DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund

NATIONAL INSTITUTES OF HEALTH

Common Fund

Budget Mechanism - Total [1/]

Dollars in Thousands

MECHANISM	FY 2011 Actual No.	FY 2011 Actual Amount	FY 2012 Enacted No.	FY 2012 Enacted Amount	FY 2013 PB No.	FY 2013 PB Amount	Change No.	Change Amount
Research Grants								
Research Projects								
Noncompeting	281	$147,970	280	$147,425	292	$153,054	12	$5,629
Administrative Supplements	*34*	5,192	*42*	6439	*42*	6439	*0*	0
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	176	141,013	193	154,799	206	163,640	13	8,841
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	176	$141,013	193	$154,799	206	$163,640	13	$8,841
Subtotal, RPGs	457	$294,175	473	$308,663	498	$323,133	25	$14,470
SBIR/STTR	0	$0	0	$0	0	$0	0	$0
Research Project Grants	457	$294,175	473	$308,663	498	$323,133	25	$14,470
Research Centers								
Specialized/Comprehensive	46	$125,655	40	$109,470	38	$104,460	-2	-$5,010
Clinical Research	9	7,001	0	0	0	0	0	0
Biotechnology	13	4,736	21	7,780	6	2,200	-15	-5,580
Comparative Medicine	3	6,249	0	6,249	0	6,249	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	71	$143,641	61	$123,499	44	$112,909	-17	-$10,590
Other Research								
Research Careers	26	$11,830	4	$2,000	4	$2,000	0	$0
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	23	19,822	31	27,112	39	33,450	8	6,338
Other Research	49	$31,652	35	$29,112	43	$35,450	8	$6,338
Total Research Grants	577	$469,468	569	$461,274	585	$471,492	16	$10,218
Research Training	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	293	11,574	0	0	0	0	0	0
Total Research Training	293	$11,574	0	$0	0	$0	0	$0
Research & Development Contracts	0	$22,681	0	$41,228	0	$41,010	0	-$218
(SBIR/STTR)	*0*	*$0*	*0*	*$0*	*0*	*$0*	*0*	*$0*
	FTEs		FTEs		FTEs		FTEs	
Intramural Research	0	$26,771	0	$26,975	0	$16,975	0	-$10,000
Research Management and Support	0	12,527	0	15,453	0	15,453	0	0
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	0	$543,021	0	$544,930	0	$544,930	0	$0

1/ All items in italics are "non-adds"; items in parenthesis are subtractions.

Major Changes in the Fiscal Year 2013 President's Budget Request

The FY 2013 budget request for the NIH Common Fund, is the same as the FY 2012 Enacted level, for a total of $544.930 million.

Research Project Grants (+$14.470 million, total $323.133 million): The NIH Common Fund expects to support a total of 498 Research Project Grant (RPG) awards in FY 2013. Noncompeting RPGs will increase by 12 awards and increase by $5.629 million. Competing RPGs will increase by 13 awards and increase by $8.841 million. Expansion of the High-Risk High-Reward program, including support for a second cohort of Early Independence Awards in FY 2013, accounts for most of this increase in funding. NIH budget policy for RPGs in FY 2013 discontinues inflationary allowances and reduces the average cost of noncompeting and competing RPGs by one percent below the FY 2012 level.

Research Centers (-$10.590 million, total $112.909 million): The NIH Common Fund plans to support a total of 44 Research Center Awards in FY 2013. The decrease in number and amount reflects a decrease in funding for the National Centers for Biomedical Computing (NCBCs), which are undergoing a planned transition from the Common Fund to the ICs as described in the original NCBC plan, and the planned transition of the Molecular Libraries Screening Centers to support via collaborations with investigator-initiated R01 grants.

Intramural Research (-$10.0 million, total $16.975 million): The requested level of funding reflects the transition of the NIH Chemical Genomics Center in the Molecular Libraries and Imaging program from Common Fund support to the National Center for Advancing Translational Sciences (NCATS).

NATIONAL INSTITUTES OF HEALTH
Common Fund by Initiative
(Dollars in Thousands)

Title of Initiative	FY 2011 Actual	FY 2012 Enacted	FY 2013 PB	Change vs. FY 2012
Epigenomics				
Mapping Centers	11,047	11,540	543	-10,997
Human Health and Disease	3,945	3,929	3,604	-325
Data Management Center for the Mapping Centers	2,915	2,838	3,000	162
Technology Development in Epigenetics	5,862	3,499	3,353	-146
Discovery of Novel Epigenetic Marks in Mammalian Cells	0	0	0	0
Subtotal, Epigenomics	23,769	21,806	10,500	-11,306
Human Microbiome				
Sequence a Reference Set of Genomes	3,028	3,798	0	-3,798
Demonstration Projects	12,269	11,755	766	-10,989
New Tools and Technologies for Metagenomic Analyses	6,204	4,094	0	-4,094
Data Coordination	2,601	3,072	0	-3,072
Resource Repository for Materials & Reagents	0	0	0	0
ELSI Studies Unique to HMP	497	0	0	0
HMP Workshops	765	1,019	441	-578
Subtotal, Human Microbiome	25,364	23,738	1,207	-22,531
Increasing Metabolomics Research Capacity				
Comprehensive Metabolomics Research Cores	0	6,435	12,435	6,000
Training in Metabolomics	0	4,316	4,316	0
Metabolomics Technology Development	0	2,015	2,015	0
Metabolomics Reference Standards Synthesis	0	54	2,083	2,029
Metabolomics Data Sharing Cloud	0	2,055	1,515	-540
Subtotal, Increasing Metabolomics Research Capacity	0	14,875	22,364	7,489
Single Cell Analysis				
Pilot Studies to evaluate cellular heterogeneity	0	4,185	4,075	-110
Exceptionally Innovative Tools and Technologies for Single Cell Analysis	0	4,065	4,075	10
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	0	4,500	7,500	3,000
Single Cell Analysis Challenges	0	0	0	0
Subtotal, Single Cell Analysis	0	12,750	15,650	2,900
Building Blocks, Biological Pathways and Networks				
National Technology Centers & Metabolomics Development	10,141	10,359	10,266	-93
Nanomedicine				
Nanomedicine Development Centers	16,000	16,000	16,000	0
Protein Capture				
Antigen Production	987	896	0	-896
Production of anti-TF Antibodies	6,450	6,455	3,875	-2,580
New Reagent Technology Development and Piloting	5,830	5,049	5,125	76
Subtotal, Protein Capture	13,267	12,400	9,000	-3,400
Structural Biology				
Membrane Protein Production	8,513	8,000	8,000	0
Knockout Mouse Phenotyping Program				
Production, Characterization, and Cryopreservation	6,428	6,443	6,449	6
Phenotyping and Data Release	4,431	4,251	4,451	200
Data Coordination	141	306	100	-206
Subtotal, Knockout Mouse Phenotyping Program	11,000	11,000	11,000	0
Science of Behavior Change				
Mechanisms of Change	4,724	5,458	4,545	-913
Bioinformatics and Computational Biology				
National Centers for Biomedical Computing	13,231	8,179	3,333	-4,846
Genotype-Tissue Expression (GTEx) Resources				
Genotype-Tissue Expression (GTEx) Resources	3,120	22,473	26,000	3,527

Title of Initiative	FY 2011 Actual	FY 2012 Enacted	FY 2013 PB	Change vs. FY 2012
Health Economics				
Changing Incentives for Consumers, Insurers, and Providers	2,564	2,787	1,620	-1,167
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	856	2,716	6,726	4,010
Economics of Prevention	2,210	3,909	4,626	717
Data Infrastructure to Enable Research on Health Reform	0	2,551	51	-2,500
Subtotal, Health Economics	5,630	11,963	13,023	1,060
HMO Research Network Collaboratory				
NIH-HMORN Coordinating Center	273	2,225	2,225	0
Expansion Activities	0	5,075	10,625	5,550
Subtotal, HMO Research Network Collaboratory	273	7,300	12,850	5,550
Library of Integrated Network-Based Cellular Signatures (LINCS)				
Large-Scale Production of Perturbation-Induced Gene Expression	5,347	5,305	6,000	695
New Laboratory-Based Technology Development	2,835	2,804	0	-2,804
Computational Tool Development and Integrative Data Analysis	1,537	1,426	0	-1,426
Integration of Existing Datasets	291	865	0	-865
Subtotal, Library of Integrated Network-Based Cellular Signatures (LINCS)	10,010	10,400	6,000	-4,400
Molecular Libraries and Imaging				
Creation of NIH Bioactive Small Molecule Library & Screening Centers	88,490	84,748	34,075	-50,673
Cheminformatics	3,900	500	0	-500
Technology Development	10,345	6,252	0	-6,252
Imaging Probe Database	500	250	0	-250
Core Synthesis Facility to Produce Imaging Probes	0	0	0	0
Subtotal, Molecular Libraries and Imaging	103,235	91,750	34,075	-57,675
NIH Center for Regenerative Medicine (NCRM)				
NIH Center for Regenerative Medicine (NCRM)	4,000	8,000	8,000	0
Re-engineering the Clinical Research Enterprise				
Clinical Research Policy Analysis and Coordination	0	0	0	0
Translational Research Core Services	15,102	11,000	5,000	-6,000
Dynamic Assessment of Patient-Reported Chronic Disease Outcomes	8,214	8,848	4,273	-4,575
Enhance Clinical Research Training via the National Multi-disciplinary CR Career Development Program and CRTP and MSTP Expansions	880	1,100	1,100	0
Clinical and Translational Science Awards	22,703	0	0	0
Subtotal, Re-engineering the Clinical Research Enterprise	46,899	20,948	10,373	-10,575
Gulf Long-term Follow-up of Workers Study				
Gulf Long-term Follow-up of Workers Study	4,251	2,500	2,500	0
Regulatory Science				
Advancing Regulatory Science Through Novel Research and Science-Based Technologies	2,697	2,515	0	-2,515
Microphysiological Systems for Drug Efficacy and Toxicity Testing	0	14,350	0	-14,350
Subtotal, Regulatory Science	2,697	16,865	0	-16,865
High-Risk Research				
NIH Director's Pioneer Awards	35,169	36,775	33,426	-3,349
NIH Director's New Innovator Awards	96,766	80,263	80,000	-263
Transformative Research Projects (TR01)	55,891	71,153	84,681	13,528
NIH Director's Early Independence Award Program	3,965	8,115	12,342	4,227
Subtotal, High-Risk Research	191,791	196,306	210,449	14,143
Global Health				
Medical Education Partnership Initiative (MEPI)	3,000	3,000	3,000	0
Human Heredity and Health in Africa (H3Africa)	223	5,943	6,291	348
Subtotal, Global Health	3,223	8,943	9,291	348
Interdisciplinary Research				
Interdisciplinary Research Centers	41,333	204	0	-204
Interdisciplinary Research Training Initiative	0	0	0	0
Innovation in Interdisciplinary Technology and Methods	0	0	0	0
Subtotal, Interdisciplinary Research	41,333	204	0	-204
Strategic Planning Funds	550	2,713	2,594	-119
Subtotal Common Fund	543,021	544,930	447,020	-97,910
New Initiatives in Common Fund	**0**	**0**	**97,910**	**97,910**
Total Common Fund	**543,021**	**544,930**	**544,930**	**0**

Justification of Budget Request

Common Fund

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

Budget Authority:

	FY 2011 Appropriation	FY 2012 Enacted	FY 2013 President's Budget	FY 2013 +/-FY 2012
BA	$543,021,000	$544,930,000	$544,930,000	$0
FTE	0	0	0	0

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

Director's Overview

The 2006 NIH Reform Act calls for the NIH Common Fund to support important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from additional research that involves collaboration between two or more national research institutes or national centers, or would otherwise benefit from strategic coordination and planning. To this end, the Common Fund programs tackle critical challenges in biomedical research and translation which affect many diseases or conditions, or which broadly relate to human health. These programs represent strategic investments aimed at solving problems or building resources to catalyze research throughout the entire biomedical research enterprise

Fostering innovation is a theme throughout the Common Fund. While this is an explicit goal of the High Risk/High Reward set of initiatives, it is an overarching goal of all of the programs. This investment in innovation is paying off economically, as well as scientifically, with patent applications, commercialization of technologies, and growth of new sectors in biomedical research. An Outcome Evaluation of the Pioneer Initiative revealed that three of the 22 awardees from the first two years of the initiative have applied for patents emanating from their Pioneer research, and a fourth has licensed his technology for commercialization. The Rapid Access to Intervention Development (RAID) program has led to 11 Investigational New Drugs, five of which have been licensed to companies for further development. The Molecular Libraries program has also led to many patent applications, and one molecule discovered through this program is now being tested in a clinical trial. This program has also contributed to a culture change in academic research by enabling all investigators to have access to chemical screening facilities equivalent to those of the pharmaceutical industry. Molecular screening centers have proliferated beyond the Common Fund set of centers, such that a 2010 evaluation indicated that 48 centers outside the Common Fund programs exist. This exemplifies how Common Fund programs can have significant impact beyond the immediate boundaries of its awards.

The Common Fund now supports over 20 programs. Most of these programs consist of a series of integrated initiatives that collectively address a set of goals that aim to transform the way research is conducted, the way that health and disease are understood, and/or the way that diseases are diagnosed or treated. Each of these programs is intended to be supported through the Common Fund for no more than ten years. At the completion of each program, the tools/technologies/data produced by the program remain available for use by the community at large, and/or, the infrastructure that the Common Fund has built transitions to other sources of support for maintenance. An exception to this ten-year limit is the High Risk/High Reward program, the only goal of which is to provide unique opportunities for innovative, ground-breaking research. Individual initiatives within this program will continue as long as they prove useful in allowing investigators to conduct pioneering research that would not be likely to be supported elsewhere at the NIH.

As the mature programs approach their last year of support through the Common Fund, the NIH has the opportunity to develop new programs which will take advantage of extraordinary opportunities that have arisen in the past few years. While some of these new Common Fund programs address fundamental biological questions and problems that have never been able to be addressed before, others take advantage of new technologies so that they may be exploited in the clinic or in translational research.

New Common Fund programs result from a planning process that engages the community at large to identify opportunities where strategic investments by the Common Fund can have a high impact. The selection of program areas to be supported by the Common Fund is based on input from this process, on input from the NIH Institute and Center Directors, and on alignment with the priorities of the NIH Director as described in the "Summary of the NIH Director's Themes" section. As a result, the diverse group of Common Fund programs includes investments in the cutting edges of basic research, technology development, translational sciences, and young investigators are specifically supported. The Common Fund strategic planning process has also resulted in the development of programs in the behavioral and social sciences, resulting in a well-rounded portfolio of programs that support the entire NIH community.

Each of the programs described below therefore represents a trans-NIH response to extraordinary opportunities. These opportunities, defined through broad community input, are in some cases the result of recent advances that allow rapid progress to be made via strategic investments. In other cases, they are opportunities for investigators to work collectively to overcome substantial hurdles or challenges so that future research will be made more efficient and effective. Each has defined goals, many of which involve substantial risk. Assessment of each program's utility and impact is critical and is therefore a focus for the Common Fund's Office of Strategic Coordination.

Overall Budget Policy: The FY 2013 President's Budget request for the Common Fund is $544.930 million, which represents no change from the FY 2012 Enacted level. The Common Fund will continue to support research consistent with the NIH Director's themes, and capitalize on the extraordinary opportunities available in FY 2013. As mature programs transition out of the Common Fund, new programs are being established through strategic planning activities that

identify cross-cutting challenges and emerging scientific opportunities where short-term investment can have a catalytic impact.

Justification Narrative

Theme 1: Investing in Basic Research

Investments in basic biomedical and behavioral research are a priority for the Common Fund, since these investments underlie the development of new therapeutic and preventive strategies. A solid understanding of basic cellular, physiological, behavioral, and pathological mechanisms is required to develop new therapeutic approaches, yet substantial hurdles often slow the pace of discovery. Some of the programs below are designed to overcome these hurdles. Others take advantage of recent advances to push the boundaries of knowledge in whole new directions.

Epigenomics

Building from the Human Genome Project, the Common Fund Epigenomics Program is intended to provide core data, tools, and technologies to explore mechanisms by which the human genome is regulated. It includes a series of complementary initiatives to generate the research tools, technologies, and infrastructure needed to accelerate our understanding of the role of epigenomics in human health and disease. Epigenetics focuses on processes that regulate how and when certain genes are turned on and turned off, while epigenomics pertains to the analysis of epigenetic changes across all of the genes in a cell. Some human diseases, such as cancer, are known to involve epigenetic changes; however, the role of epigenetics in other diseases is largely unknown and is difficult to study because researchers lack the tools to efficiently detect and correlate changes in the epigenome to specific diseases or health conditions. The Common Fund Epigenomics Program supports four initiatives, described below.

First, the Reference Epigenome Mapping Centers, funded through FY 2012, are focused on developing maps of epigenetic changes in specific cell types that can be used to identify epigenomic changes that underlie biology and disease, and may be targeted in new therapeutics. To date, the researchers have identified a core set of epigenomic changes in 25 different cell and tissue types that represent “reference maps” of non-diseased cells. By comparing reference maps to epigenomic maps of diseased cells, researchers are able to pinpoint specific parts of the genome and epigenomic changes that correlate with disease. Data generated by the Centers are standardized and made publicly available by the Epigenomics Data Analysis and Coordination Center as a way to stimulate other researchers to analyze and use the data in follow-up studies.

Two other initiatives support projects on Technology Development in Epigenetics and on the Epigenomics of Human Health and Disease, to determine how or whether epigenomic changes correlate with disease. A fourth initiative, focused on Discovery of Novel Epigenetic Marks in Mammalian Cells, was completed in FY 2010.

Budget Policy: The FY 2013 President's Budget request of $10.500 million for the Epigenomics program represents a decrease of $11.306 million, or 51.85 percent less than the FY 2012 Enacted level. This decrease is due to the planned completion of the Reference Epigenome Mapping Centers. The epigenomics reference maps generated by the Centers will continue to be made available to the scientific community through NCBI.

Human Microbiome Project

Microbes such as bacteria, viruses, and fungi found naturally in the human body outnumber human cells by a factor of 10. Advances in sequencing technologies and computation have provided the opportunity to explore the relationship of these microbes to human health and disease in a way that has never before been possible. Many of the microbes living in our bodies are beneficial whereas others cause disease. Bacteria have been implicated in conditions as diverse as asthma, cancer and obesity; yet the great majority of bacteria and viruses that reside on and in people are unidentified and uncharacterized.

The Common Fund Human Microbiome Project (HMP) was launched in FY 2008 to leverage advances in high throughput genomic technologies to create a national resource of microbial sequencing data, analysis tools, and methods, to enable studies to identify and characterize hundreds of new human microbes, and to explore causal links between changes in the microbiome and disease. The program samples microbes from several different body sites from many different individuals to determine whether there is a common set of microbes, or so-called microbiome, that is shared by all people or whether each person has a unique microbiome.

To date, the HMP researchers have completed sequencing the genomes of 800 microbial strains, discovered more than 29,000 novel proteins encoded by the human microbiome, and initiated a series of disease-specific studies on obesity, dermatitis, Crohn's disease, inflammation, acne, and undiagnosed fever. The program investigators have sequenced and cataloged the microbiome samples, established links between the microbiome and disease, and developed technologies to isolate and identify unknown microbes.

In FY 2013, the program will provide the last year of support for a demonstration project that is examining the relationship between the skin microbiome and skin disease.

Budget Policy: The FY 2013 President's Budget request of $1.207 million for HMP represents a decrease of $22.531 million, or 94.92 percent less than the FY 2012 level. The estimated decrease in funding reflects the planned FY 2012 conclusion of all but one of the awards. This award had a late start, and therefore will continue into FY 2013. There is a possibility of supporting a second phase of the HMP program, pending an analysis of current needs.

Increasing Metabolomics Research Capacity (new in FY 2012)

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. 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 which 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. The field is also hampered by a lack of uniform standards for identifying unknown metabolites.

The Common Fund's Metabolomics program, initiated in FY 2012, 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.

Budget Policy: The FY 2013 President's Budget request of $22.36 million for the Metabolomics program represents an increase of $7.489 million, or 50.35 percent more than the FY 2012 Enacted level. The increased level of funding will be used to support new awards for Comprehensive Metabolomics Research Cores and an expansion of the Metabolomics Reference Standards Synthesis initiative.

Program Portrait: Increasing Metabolomics Research Capacity

FY 2012 Level: $14.9 million
FY 2013 Level: $22.4 million
Difference: +$07.5 million

Metabolites are the output of biological processes, and when studied collectively, provide a wealth of information about nutrition, environmental insult, infection, health, and disease status. Current technologies allow researchers to identify "fingerprints" or molecular profiles of metabolites that can be used for disease diagnosis, progression, and response to treatment. They are limited in their ability to pinpoint specific metabolites and pathways that, if known, could be targeted in treatment. Next generation technologies are needed to enhance the sensitivity and speed with which specific elements of the cellular metabolome can be identified and quantified. In response, the Common Fund's Metabolomics program was created to increase national capacity in metabolomics, bringing it on par with genomics and proteomics, by providing high quality measurement tools, data, standards, and training of the biomedical workforce needed to catalyze its use in scientific discovery and clinical practice. The program goals are to:

- Establish comprehensive metabolomics resource cores by expanding existing metabolomics resources by adding and improving instrumentation, increasing faculty expertise, and developing new training programs to meet the need for expertise;
- Increase the workforce of investigators with metabolomics expertise;
- Identify and address current limitations in metabolomics technologies so they can be easily and widely adapted by multiple laboratories; and,
- Create a repertoire of chemically-identifiable metabolites to serve as analytical standards for the metabolomics community.

Single Cell Analysis (new in FY 2012)

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, initiated through the Common Fund in FY 2012, seeks to overcome the scientific and technological hurdles to understanding how cells vary normally and how they respond to their microenvironment, both in isolation and within populations of tissues and networks.

Budget Policy: The FY 2013 President's Budget request of $15.650 million for the Single Cell Analysis program represents an increase of $2.900 million, or 22.75 percent more than the FY 2012 Enacted level. The increased level of funding will be used to support expansion of the initiatiave to Accelerate the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level.

Program Portrait: Single Cell Analysis

FY 2012 Level: $12.8 million
FY 2013 Level: $15.7 million
Difference: +$02.9 million

The ability to study single cells in isolation has eluded researchers for decades, yet differences in the way a cell behaves in isolation versus in a population can have profound effects on the health and function of tissues and organs. Most biological experiments are performed on groups of cells because, until recently, it was thought that all cells of a particular "type" are identical. New findings show that individual cells within the same population may function very differently. Traditional approaches to study cells based on analyses of populations can obscure these crucial differences. The Common Fund's Single Cell Analysis program aims to accelerate the discovery, development, and translation of innovative technologies and approaches to study single cells in isolation and within populations in an effort to uncover fundamental biological principles and ultimately improve the detection and treatment of disease. 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 goals of the program are to:

- Use gene expression to evaluate cell-to-cell variation within a population and define molecular fingerprints or profiles of specific cell types;
- Develop new tools and technologies to catalyze studies of single cells; and,
- Engage the biomedical research community in identifying roadblocks and opportunities to accelerate discovery and synergize ongoing efforts.

Building Blocks, Pathways, and Networks

The basic building blocks of the human body, from individual genes to entire organs, work together to promote normal development and sustain health. This amazing feature of biological systems is accomplished mainly through ever-changing relationships between the proteins that make up biological pathways. Understanding how these pathways are interconnected and maintained, how they can become disturbed, and what might be done to restore disturbed pathways to their normal functions is key to understanding health and disease. Although scientists can currently study interactions between proteins within cells, their ability to do this is equivalent to taking a snapshot – looking at a single, isolated moment in time.

The National Technology Centers for Networks and Pathways (TCNP) initiative supports the development of new technologies to help researchers view dynamic events, such as protein-protein interactions, in cells to better understand how these processes work under normal conditions and in disease. The centers serve as an important overall resource for NIH-supported investigators by promoting collaboration amongst biomedical researchers and expediting the transfer of new technologies to other laboratories.

Common Fund support ends in FY 2013, with the technologies created through this program being adopted by researchers supported by the NIH Institutes/Centers (ICs) to solve complex biological problems and better understand dynamic cellular processes that contribute to health and disease.

Budget Policy: The FY 2013 President' Budget request of $10.266 million for the Building Blocks, Pathways, and Networks program represents a decrease of $0.930 million, or 0.89 percent less than the FY 2012 Enacted level. FY 2013 funds will be used for the continued development of new technology at the TCNPs and dissemination of these research tools to scientists supported by many of the individual NIH IC, with the small decrease in funding reflecting normal year-to-year cost variability in the awards. FY 2013 will be the final year for Common Fund support of this program.

Nanomedicine

Nanotechnology, the study and manipulation of molecules less than 100 nanometers in size, holds tremendous promise for use in diagnosing and treating disease. The goal of this program is to use nanotechnology to understand and manipulate biological processes in a cell for specific medical purposes. For example, nanoscale protein folding machines are being developed for the treatment of diseases such as Alzheimer's and Huntington's, where misfolded proteins are thought to play a role.

In FY 2005, a network of eight Nanomedicine Centers at academic institutions across the country was established. The program underwent an extensive review in 2009 to inform the next phase, which is focusing on making the nanobiological structures developed in first phase more clinically useful. The second phase of the program constitutes a more focused effort involving a smaller number of centers to maximize the opportunity for development of potential new clinical applications. This program uses the Flexible Research Authority or Other Transaction Mechanism, which will continue in FY 2013.

Budget Policy: The FY 2013 President's Budget request of $16.000 million for the Nanomedicine program represents no change from the FY 2012 Enacted level. The estimated funding reflects ongoing support of the nanomedicine development centers that are currently funded. Funds in this second phase of the program are specifically targeted at using the nanobiological structures developed in the first phase for novel clinical applications.

Protein Capture

This program is designed to stimulate basic research discovery and clinical translation through the development and dissemination of molecules that bind and "capture" proteins. A renewable resource of protein capture reagents is greatly needed by researchers for protein isolation, high-throughput assays, diagnostics, and biomarker development. To have the maximum benefit, such reagents need to be high quality, affordable, and reliable. This program provides support for the development of new technologies and for the provision of monoclonal antibodies, which have been used historically for protein capture but can be difficult to generate.

Ongoing initiatives in FY 2013 are aimed at producing antibodies for a special class of proteins called transcription factors, as well as testing the quality, utility, cost, and ability to scale-up the production of alternative protein capture reagents.

Budget Policy: The FY 2013 President's Budget request of $9.000 million for the Protein Capture program represents a decrease of $3.400 million, or 27.42 percent less than the FY 2012 Enacted level. This decrease reflects the completion of an initiative to produce transcription factor antigens for making monoclonal and recombinant anti-body protein capture reagents. On-going anti-body production initiatives are directly building upon the transcription factor initiative, with the goal of optimizing and scaling-up production of anti-transcription factor protein capture reagents to build a community resource.

Structural Biology

Proteins embedded in the cell surface membrane represent a large class of targets for drugs, since they may be more accessible to drugs than proteins inside the cell, and since they regulate many fundamentally important cellular processes. However, these proteins are difficult to purify and characterize, and this makes the design of drugs that bind them difficult. The Structural Biology program is addressing a critical hurdle to understanding how membrane-bound proteins function normally and can be targeted in disease therapy by creating new methods and approaches for producing membrane-bound proteins in sufficient quantity and quality for use in research studies. The ability to produce membrane-bound proteins to meet this need has led to the discovery of structures for proteins involved in HIV, cancer, neurological disorders, and more.

In FY 2009, the Structural Biology Centers began a second five-year phase of support through the Common Fund. The second five years of this program are intended to discover innovative methods for membrane protein production as well as structure determination, including methodologies that can be applied to protein complexes made up of multiple components, such as different types of proteins..

FY 2013 is the last year of funding, with the expectation that IC-funded scientists will continue to use the methods and approaches developed by the program.

Budget Policy: The FY 2013 President's Budget request of $8.000 million for the Structural Biology program represents no change from the FY 2012 Enacted level. FY 2013 funds will be used for the continued development of approaches to membrane protein production and structure determination, with a particular focus on protein complexes.

Knockout Mouse Phenotyping Program

Recognizing the value and utility of a readily-accessible, genome-wide collection of mouse mutants as very important in determining how mammalian genes function, several international programs were launched in 2006 to develop mutant mouse strains. Collectively, these programs have created more than 8,000 prototype knockout mice. The Common Fund program builds upon this resource by expanding the efforts to characterize the mutant strains. The data are being made rapidly available to the entire research community through an internationally-coordinated data coordinating center as a way to catalyze additional analyses of how specific genes contribute to health and disease conditions. Some of the genes to be characterized are expected to suggest novel drug targets and increase understanding of genetic pathways that drugs may affect.

Budget Policy: The FY 2013 President's Budget request of $11.000 million for the Knockout Mouse Phenotyping program represents no change from the FY 2012 Enacted level. FY 2013 funds will continue to support the characterization of mutant strains, and the dissemination of this data to the broader research community.

Science of Behavior Change

Human behaviors contribute enormously to health and disease, and most people are aware that over-eating, smoking, drug and alcohol abuse, failing to exercise, etc. represent unhealthy behaviors. However, it can be very difficult to change one's behavior and/or to motivate behavior change in others. The Common Fund Science of Behavior Change program is intended to improve our understanding of human behavior change across a broad range of health-related behaviors. This is being accomplished by supporting basic research to improve our understanding of human motivation and the maintenance of behavior change across multiple diseases and conditions, and then using this knowledge to develop more effective and economical behavioral interventions.

Budget Policy: The FY 2013 President's Budget request of $4.545 million for the Science of Behavior Change program represents a decrease of $0.913 million, or 16.73 percent less than the FY 2012 Enacted level. The decrease in funding is due to the completion of one award in FY 2012.

Theme 2: Accelerating Discovery Through Technology

Advances in technologies often precede significant advances in other arenas, so Technology Development is often emphasized in Common Fund programs. Most of the programs described above have a Technology Development component. These technologies are "opportunity generators" which, if developed within the context of active research, can propel the research forward with ever-increasing efficiency. For example, a technology developed in the Epigenomics program allows the efficient and inexpensive identification of regulatory changes to DNA in specific regions of the chromosome that are of interest. This technology has been cited in over 100 other publications as other investigators adopt it for their own studies.

Since technology development can be difficult to find support for elsewhere at the NIH, and yet can have exceptionally high impact, it has frequently been a focus for investigators funded via the Common Fund High Risk/High Reward Program. A technology called "optogenetics," was developed through the Pioneer program and allows the precise control of neurons in the brain of living animals using light. This has revolutionized the ability to study neural networks and brain function, and this technology is now being extended to other tissues.

In addition to these programs which address technology development, but do not have it as an explicit goal, the **Bioinformatics and Computational Biology Program** addresses technology development in the ever-expanding realm of informatics and computation. In an age where the ability to manage and organize large amounts of varied biomedical data is necessary for research, the need for informatics tools is critical. These tools must be tailored to handle the large amounts of data and use engineering systems that are adapted to handle the type of data that are generated from studies of biological systems. The Bioinformatics and Computational Biology program, which supports the National Centers for Biomedical Computing (NCBCs), was funded beginning in 2003-2004 and completed its first phase of funding through the Common Fund in 2008.

The first phase established the utility of a network of integrated centers that collectively addressed a broad range of biological problems that revolved as the tools were developed. In the second phase of the program, which ends in 2013, the network of centers will transition to NIH's Institutes and Centers (ICs) for support, and function as core resources for the development of novel software and computational tools that address IC-specific problems.

Budget Policy: The FY 2013 President's Budget request of $3.333 million for NCBCs represents a decrease of $4.846 million, or 59.25 percent less than the FY 2012 Enacted level. The estimated decrease is consistent with the natural transition of NCBC support from the Common Fund to the ICs as described in the original NCBC plan.

Theme 3: Advancing Translational Sciences

As with Technology Development, the support for translational science is an underlying theme in some of the Basic Science Programs. For example, the Structural Biology of Membrane Proteins Program is intended to support the identification of new drug targets and aid in drug design. However, the programs below have as a specific focus the development of resources or tools that

will be broadly useful for investigators who seek to establish new drug targets and/or determine disease pathways for which drugs may be developed.

Genotype-Tissue Expression (GTEx)

Although genome-wide studies are an effective way to identify specific genes that may be associated with a disease, many diseases involve changes in DNA that lie outside of a specific gene region, making it difficult to determine how the change leads to disease. The Genotype-Tissue Expression (GTEx) project provides the scientific community with data on how DNA variation correlates with variation in gene activity levels. This is intended to strengthen the power of genome-wide association studies to identify potential new gene targets for therapies.

The GTEx project was initiated in FY 2010 as a two-year pilot to test the feasibility of collecting high-quality RNA and DNA from multiple tissues from approximately 160 donors identified through autopsy or organ transplant. The project is also exploring ethical, legal, and social issues raised by the research which can inform other genomics programs. Support is provided for new statistical methods, creation of a database of genetic and clinical data generated by the program and obtained from other sources, and a new tissue repository resources intended to stimulate new studies to identify genetic contributions to health and disease.

Budget Policy: The FY 2013 President's Budget request of $26.000 million for the GTEx program represents an increase of $3.527 million, or 15.69 percent more than the FY 2012 Enacted level. In FY 2012, this program underwent a transition from the feasibility stage to a full scale program. The increased funding level in FY 2013 will be used to scaleup the number and types of samples collected, as well as the development of new methods to analyze the genetic data; the storage, collection, and distribution of tissues; and the population of the database to disseminate information. FY 2013 funds will also support continued research on the ethical, legal, and social implications of the research.

Health Economics

This program addresses questions of how patients and healthcare providers respond to various incentives, and how their responses influence the cost of healthcare. This is intended to lead to recommendations for more efficient and effective healthcare policies and practices. In FY 2011, the program initiated a series of developmental research projects to identify and develop approaches to improve health and increase efficiency in delivery of healthcare. Common Fund support continues in FY 2013 for initiatives investigating the economics of prevention strategies, costs and outcomes of healthcare delivery, and improvement of data resources for the health economics research community.

Budget Policy: The FY 2013 President's Budget request of $13.023 million for the Health Economics program represents an increase of $1.106 million, or 8.86 percent more than the FY 2012 Enacted level. The increased level of funding will be used to support expansion of the Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare initiative, which fosters research on scientific questions about the effects on costs and outcomes of changes in the way health care is organized and delivered.

Health Care Systems (HCS) Collaboratory

In an effort to leverage the resources and expertise of networks of healthcare organizations for the benefit of research, the Common Fund launched this program, which provides support for improved informatics and other networking resources in health care delivery organizations with significant research interests. Although initially intended to support an existing network of HMOs, the funding opportunity was later opened to any network of healthcare delivery organizations, since it became apparent that non-HMO networks may be equally suited to the task of coordinating large patient populations and investigators. A coordinating center and a set of demonstration projects were funded in FY 2012. The goal is to develop capacity in the healthcare delivery system for networking among providers for the benefit of research. This capacity is being tested within the context of practical clinical trials, with plans to pilot networking mechanisms for mega-epidemiology studies beginning in FY 2013.

Budget Policy: The FY 2013 President's Budget request of $12.850 million for the HCS Collaboratory program represents an increase of $5.550 million, or 76.02 percent more than the FY 2012 Enacted level. This estimated increase will support a second round of demonstration projects focused on epidemiology studies that require large patient cohorts to test the ability of the HCS Collaboratory to identify and recruit these patients.

Library of Integrated Network-Based Cellular Signatures (LINCS)

The LINCS program aims to develop a resource "library" of molecular signatures -- gene expression and other cellular traits, as well as new data analysis and computational tools, to understand how biological pathways interact and change or respond to genetic and environmental stressors, or to drugs. The molecular signatures represent the response that different types of cells elicit when exposed to various perturbing agents, including small interfering RNAs (siRNAs), which are short RNA molecules that can inhibit the expression of specific genes, and small bioactive molecules.

Since its inception, the program's researchers have developed molecular signatures in thousands of cell types and have created novel approaches to store, analyze, and integrate different types of large, complex data sets. The approach has led to the discovery of new relationships between compounds that bind and inhibit specific receptors in cells, providing insights into cell-to-cell variability and how cell function can be targeted in new therapies.

The LINCS program began in FY 2010 as a three-year pilot to develop molecular and cellular signatures for specific perturbing agents, create a database and standards, and develop new tools and assays. Common Fund support for this first phase of the program ends in FY 2012. A review of pilot phase activities will inform the need for a second phase, to start in FY 2013.

Budget Policy: The FY 2013 Pressident's Budget request of $6.000 million for the LINCS program represents a decrease of $4.400 million, or 42.31 percent less than the FY 2012 Enacted level. This estimated decrease reflects the end of the first phase of the program in FY 2012. In FY 2013, data generated through the first phase will be analyzed using computational tools

developed by the program. This analysis will inform the need and feasibility for a second phase, which would begin in FY 2014.

Molecular Libraries and Imaging

For years, the pharmaceutical industry has used a process known as high-throughput screening (HTS) to identify new small molecule probes that can be used for drug development and to study biological processes involved in disease. Prior to the launch of the Molecular Libraries and Imaging Program, HTS capabilities were not available to most academic researchers. This program provides public sector biomedical researchers much needed access to HTS approaches to develop small molecule probes. Data about the structure and function of the probes are deposited in a free, on-line public database called PubChem (http://pubchem.ncbi.nlm.nih.gov/), which was designed and implemented by the Molecular Libraries and Imaging program.

The program provides a boost to economic growth and scientific advancement, resulting in many new patent applications for small molecule probes and methods, stimulating the creation of new molecular screening centers outside of the Molecular Libraries and Imaging program, and 87 compounds into pre-clinical tests as new leads for drug development.

FY 2013 is the final year of support for this program from the Common Fund. However, the robust small molecule screening enterprise which the Common Fund has helped to create will continue via other sources of support. The National Library of Medicine is continuing the PubChem database as an on-going resource for the community; the National Cancer Institute supports small molecule screening efforts through a dedicated program, and other ICs support individual screening centers as well. Support for screening is also provided through investigator-initiated applications from investigators who collaborate with screening centers for specific questions.

Budget Policy: The FY 2013 President's Budget request of $34.075 million for the Molecular Libraries and Imaging program represents a decrease of $57.675 million, or 62.86 percent less than the FY 2012 Enacted level. This estimated reduction is due to the transition of the Molecular Libraries and Imaging program from Common Fund support to IC support, as planned. Common Fund support for the chemical diversity initiative ends in FY 2012, with support for the synthesis of novel chemicals transitioning to the National Institute of General Medical Sciences. In FY 2013, the National Library of Medicine will support the PubChem database and NCATS will support the NIH Chemical Genomics Center. In FY 2013, Common Fund support will allow extramural centers to complete screening projects initiated in FY 2012. New screening projects will be funded as collaborations with investigator initiated research supported by the ICs, solicited in part through program announcements released in the fall of 2011. Additionally, in FY 2013, the Common Fund will support the small molecule repository and the cheminformatics initiative.

NIH Center for Regenerative Medicine (NIH CRM)

This program, initiated in FY 2010 and housed in the NIH Intramural Research Program (IRP), provides a national resource for stem cell science that is specifically focused on accelerating the development of new medical applications and cell therapies. The Center is designed to help the biomedical community work through the procedural and regulatory issues that hamper the use of stem cells in medicine; develop induced pluripotent stem cells from a genetically-diverse set of patients, and make these cells available to the community; create standards to streamline stem cell development on a national and international scale; and build a cadre of intramural investigators working to advance the field of regenerative medicine. In FY 2013, the Center will establish induced pluripotent stem cells (iPSCs) from healthy and sick patients of diverse genetic backgrounds and will make these cells and differentiated derivatives of them available to the community to stimulate new clinical studies. These cells may also be incorporated into the "human-on-a-chip" platform to be developed through the Regulatory Science Program (see below) used to conduct projects that address common hurdles in the development and use of cell therapies in clinical practices.

Budget Policy: The FY 2013 President's Budget request of $8.000 million for NIH CRM represents no change from the FY 2012 Enacted level. FY 2013 funds will be used to continue to build a stem cell resource for the scientific community, as well as to support intramural investigators piloting projects on clinical applications of iPSCs.

Re-engineering the Clinical Research Enterprise

This program seeks to enhance the efficiency and effectiveness of clinical research. The initiatives within Re-engineering the Clinical Research Enterprise have strived to transform the entire system of clinical research in order to fulfill the potential of modern medicine. The goal of these initiatives has been to foster the creation of new partnerships and a higher level of institutional integration in order to improve the working relationships among the numerous entities that are part of the clinical research process. All but two of the initiatives have ended or transitioned to other sources of support.

Translational Research Core Services: NIH Rapid Access to Intervention Development (RAID) (Renamed for FY 2012: Bridging Interventional Development Gaps or BrIDGs)

Many new promising therapeutics encounter roadblocks during clinical development. Especially vulnerable are therapeutic approaches that involve high risk ideas or therapies for uncommon disorders that cannot attract private sector investment. Where private sector support for drug development is limited or not available, the NIH-RAID/BrIDGs program can help fill the gap and reduce some of the common barriers that block progress of therapeutic discoveries from the bench to the bedside. BrIDGs is not a grant program. Instead, it makes available critical resources that are needed to develop new therapeutic agents, including ones that can generate bulk amounts of the drug candidate or test its stability or toxic effects. It also provides researchers with access to experts at the Food and Drug Administration on document preparation and submission. The investments are

paying-off with several new Investigational New Drugs, some of which have been licensed for commercialization. FY 2013 is the last year of Common Fund support for this program.

Budget Policy: The FY 2013 President's Budget request of $5.000 million for the BrIDGs program represents a decrease of $6.000 million, or 54.55 percent less than the FY 2012 Enacted level. This reduced funding level will support the completion of projects initiated in FY 2012. New projects for this program will be solicited via funding opportunity announcements through NCATS.

Dynamic Assessment of Patient-Reported Chronic Disease Outcomes: Patient-Reported Outcomes Measurements Information System (PROMIS)

PROMIS is a revolutionary effort to enhance the precision of measures of patient-reported symptoms and function or outcomes. Patient-reported outcomes are essential for proper medical care but are often difficult to collect reliably. The PROMIS program has developed an interactive, computerized testing system that accurately reports patient-reported outcomes by adapting questions to the responses of each individual patient. This standardized measurement tool will increase the comparability of studies while reducing the reporting burden on patients. The initial PROMIS network of seven research sites and one coordinating center developed questionnaires tailored to a number of symptoms of chronic diseases and conditions including anxiety, pain, and fatigue. In FY 2009, the second phase of the PROMIS program began with an expansion of the network to 14 research sites and three supporting centers to extend the PROMIS system to several new areas with an emphasis on questionnaires tailored to children, minorities, women, and the underserved.

Budget Policy: The FY 2013 President's Budget request of $4.273 million for this program represents a decrease of $4.575 million or 51.71 percent less than the FY 2012 Enacted level. This estimated funding reflects bridge support for the PROMIS program as it transitions to IC support in FY 2014. In FY 2013, PROMIS will continue to validate its questionnaires in clinical trials, further establishing the utility of these new tools.

Clinical Research Training Program

The Common Fund supports the Clinical Research Training Program, which is a 12-month residential program that provides training for the next generation of clinician-scientists to learn about translational research, from the bench to the bedside, and back to the bench. The program is designed to attract the most creative, research-oriented medical and dental students, called "*fellows*", to the intramural NIH campus in Bethesda, Maryland. The fellows become engaged in a mentored clinical or translational research project in an area that matches their personal research interests and goals.

Budget Policy: The FY 2013 President's Budget request of $1.100 million for the Clinical Research Training program represents no change from the FY 2012 level. FY 2013 funds will continue to cultivate a pipeline of clinician-scientists by educating medical and dental students on the principles of clinical research and long-term career opportunities.

Clinical and Translational Science Awards (CTSAs)

The CTSA program was established through Common Fund support as an effort to is a unique and bold venture to restructure and improve the clinical research enterprise. The CTSA program is enabling researchers to provide and deliver new treatments more efficiently and quickly to patients. Common Fund support for this program has ended, with the final year of support being FY 2011. Funding and management have transitioned first to NCRR, and now to NCATS in FY 2013.

Budget Policy: The CTSA program will receive no funds from the Common Fund in FY 2013, which is consistent with FY 2012 Enacted level.

Gulf Long Term Follow-Up (GuLF) of Workers Study

The oil spill that resulted from the April 20, 2010 explosion on the Deepwater Horizon oil rig in the Gulf of Mexico contaminated the Gulf and has settled along the coastline and marshes of Alabama, Louisiana and Florida. In Dr. Collins' testimony before the Senate Subcommittee on Health, Committee on Energy and Commerce on June 15, 2010, the NIH Director pledged support from the Office of the Director and the NIH Common Fund for research into the environmental health hazards posed by the Gulf oil spill. The GuLF program, initiated with FY2010 funds, includes a prospective study of clean-up workers and toxicological studies. The NIH efforts for GuLF are coordinated and complemented with response efforts of other agencies and institutions working in the Gulf region. The study findings will not only advance our understanding of link between environmental hazards and health, but also make us better equipped to deal with future disasters.

Budget Policy: The FY 2013 President's Budget request of $2.500 million for the GuLF program represents no change from the FY 2012 Enacted level. This estimated budget level reflects the continuation of the prospective study of clean-up workers, including efforts to define biomarkers of chemical exposure in a subset of the study population, and toxicological studies.

Regulatory Science

The NIH and the U. S. Food and Drug Administration (FDA) have formed an inter-agency partnership to foster regulatory science, a specialized and inter-disciplinary area of biomedical research that serves to generate new knowledge and tools for assessing experimental therapies, preventions, and diagnostics. The broad goal of the Regulatory Science program, initiated in FY 2010, is to accelerate the development and use of new tools, standards, and approaches to develop products efficiently and to evaluate product safety, efficacy, and quality more effectively. The program expanded in FY 2012 to jump-start a specific, high priority challenge to develop a "human-on-a-chip" micro-platform containing artificial organ models to be used in a variety of regulatory and research situations, including the evaluation of toxicity and efficacy of new therapies. The program involves a new inter-agency collaboration between the NIH, FDA, and the Defense Advanced Research Projects Agency (DARPA). Begun through the Common Fund, the program transitions to NCATS beginning in FY 2013.

Budget Policy: The Regulatory Science program will receive no funds from the Common Fund in FY 2013, as all components will transition to NCATS support, and represents a decrease of $16.865 or 100 percent less than the FY 2012 Enacted level.

Theme 4: Encouraging New Investigators and New Ideas

Providing support for both highly creative researchers and potentially transformative ideas is the goal of several Common Fund programs, but the programs below specifically seek to invigorate and support the workforce so that innovation is encouraged and fostered, and so that the best and the brightest are engaged in biomedical research.

High-Risk High-Reward Investigator-Initiated Research

Research that aims to transform science is inherently difficult; if it was either obvious or easy, the need for transformation would not exist. A primary goal of the Common Fund is to provide opportunities for investigators to take risks when the potential impact is high, to think outside the box, and to try things that may not fare well in standard peer review, which relies on solid preliminary data to support proposed hypotheses. Although all of the Common Fund programs encourage risk-taking to overcome significant challenges in research, most of them involve designated funds for particular high risk objectives (such as clinical applications of nanobiology) or approaches (such as screening for new drugs or probes in the Molecular Libraries Program). However, four initiatives within the Common Fund foster innovation, risk-taking, and transformative research in any area of health research chosen by the investigators: the NIH Director's Pioneer Program, the NIH Director's New Innovator Program, the Transformative Research Projects program, and the NIH Director's Early Independence Award program. These initiatives represent complementary approaches to foster innovation and promote transformation.

An Outcome Evaluation of the Pioneer Initiative shows the investment is producing a high yield, with development of software, vaccines, patents, and commercialized products that are fueling collaboration and economic and scientific progress at the national and international level.

Two of these initiatives support early career-stage investigators specifically. The New Innovator initiative supports investigators who are within ten years of their terminal degree and who have tenure-track or equivalent research positions. Preliminary evaluation data indicate that these awardees are more likely to conduct research that is interdisciplinary and that crosses boundaries of individual ICs. Many of them have been recognized for exceptional creativity and innovation in other ways, such as through the receipt of Presidential Early Career Awards for Scientific Excellence (PECASE) or through the receipt of other Common Fund High Risk awards.

The Early Independence Awards program is designed specifically to invigorate the workforce by fostering independence of exceptional young scientists immediately after completion of their doctoral degrees. These awards, first issued in FY 2011, are being closely monitored by NIH staff to follow the impact of the awards on the career trajectories of the recipients. These awards are intended to foster innovation at a time in the investigators' lives when they may be expected to be the most creative and energetic. The receipt of these awards is therefore expected to put

them in an excellent position to obtain tenure-track or equivalent positions at the end of the award period.

The TR01 award is re-named the "NIH Director's Transformative Research Award" beginning in FY 2012 to emphasize that although investigator-initiated, these projects are expected to be different from traditional R01 awards. These awards provide unique opportunities for interdisciplinary, inter-IC projects that may require large budgets to address exceptionally high pay-off questions and that involve more risk than traditional IC-supported research.

Budget Policy: The FY 2013 budget estimate of $210.449 million for the High-Risk High-Reward program represents an increase of $14.143 million, or 7.20 percent more than the FY 2012 Enacted level. This estimated increase in funding is due to an expansion of the NIH Director's Early Independence Award program to support another cadre of exceptional young scientists in independent research positions, as well as an expansion of the Transformative Research Award program to support exceptionally innovative or unconventional research projects that have the potential to create or overturn fundamental paradigms.

Global Health

The NIH Common Fund Global Health Program is partnering with other NIH Institutes, Centers, and Offices as well as other federal agencies and the UK Wellcome Trust to support two initiatives that will expand research capacity in Africa, largely through the support of training and career development. The Medical Education Partnership Initiative was funded beginning in FY 2010 and is developing and strengthening models of medical education and building research and clinical capacity in countries of Sub-Saharan Africa that are part of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

The Common Fund investments leverage other sources of funds to train healthcare providers and researchers in non-AIDS areas of research. The Human Heredity and Health in Africa (H3Africa) initiative was funded beginning in FY 2010 and involves collaboration with the Wellcome Trust to build research capacity in Africa by supporting career development and training, informatics, and laboratory equipment to researchers studying the genetic and environmental contributions to health and disease. Both communicable and non-communicable diseases and conditions are being addressed through this initiative.

Budget Policy: The FY 2013 President's Budget request of $9.291 million for the Global Health program represents an increase of $0.348 million, or 3.89 percent more than the FY 2012 Enacted level. This estimated increase is due to an expansion of the H3Africa program to study the societal implications of the genetics research being conducted by the H3Africa initiative.

Interdisciplinary Research Consortia

A major focus of the NIH Common Fund has been to foster new modes of conducting research, with emphasis on the need for interdisciplinary approaches to address complex health problems. In FY 2007, the NIH awarded funds to nine Interdisciplinary Research Consortia to explore new ways to integrate different scientific disciplines to address critical health challenges. This

program piloted new award mechanisms for Interdisciplinary Research and Training as well as new methods of review for Interdisciplinary Research. It also resulted in a change of policy within the NIH to recognize multiple Principal Investigators on NIH grants and developed new methods of inter-IC award management. Common Fund support of this program ended in FY 2011, with the expectation that ICs will continue to use the award mechanisms as needed to support interdisciplinary approaches, working together to foster research that cuts across IC mission boundaries.

Budget Policy: The Interdisciplinary Research program will receive no funding in FY 2013 from the Common Fund and represents a decrease of $0.204 or 100 percent less than the FY 2012 Enacted level.

Strategic Planning and Evaluation Funds

A core mission of the NIH Common Fund is to foster collaboration, coordination, evaluation, and strategic planning activities across the NIH. New research opportunities that would benefit from Common Fund support are being envisioned for FY2013. To facilitate these planning efforts, the NIH Director is conducting a variety of activities to gather input from external and internal experts, public and private sector partners, and stakeholders. These planning efforts are being supported through the Common Fund Strategic Planning and Evaluation Funds. In addition, the Strategic Planning and Evaluation Funds will be used to evaluate programs that are coming to an end or that are in a pilot phase that is ending. Assessment of mature programs is critical for on-going management of the Common Fund, and assessment of the pilot programs will be important for the prioritization of a second phase relative to potential new programs.

Budget Policy: The FY 2013 President's Budget request of $2.594 million for Strategic Planning and Evaluation funds represents a decrease of $0.119 million, or 4.39 percent less than the FY 2012 Enacted level. These funds will be used to implement a strategic planning process for gathering bold and innovative ideas to address cross-cutting challenges and promote emerging scientific opportunities. Funds will also be used to evaluate and assess the outputs and outcomes of ongoing and mature programs.

Funds Available for New Programs

As mature initiatives end or transition out of the Common Fund, funds are available to address new challenges. The FY 2013 strategic planning process described above has produced new potential program areas where Common Fund investment could have a broad, transformative impact. These topics are continuing to be pursued through additional planning activities, and new programs will be selected in the Spring of 2012. The following topics are being pursued through additional planning activities to identify and understand ongoing work in each scientific area and to determine whether opportunities exist for the Common Fund to have a significant impact. New programs will be selected in the Spring of 2012:

- Disruptive Proteomics Technologies – The explosion of genomics research has been possible because of highly innovative technologies in gene sequencing. These technologies, which involve disruption of the DNA molecules and computational re-

assembly, have made genetic sequencing faster and cheaper, enabling increasing use in the clinic and all aspects of medical research. A potential new Common Fund program would seek to develop similar breakthrough technologies for the study of proteins.

- Exosomes – Exosomes are small membrane-bound droplets of material that are extruded from cells, along with cargos of large and small molecules. Recognized in recent years for their potential ability to deliver therapeutic compounds to targeted cell types and for their importance in cell-to-cell communication, exosomes are at the leading edge of mechanistic studies of basic cell biology and studies that seek to develop targeted drug delivery approaches. A potential new Common Fund program would take advantage of recent discoveries on exosomes to expand this field of research.

- Mobile Health – Recognition that cellular phones and other portable electronic devices have tremendous potential for health research has prompted the development of many devices and software applications that could be useful in the clinic. A potential Common Fund program would take advantage of these devices to establish, through public-private partnerships and partnerships with NIH ICs, studies that would validate existing devices in clinical settings. It might also develop improved software applications for use in recruiting and monitoring patients in clinical studies.

- A Synthetic Clinical Cohort for Human Genetic Studies – Recent genetic analyses of human populations have shown that healthy individuals harbor many gene mutations. Although some of these mutations may confer susceptibility toward disease, others may actually be protective. In most cases, the impact of the mutations is not clear. In order to understand the impact of mutations that occur naturally in the population, a large number of patients is needed for which genomic and medical information is available. Establishment of such a patient cohort would be prohibitively expensive. However, NIH wide, thousands of patients have been recruited for various studies, and genetic information is available for many of them. A potential Common Fund program would facilitate the combination of data from existing studies to enable broader utility of the data.

Budget Policy: In the FY 2013 President's Budget request, the Common Fund has $97.910 million available to support new programs. These new programs will be identified through the strategic planning process where targeted investment by the Common Fund can have a high impact.