.gov/pdf/Nanomed_summaries_Mid-Course.pdf). In its final phase of support, each Center is assessed and advised annually by a Clinical Consulting Board. These panels provide an assessment of the likely clinical utility of each project.

NIH Rapid Access to Intervention Development (RAID) (now renamed as Bridging Interventional Development Gaps (BrIDGs) – A mid-course review was conducted in 2007 to inform the need for continued support for the program. External panelists emphasized the need to include small businesses as eligible applicants and the need to reduce the time for decision-making. Overall, the panelists voiced strong support for continuing the program and for increasing awareness of its existence as a valuable opportunity for the community (http://commonfund.nih.gov/pdf/NIH-RAID_Midcourse_Review_Report_Final.pdf).

NIH Director's Early Independence Award program – An evaluation of the Early Independence Program application and review process was undertaken in 2011. Although many individual applicants and host institutions were satisfied with the process, several suggestions for improvement were recommended. These included promoting awareness of the program, as well as having NIH assist in the "match-making" between applicants and host institutions (http://commonfund.nih.gov/pdf/EIA_Program_Process.pdf). To facilitate this

process, the Common Fund hosted a matching portal that aims to connect applicants and host institutions. To date, ten institutions have joined the Common Fund-hosted matching portal. An extensive outreach campaign was launched to reach potential applicants for the 2012 funding opportunity.

NIH Director's New Innovator Award program – An evaluation of the New Innovator Award process in 2008 revealed that the program is having a positive impact on fostering innovation. Most applicants proposed riskier aims than they normally would have, and many proposed projects outside their existing area of research. Although it is still too early to determine long-term outcomes of this award program, many high-impact publications have been produced (http://commonfund.nih.gov/pdf/NIA_PE.pdf).

NIH Director's Pioneer Award program – Since the Pioneer program has piloted novel review processes, annual process evaluations were undertaken from 2004-2008, which informed gradual evolution of the application and review processes (http://commonfund.nih.gov/pdf/PioneerAwardProcessEvaluation_2004-2008.pdf). An evaluation of the outcomes of the first two rounds of Pioneer Awards made in 2004 and 2005 revealed that the initiative is having a positive impact on program awardees and the NIH as a whole. Pioneer awardees are pursuing bigger and more high-risk research that is often more multidisciplinary; and they are working outside their traditional areas of research to pursue new ideas, theoretical concepts, methodologies, and technologies and to discover new phenomena through the synthesis of diverse concepts spanning many different disciplines (http://commonfund.nih.gov/pdf/Pioneer_Award_Outcome%20Evaluation_FY2004-2005.pdf). The Pioneer Comparison Evaluation, conducted in 2012, indicated that this program provides important opportunities for innovation, allowing investigators to conduct research that is more pioneering—highly innovative with higher impact—than traditional grant programs such as R01s. Their level of innovation is similar to that of investigators supported by the Howard Hughes Medical Institute, also known for fostering innovation, when efforts are made to control for the total level of support received. These results suggest that both R01s and the Pioneer Awards should be utilized to best provide a balance of depth and breadth of the NIH scientific research portfolio while allowing the best opportunities for trail blazing research (http://commonfund.nih.gov/pioneer/evaluations.aspx).

Patient-Reported Outcomes Measurement Information System (PROMIS) – The mid-course review for PROMIS was released in 2007. The review was conducted from May to September 2007 and assessed the progress of the Network over the first two-and-a-half years of funding. The mid-course review helped assess short- and long-term needs. The review panel consisted of federal employees and outside experts, none of whom were directly involved in or funded by the program. The review determined that the PROMIS program exceeded expectations, and the investigators have developed and organized a functional and productive network (http://commonfund.nih.gov/pdf/PROMIS_Mid_Course_Review.pdf).

Technology Centers for Networks and Pathways (TCNPs) (part of the Building Blocks, Biological Pathways, and Networks program) – In August 2007, a mid-course review was conducted for the TCNP initiative. The review panel was composed of outside experts, and they found that the program goals are laudable and that the awardees are investigating issues that will result in new knowledge and understanding of gap areas (http://commonfund.nih.gov/bbpn/coursereview.aspx).

Structural Biology – An expert scientific panel conducted a mid-course review of the Structural Biology program in 2008. Panel members found that the program was successfully promoting research on membrane protein expression, purification, characterization, and structure determination. Additionally, they concluded that the approaches and reagents being developed will be useful to the membrane protein community at large (http://commonfund.nih.gov/structuralbiology/midcoursereview/summary2008.aspx).