DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund (CF)

FY 2014 Budget — Page No.

NATIONAL INSTITUTES OF HEALTH
Common Fund
Budget Mechanism - Total [1]
(Dollars in Thousands)

MECHANISM	FY 2012 Actual No.	FY 2012 Actual Amount	FY 2013 CR No.	FY 2013 CR Amount	FY 2014 PB No.	FY 2014 PB Amount	Change vs. FY 2012 No.	Change vs. FY 2012 Amount
Research Grants								
Research Projects								
Noncompeting	281	$149,193	291	$154,488	272	$151,154	-9	$1,961
Administrative Supplements	*58*	7,029	*73*	8,854	*58*	7,029	*0*	-
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	194	156,288	196	158,070	231	185,969	37	29,681
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	194	$156,288	196	$158,070	231	$185,969	37	$29,681
Subtotal, RPGs	475	$312,510	487	$321,412	503	$344,152	28	$31,642
SBIR/STTR	0	$0	0	$0	0	$0	0	$0
Research Project Grants	475	$312,510	487	$321,412	503	$344,152	28	$31,642
Research Centers								
Specialized/Comprehensive	36	$113,201	24	$75,832	21	$67,454	-15	-$45,747
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	14	7,788	4	2,329	4	2,268	-10	-5,520
Comparative Medicine	3	6,249	3	6,249	3	6,249	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	53	$127,238	31	$84,410	28	$75,971	-25	-$51,266
Other Research								
Research Careers	4	$554	12	$1,700	12	$1,700	8	$1,146
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	26	26,785	42	43,458	69	71,017	43	44,232
Other Research	30	$27,339	54	$45,158	81	$72,717	51	$45,378
Total Research Grants	558	$467,087	572	$450,980	612	$492,840	54	$25,754
Ruth L. Kirschstein Training Awards	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	0	0	0	0	0	0	0	0
Total Research Training	0	$0	0	$0	0	$0	0	$0
Research & Development Contracts	0	$37,178	0	$45,196	0	$37,178	0	$0
(SBIR/STTR)	*0*	*$0*	*0*	*$0*	*0*	*$0*	*0*	*$0*
	FTEs		FTEs		FTEs		FTEs	
Intramural Research	0	$28,890	0	$38,049	0	$28,890	0	$0
Research Management and Support	0	11,775	0	14,040	0	14,040	0	2,264
Construction		0		0		0	0	0
Buildings and Facilities		0		0		0	0	0
Total, Common Fund	0	$544,930	0	$548,265	0	$572,948	0	$28,018

1 All items in italics are "non-adds."

Major Changes in the Fiscal Year 2014 President's Budget Request

Major changes by budget mechanism and / or budget activity detail are briefly described below. Note that there may be overlap between budget mechanisms and activity detail and these highlights will not sum to the total change for the FY 2014 President's Budget for CF, which is $28.0 million more than the FY 2012 level, for a total of $572.9 million.

Research Project Grants (+$31.642 million; total $344.152 million): The NIH Common Fund expects to support a total of 503 Research Project Grant (RPG) awards in FY 2014. Noncompeting RPGs will decrease by nineawards and increase by $1.961 million. New Common Fund programs to be launched in FY 2014 accounts for most of this increase in funding.

Research Centers (-$51.266 million; total $75.971 million): The NIH Common Fund plans to support a total of 28 Research Center Awards. The decrease in number and amount reflects a planned decrease in the number and amount of support provided to Research Centers within the Protein Capture, Human Microbiome, Molecular Libraries, and Bioinformatics and Computational Biology programs between FY 2012 and FY 2014. Resources, tools, technologies, and data produced by these Research Centers have been taken up by the scientific community to support investigator-initiated research throughout the NIH, and ongoing infrastructure costs have transitioned to other sources of support for maintenance.

Other Research (+$45.378 million; total $72.717 million): The estimated increase in Common Fund support for Other Research reflects a new funding opportunity for Metabolomics Career Development Awards within the Other Research, Research Careers mechanism. Additionally, new programs in Strengthening the Biomedical Research Workforce and Increasing the Diversity of the NIH-Funded Workforce, along with a planned increase in the number of Regional Metabolomics Resource Cores, results in the estimated increase within the Other Research, Other mechanism.

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

Title of Initiative	FY 2012 Actual	FY 2013 CR	FY 2014 PB	Change vs. FY 2012
Single Cell Analysis				
Pilot Studies to Evaluate Cellular Heterogeneity	5,656	5,601	5,986	330
Exceptionally Innovative Tools and Technologies for Single Cell Analysis	3,345	3,174	6,800	3,455
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	6,134	5,648	5,674	(460)
Single Cell Analysis Challenges	0	60	1,100	1,100
Subtotal, Single Cell Analysis	15,135	14,483	19,560	4,425
Epigenomics				
Mapping Centers	11,839	183	0	(11,839)
Human Health and Disease	3,891	3,679	0	(3,891)
Data Management Center for the Mapping Centers	2,861	3,062	3,000	139
Technology Development in Epigenetics	3,452	3,576	3,500	48
Pharmacology	0	4,000	4,000	4,000
Subtotal, Epigenomics	22,043	14,500	10,500	(11,543)
Big Data to Knowledge (BD2K)				
Big Data to Knowledge (BD2K)	0	800	40,891	40,891
Bioinformatics and Computational Biology				
National Centers for Biomedical Computing	8,425	3,555	0	(8,425)
Building Blocks, Biological Pathways and Networks				
National Technology Centers for Networks and Pathways (TCNPs)	10,140	10,068	0	(10,140)
Extracellular RNA Communication				
Data Management and Resource/Repository (DMRR)	0	2,676	2,611	2,611
Reference Profiles of Human Extracellular RNA	0	4,083	4,078	4,078
Extracellular RNA Biogenesis, Biodistribution, Uptake, and Effector Function	0	7,319	7,328	7,328
Clinical Utility of Extracellular RNAs as Biomarkers and Therapeutic Agents	0	8,136	10,132	10,132
Subtotal, Extracellular RNA Communication	0	22,214	24,149	24,149
Human Microbiome				
Sequence a Reference Set of Genomes	4,385	0	0	(4,385)
Demonstration Projects	11,516	766	0	(11,516)
New Tools and Technologies for Metagenomic Analyses	4,060	0	0	(4,060)
Data Coordination	3,091	0	0	(3,091)
ELSI Studies Unique to HMP	10	0	0	(10)
HMP Workshops	587	0	0	(587)
Evaluation of multi-'omic data in understanding the microbiome's role in health and disease	0	5,000	5,000	5,000
Subtotal, Human Microbiome	23,649	5,766	5,000	(18,649)
Metabolomics				
Comprehensive Metabolomics Research Cores	7,358	12,419	12,450	5,092
Interdisciplinary Training in Metabolomics	2,899	3,933	3,933	1,034
Metabolomics Technology Development	2,540	2,519	2,513	(27)
Metabolomics Reference Standards Synthesis	53	2,050	2,084	2,031
Metabolomics Data Sharing and Program Coordination Core	2,030	1,443	1,401	(629)
Subtotal, Metabolomics	14,880	22,364	22,381	7,501
Knockout Mouse Phenotyping Program				
Production, Characterization, and Cryopreservation	6,443	6,458	6,449	6
Phenotyping and Data Release	4,251	8,065	6,701	2,450
Data Coordination	306	677	550	244
Subtotal, Knockout Mouse Phenotyping Program	11,000	15,200	13,700	2,700
Nanomedicine				
Nanomedicine Development Centers	16,000	16,000	16,000	0
Protein Capture				
Antigen Production	1,346	50	0	(1,346)
Production of anti-TF antibodies	6,545	4,204	4,875	(1,670)
New Reagent Technology Development and Piloting	5,147	5,058	6,125	978
Subtotal, Protein Capture	13,038	9,312	11,000	(2,038)
Science of Behavior Change				
Mechanisms of Change	5,458	4,282	3,674	(1,784)
Structural Biology				
Membrane Protein Production	8,663	8,064	0	(8,663)

Title of Initiative	FY 2012 Actual	FY 2013 C.R.	FY 2014 PB	Change vs. FY 2012
Genotype-Tissue Expression (GTEx) Resources				
Genotype-Tissue Expression (GTEx) Resources	22,475	32,014	35,614	13,139
Gulf Long-term Follow-up of Workers Study				
Gulf Long-term Follow-up of Workers Study	455	4,545	2,500	2,045
Health Care Systems Research Collaboratory				
NIH-HMORN Coordinating Center	2,378	2,440	2,786	408
Expansion Activities	5,191	100	10,615	5,424
Subtotal, Health Care Systems Research Collaboratory	7,569	2,540	13,401	5,832
Health Economics				
Changing Incentives for Consumers, Insurers, and Providers	2,434	1,360	712	(1,722)
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	2,372	5,017	5,057	2,685
Economics of Prevention	3,914	4,711	4,649	735
Data Infrastructure to Enable Research on Health Reform	51	1,552	501	450
Subtotal, Health Economics	8,771	12,640	10,919	2,148
Library of Integrated Network-Based Cellular Signatures (LINCS)				
Large-scale Production of Perturbagen-Induced Gene Expression	5,110	4,678	0	(5,110)
New laboratory-based technology development	2,835	2,800	0	(2,835)
Computational Tool Development and Integrative Data Analysis	1,501	2,507	0	(1,501)
Integration of existing datasets	1,138	15	0	(1,138)
Subtotal, Library of Integrated Network-Based Cellular Signatures (LINCS)	10,584	10,000	0	(10,584)
Molecular Libraries and Imaging				
Creation of NIH Bioactive Small Molecule Library & Screening Centers	84,603	46,825	0	(84,603)
Cheminformatics	500	250	0	(500)
Technology Development	6,625	0	0	(6,625)
Imaging Probe Database	450	0	0	(450)
Subtotal, Molecular Libraries and Imaging	92,178	47,075	0	(92,178)
NIH Center for Regenerative Medicine (NCRM)				
NIH Center for Regenerative Medicine (NCRM)	7,475	8,000	10,000	2,525
Re-engineering the Clinical Research Enterprise				
Translational Research Core Services	11,000	5,000	0	(11,000)
Dynamic Assessment of Patient-Reported Chronic Disease Outcomes	8,841	4,273	0	(8,841)
Enhance Clinical Research Training via the National Multi-disciplinary CR Career Development Program and MRSP Expansions	1,099	1,100	1,100	1
Subtotal, Re-engineering the Clinical Research Enterprise	20,940	10,373	1,100	(19,840)
Regulatory Science				
Advancing Regulatory Science through novel research and science-based technologies	2,452	25	0	(2,452)
Microphysiological Systems for Drug Efficacy and Toxicity Testing	4,350	4,151	0	(4,350)
Drug Repurposing	0	18,000	0	0
Subtotal, Regulatory Science	6,802	22,176	0	(6,802)
Undiagnosed Disease Program				
Undiagnosed Diseases Program Network	0	11,150	16,750	16,750
Training in the Use of Contemporary Genomic Approaches to Rare Disease Diagnostics	0	600	900	900
Subtotal, Undiagnosed Disease Program	0	11,750	17,650	17,650
Increasing the Diversity of the NIH-Funded Workforce				
Increasing the Diversity of the NIH-Funded Workforce	0	3,800	32,300	32,300
Strengthening the Biomedical Research Workforce				
Strengthening the Biomedical Research Workforce	0	3,815	6,939	6,939
Global Health				
Medical Education Partnership Initiative (MEPI)	3,000	3,000	3,000	0
Human Heredity and Health in Africa (H3Africa)	5,943	6,406	7,652	1,709
Subtotal, Global Health	8,943	9,406	10,652	1,709
High-Risk Research				
NIH Director's Pioneer Award	34,503	33,426	31,889	(2,614)
NIH Director's New Innovator Award Program	91,403	90,480	90,815	(588)
Transformative R01's	73,510	84,681	70,064	(3,446)
NIH Director's Early Independence Award Program	9,175	12,342	17,419	8,244
Subtotal, High-Risk Research	208,591	220,929	210,187	1,596
Interdisciplinary Research				
Interdisciplinary Research Centers	204	0	0	(204)
Strategic Planning Funds	1,512	2,594	2,594	1,082
Subtotal Common Fund	544,930	548,265	520,711	(24,219)
New Initiatives in Common Fund	0	0	52,237	52,237

Justification of Budget Request

Common Fund

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

Budget Authority (BA):

	FY 2012 Actual	FY 2013 CR	FY 2014 President's Budget	FY 2014 + /- FY 2012
BA	$544,930,000	$548,265,000	$572,948,000	+$28,018,000
FTE	0	0	0	0

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

Director's Overview

Begun in 2004 as the NIH Roadmap and re-named in the 2006 NIH Reform Act, the NIH Common Fund supports research in areas of emerging scientific opportunities, rising public health challenges, and knowledge gaps that deserve special emphasis and would benefit from strategic coordination and planning across the NIH Institutes and Centers (ICs). To this end, the Common Fund programs tackle high-priority 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.

The Common Fund currently supports over 25 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 10 years. 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 maintenance. An exception to the 10-year limit is the High-Risk, High-Reward program, which includes the Pioneer, New Innovator, Transformative Research, and Early Independence Awards. Although individual investigators within this program are funded for no longer than five years, the program as a whole supports new cohorts of investigators each year. A recent evaluation of the Pioneer initiative has indicated that this program provides important opportunities for innovation, yielding high impact achievements and therefore warrants continuation (http://commonfund.nih.gov/pioneer/evaluations.aspx).

Common Fund programs that were funded in prior years, but are not included in the Common Fund FY 2014 budget request include Bioinformatics and Computational Biology; Bridging Interventional Development Gaps (BrIDGs); Building Blocks, Biological Pathways, and Networks; Molecular Libraries and Imaging; Patient-Reported Outcomes Measurement Information System (PROMIS); and Structural Biology. The data, tools, technologies and resources generated by these programs continue to stimulate and support investigator-initiated studies across the NIH, and funds for infrastructure established by these programs are being requested from other sources, including funds requested in the National Center for Advancing Translational Sciences (NCATS) Congressional Justification for Molecular Libraries and Imaging and BrIDGs.

New Common Fund programs result from a planning process that engages the broad scientific community 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, input from the NIH IC Directors, and 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 that span the continuum from basic science to translational science, and covers a broad range of biomedical and behavioral research. The Common Fund also supports a number of programs that help create and sustain a vibrant and robust biomedical workforce, including programs that have this focus as a main goal, such as the High-Risk, High-Reward program, and programs that include training as one component, such as the Metabolomics program. Collectively, Common Fund programs address challenges and opportunities that have been identified as being the highest priority for the scientific research community and the NIH.

Common Fund programs have been designed to achieve high impact results within a defined timeframe. Significant efforts have been made to evaluate these programs during their lifetime and as programs end, the outcomes are being assessed. Funds freed as the completed programs areas move to other sources of support, or as tools are taken up by the investigator community, will be available in FY 2014 for new challenges and opportunities. The Common Fund undergoes an annual strategic planning process to identify new program areas ripe for Common Fund investment. In FY 2014, strategic planning efforts will identify the most high-priority areas in which to invest the funds made available through the planned turnover of initiatives and through the completion of programs that have concluded their final of support. Strategic planning is therefore a substantial activity as the NIH works with stakeholders to identify the next wave of NIH-wide priorities for the Common Fund.

Overall Budget Policy: The FY 2014 President's Budget request for the Common Fund is $572.948 million, an increase of $28.018 million, or 5.1 percent above the FY 2012 Actual level. The Common Fund will continue to support research consistent with the NIH Director's themes, and capitalize on the emerging scientific opportunities available in FY 2014. As mature programs transition out of the Common Fund, new programs are being established through strategic planning activities that identify potentially transformative areas of research where short-term Common Fund investment can have a catalytic impact.

Theme 1: Today's Basic Science for Tomorrow's Breakthroughs

Investments in basic biomedical and behavioral research are a priority for the Common Fund, since these investments are the basis for future therapeutic and preventative strategies. Common Fund programs focused on basic research are designed to overcome barriers to discovery, or to capitalize on emerging opportunities to catalyze the rate of scientific progress. The programs listed below have basic research as a primary focus, although the requirement that Common Fund programs be goal-driven and relevant to multiple diseases and conditions means that many basic research programs also have overlap with translational research as well.

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, 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 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. In FY 2014, the Single Cell Analysis program undergoes a planned increase to include a new funding opportunity on methods for the spatiotemporal tracking, characterization, and analysis of live cells in situ.

Budget Policy: The FY 2014 President's Budget estimate is $19.560 million for the Single Cell Analysis program, an increase of $4.425 million, or 29.2 percent above the FY 2012 Actual level. This estimated increase in funding will be used to support additional research to develop exceptionally innovative tools, technologies, and methods for single cell analysis, including methods to enable single cell analysis in situ.

Epigenomics

Modifications to DNA that do not change the underlying gene sequence, but instead alter gene expression, are called epigenetic modifications, and are known to play an important role in many diseases and during normal development. The Common Fund Epigenomics Program is intended to provide core data, tools, and technologies to the biomedical research community so that researchers can explore mechanisms by which epigenetic modifications regulate the human genome.

In FY 2008, four Reference Epigenome Mapping Centers were selected through peer review based on their ability to conduct genome-wide analysis of epigenetic modifications in diverse

cell types. To date, the Centers have identified a core set of epigenomic changes in 61 different cell and tissue types that represent "reference maps" of non-diseased cells. By comparing these reference epigenomic maps to epigenomic maps of diseased cells, researchers will be able to pinpoint specific parts of the epigenome that correlate with disease. Data generated by the Centers are standardized through the Epigenomics Data Analysis and Coordination Center, and made publicly available through the National Center for Biotechnology Information NCBI as a way to stimulate other researchers to analyze and use the data in follow-up studies. Researchers in the Epigenomics program have developed numerous resources for investigators, including several web browsers for viewing and analyzing epigenomics data, experimental protocols, and novel technologies for detecting epigenomic changes with high resolution or in extremely small samples. Recent research from the Epigenomics program has suggested 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, providing an important breakthrough in our understanding of the relationship between genetic and epigenetic factors contributing to disease.

In FY 2014, the Epigenomics program will continue to support the Epigenomics Data Analysis and Coordination Center, as well as Technology Development for Epigenetics. Input from the scientific community has identified a critical need for tools to manipulate the epigenome in a precise, cell-specific manner. Current planning activities within the Epigenomics program are exploring how Common Fund investment could build on recent advances in epigenomics research to capitalize on this emerging opportunity and accelerate the development of new cell- and gene-specific tools to manipulate the epigenome.

Budget Policy: The FY 2014 President's Budget estimate is $10.5 million for the Epigenomics program, a decrease of $11.543 million, or 52.4 percent below the FY 2012 Actual level. The estimated decrease in funding reflects the planned completion of the Reference Epigenome Mapping Centers, as well as the completion of an initiative on the Epigenomics of Human Health and Disease. Funds requested in FY 2014 will be used for data coordination and management, technology development, and to explore the emerging scientific opportunities in the area of epigenomic pharmacology.

Big Data to Knowledge (BD2K) (New in FY 2013)

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

In response to the needs articulated by the Advisory Committee to the Director 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. The BD2K program is being supported in large part by the Common Fund, with contributions to the centers from all NIH ICs. Supported through a planning phase in FY 2013, the BD2K program will expand in FY 2014.

Budget Policy: The FY 2014 President's Budget estimate is $40.891 million for the BD2K program from the Common Fund, an increase of $40.891 million, since the program was not supported in FY 2012. Support for BD2K will be used to develop new methods, approaches, and resources for analysis of big data, as well as training in disciplines relevant for large-scale data analysis to increase the number of researchers with this much-needed expertise.

Extracellular RNA Communication (New in FY 2013)

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, recent research indicates that RNAs can play a role in a variety of complex functions, including newly discovered mechanisms of cell-to-cell communication. The impact of these extracellular RNAs, or 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 in FY 2013.

Budget Policy: The FY 2014 President's Budget estimate is $24.149 million, an increase equal to the total request for the program, which was not supported in FY 2012. The requested level of funds will be used to support the Data Management and Resource/Repository (DMRR), as well as the investigation of fundamental biological principles of exRNA, development of reference profiles exRNAs from healthy humans, and exploration of the potential clinical utility of exRNAs as biomarkers or therapeutic delivery vehicles.

Program Portrait: Extracellular RNA Communication

FY 2012 level: $0.0 million
FY 2014 level: $24.1 million
Change: +$24.1 million

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. This recent research suggests exRNAs may represent a previously undiscovered mechanism of intercellular and even inter-species information exchange.

To explore how exRNAs may mediate this novel type of cell-to-cell communication, and to identify the potential impact on human health and disease, the Common Fund has launched the Extracellular RNA Communication program. This program is composed of a series of coordinated initiatives aiming to:

- Establish a central repository for data collection and analysis
- Develop reference profiles for healthy human exRNAs in a variety of body fluids
- Support analyses to define fundamental principles of exRNA generation, distribution, uptake, and effector function
- Investigate the possible clinical utility of exRNAs as biomarkers or therapeutic delivery vehicles.

Human Microbiome Project

Microbes such as bacteria, viruses, and fungi found naturally in the human body outnumber human cells by a factor of 10. Many of the microbes living in our bodies are beneficial, whereas others are implicated in diseases such as asthma, cancer, and obesity. However, 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 microbiome, that is shared by all people or whether each person has a unique microbiome.

HMP researchers have sequenced the genomes of 1,600 microbial strains, discovered more than 29,000 novel proteins encoded by the human microbiome, and discovered links between changes in the microbiome and dermatitis, Crohn's disease, and gastrointestinal reflux disease (GERD). The program's investigators have sequenced and cataloged the microbiome samples and developed technologies to isolate and identify unknown microbes.

Common Fund support for the program continued in FY 2013 to address remaining high-priority issues that affect the field as a whole, such as the extent to which genomic analysis of microbial species can predict the function of the microbes versus the extent to which analysis of other

parameters is required. The effort to gather data on the proteins and metabolites that are produced by microbes will complement the data gathered on the genomes during the initial phase of HMP. In FY 2014, support will continue for evaluation of this "multi-'omic" data in understanding human health and disease.

Budget Policy: The FY2014 President's Budget estimate is $5.0 million for the HMP program, a decrease of $18.649 million, or 78.9 percent below the FY 2012 Actual level. The estimated decrease in funding reflects the planned completion of several major initiatives, including the Data Analysis and Coordinating Center (DACC); initiatives to generate new tools, technologies, and methods for studying the human microbiome; development of a reference set of microbial genomes; and research on the relationship between changes in the human microbiome and disease. Funds requested in FY 2014 will be used to evaluate "multi-'omic" data, including proteins and metabolites that are produced by the microbiome.

Increasing Metabolomics Research Capacity

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 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, and the 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 2014 President's Budget estimate is $22.381 million for the Metabolomics program, an increase of $7.501 million, or 50.4 percent above the FY 2012 Actual level. The estimated increase in funding will be used to support an expansion of the Comprehensive Metabolomics Resource Cores, as well as an increase in support for interdisciplinary training in metabolomics and synthesis of metabolomics reference standards.

Knockout Mouse Phenotyping Program

Recognizing the value and utility of a readily-accessible, genome-wide collection of mouse mutants for determining how mammalian genes function, several international programs were launched in 2006 to develop mutant mouse strains. Collectively, these programs have generated

more than 8,000 prototype knockout mice. The Common Fund has joined together with multiple NIH ICs to support the Knockout Mouse Phenotyping Program, which builds upon this existing 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 2014 President's Budget estimate is $13.7 million for the Knockout Mouse Phenotyping Program, an increase of $2.7 million, or 24.5 percent above the FY 2012 Actual level. The estimated increase in funding reflects the discovery that approximately one-third of the engineered genetic mutations resulted in embryonic lethality; therefore, support will be provided for an expansion of phenotyping efforts to include these embryonic-lethal mutations, as well as a concomitant scale-up of data release and data coordination.

Nanomedicine

Nanotechnology, the study and manipulation of systems less than approximately 100 nanometers in size, about $1/100^{th}$ the diameter of a red blood cell, holds tremendous promise for use in diagnosing and treating disease. The goal of the Nanomedicine program is to use nanotechnology to understand and manipulate biological processes in a cell for specific clinical purposes. For example, nanoscale protein folding machines are being manipulated for the treatment of diseases such as Alzheimer's and Huntington's, where misfolded proteins are thought to play a role, and nanoscale photoswitches are being developed to help restore vision in people with degenerative retinal diseases.

In FYs 2005 and 2006, a network of eight Nanomedicine Centers at academic institutions across the country was established. The first phase of the program was heavily focused on basic science, with an increased emphasis on application of this knowledge in the second phase. The program underwent an extensive review in 2009 to inform the selection of Centers that were best positioned to apply their findings to translational studies in the second phase. The second phase of the program constitutes a more focused effort involving a smaller number of centers, currently four, 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 2014. The Flexible Research Authority provides NIH flexibility in funding mechanisms and review process to pursue research of high priority to the NIH.

Budget Policy: The FY 2014 President's Budget estimate is $16.0 million for the Nanomedicine program, no change from the FY 2012 Actual level. The estimated funding level reflects ongoing support for the four currently funded Nanomedicine Centers, which are focusing on exploring novel clinical applications of nanobiological structures developed during the first phase of the Nanomedicine program.

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, which can be used by researchers in protein isolation, high-throughput assays, diagnostics, and biomarker development. These resources will support a wide-range of research and clinical applications that will enable the isolation and tracking of proteins of interest and permit their use as diagnostic biomarkers of disease onset and progression. To have the maximum benefit, such reagents need to be high quality, affordable, and reliable. This program provides support for two production centers to achieve just this; comparing the utility of monoclonal antibodies, which have been widely used to capture proteins but are time-consuming and expensive to generate, with recombinant antibodies, a newer technology that holds great promise for making affordable reagents in less time. The program also supports the development of new technologies to capture proteins.

Budget Policy: The FY 2014 President's Budget estimate is $11.0 million for the Protein Capture program, a decrease of $2.038 million, or 15.6 percent below the FY 2012 Actual level. The estimated decrease in funding reflects the completion of an initiative to produce transcription factor antigens, as well as a planned decrease in support of the antibody production initiative. Ongoing initiatives will support the development and testing of new technologies for reagent production.

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. The Common Fund's Science of Behavior Change program is intended to improve our understanding of human behavior change across a broad range of health-related behaviors. This goal 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 behavioral interventions.

Budget Policy: The FY 2014 President's Budget estimate is $3.674 million for the Science of Behavior Change program, a decrease of $1.784 million, or 32.7 percent below the FY 2012 Actual level. This estimated decrease in funding reflects the planned completion of several awards at the end of FY 2013.

Theme 2: Translational Science

Building upon scientific discoveries and advances made in large part by basic research studies, programs with a focus on translational science aim to develop tools, technologies, or resources that will aid in the development of new therapeutics, diagnostics, or preventative strategies. Common Fund programs primarily focused on translational research span a wide range of

activities with the ultimate goal of improving public health, from the identification of biological pathways that may be perturbed in disease and could be targeted to restore health, to identifying mechanisms of behavior change that can promote and sustain healthy lifestyle choices.

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 any gene coding region, making it difficult to determine how the change leads to disease. The Genotype-Tissue Expression (GTEx) project provides data on how human DNA variation correlates with variation in gene activity levels. This program 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 human tissues from approximately 160 donors identified through autopsy or organ transplant. Based on the success of this pilot study, the program underwent an expansion in FY 2013. Support in FY 2014 will be used to continue to build a comprehensive data and sample resource of genetic variation and gene expression profiles in multiple tissues. Support is also provided for development of new statistical methods, creation of a database of genetic and clinical data generated by the program and obtained from other sources, and a tissue repository intended to stimulate new studies to identify genetic contributions to health and disease. The project is also exploring ethical, legal, and social implications raised by the research, which can inform other genomics programs.

Budget Policy: The FY 2014 President's Budget estimate is $35.614 million for the GTEx program, an increase of $13.139 million, or 58.5 percent above the FY 2012 Actual level. The estimated increase in funding reflects the expansion of this program from a feasibility phase to a full-scale program. Support for GTEx in FY 2014 will be used to expand the comprehensive data and sample resource of genetic variation and gene expression profiles in multiple tissues from post-mortem donors, to support development of new approaches and methods for data analysis, and to support molecular analysis of stored biospecimens from the GTEx project.

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

The oil that spilled following 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 his 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, in order to augment research commitments from the National Institute for Environmental Health Sciences. The GuLF program, launched in FY 2010 with Common Fund support, 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 is the largest health outcome study ever conducted following an oil spill and the findings will not only advance our understanding of links between environmental hazards and health, but also make us better

equipped to deal with future disasters. FY 2014 will be the final year of Common Fund support for this program as it moves to NIEHS for long term follow up.

Budget Policy: The FY 2014 President's Budget estimate is $2.5 million for the GuLF program, an increase of $2.045 million, or 449.5 percent above the FY 2012 level. This estimated increase in funding reflects support for a contract to study the health effects of clean-up workers and increased recruitment of participants.

Health Care Systems Research Collaboratory

The overall goal of the NIH Common Fund Health Care Systems (HCS) Research Collaboratory program is to strengthen the national capacity to implement cost-effective large-scale research studies that engage health care delivery organizations as research partners. The aim of the program is to provide a framework of implementation methods and best practices that will enable the participation of many health care systems in clinical research. These methods and practices are being tested and honed within the context of pragmatic clinical trials, which measure the effectiveness of treatments in real world settings. A Coordinating Center serves as the central resource for the development of technical and policy guidelines and best practices for the effective conduct of research studies in partnership with health care systems. The Coordinating Center will also foster approaches to increase the effective use of health information technologies, including Electronic Health Records (EHRs). Effectively leveraging EHRs across health systems will require the identification of the relevant standards used by participating health systems and the development of approaches to enable cross-system interoperability.

Recent input from the scientific community has identified the management of chronic diseases in clinical trials as a critical roadblock to progress in this field. Although having two or more co-morbid conditions is often an exclusion criterion for clinical trials, many patients who will ultimately be prescribed medications studied in these trials have multiple chronic conditions. There is uncertainty about how these co-morbid conditions could affect drug efficacy and toxicity, and a lack of information about co-morbidities in the context of chronic diseases and their treatments. Within the HCS Research Collaboratory program, a potential new initiative is being explored to develop novel models of clinical trials that consider the approaches, data collection methods, and analysis tools needed to provide information on the biological and clinical consequences of therapeutic intervention on patients with multiple chronic conditions.

Budget Policy: The FY 2014 President's Budget estimate is $13.401 million, an increase of $5.832 million, or 77.1 percent above the FY 2012 Actual level. The estimated increase in funding reflects an expansion of the pragmatic clinical trials demonstration projects, as well as a planned new initiative to develop novel models of clinical trials that adequately address the issue of patients with multiple chronic conditions.

Health Economics

The Common Fund's Health Economics program aims to support basic and applied research to understand how innovations in treatments, diagnosis, and preventive strategies can be most effectively implemented in a health care setting. Research supported by this program will

identify factors determining optimal adoption of highly effective health technologies, innovations, and discoveries, so that past and future investments by NIH may have greater public health impact. The program seeks to analyze factors that are likely to affect the adoption of personalized medicine approaches, including research to understand individual characteristics and preferences of patients and their families, as well as factors influencing health care provider decisions. Understanding these responses will inform the development of future treatments, diagnostic, and preventive strategies to ensure that innovations are implementable in a real world environment. The Health Economics program also aims to build research capacity in health economics so that future NIH-supported research can be informed by economic analysis of factors that influence health and the uptake and adoption of NIH-supported innovations.

In FY 2011, the program initiated a series of developmental research projects to add to our understanding of the behavioral responses to various innovations in health care, including diagnosis, treatment, and prevention. Studies are investigating whether implementation of these innovations is practical and affordable, and will identify reasons why various NIH-supported innovations are or are not being implemented in practice.

Budget Policy: The FY 2014 President's Budget estimate is $10.919 million, an increase of $2.148 million, or 24.5 percent more than the FY 2012 Actual level. The estimated increase in funding reflects support for a contract to enable the development of a database to gather the most relevant state-level variables that contribute to uptake and use of NIH-supported medical strategies. In addition, support will be provided for research on the determinants and consequences of personalization in health care and prevention, as well as research designed to explore the diffusion of health technologies to improve the process leading from scientific advances to health benefits.

Library of Integrated Network-Based Cellular Signatures (LINCS)

The LINCS program aims to develop a resource "library" of molecular signatures, including gene expression and other cellular traits to understand how biological pathways interact and respond to a variety of genetic, environmental, and pharmacological influences. Since its inception, the program's researchers have developed molecular signatures in thousands of cell types and have pioneered novel bioinformatics 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 experimental therapies. LINCS data will accelerate the pre-clinical drug development pipeline by facilitating the identification of biological targets for new disease therapies.

The pilot phase of the LINCS program is aimed towards defining signatures for specific perturbing agents, establishing a database and standards, and developing new tools and assays. This pilot was begun in FY 2010 and extended through FY 2013. A review of pilot phase activities will inform the need for a second phase that is planned to start in FY 2014. The planned review will assess the usability of the data resource to the research community.

Budget Policy: The FY 2014 President's Budget estimate is $0.0 million, a decrease of $10.584 million, or 100.0 percent below the FY 2012 Actual level. This estimated decrease in support reflects the planned completion of the pilot phase of the LINCS program. The planned review of the pilot phase will inform the need for a possible second phase of LINCS to be supported in FY 2014 using funds for new initiatives.

NIH Center for Regenerative Medicine (NCRM)

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-based therapies. The Center is designed to: 1) develop strategies for induced pluripotent stem cell (iPSC)-based therapies, using specific rare diseases as test cases; 2) assist the biomedical community in negotiating the procedural and regulatory issues currently hampering stem cells usage in the clinic; 3) make a variety of iPSCs available to the scientific community for research purposes; 4) establish standards to streamline stem cell development on a national and international scale; 5) and build a cadre of intramural investigators working to advance the field of regenerative medicine.

Budget Policy: The FY 2014 President's Budget estimate is $10.0 million, an increase of $2.525 million, or 33.8 percent above FY 2012 Actual levels. The estimated increase in funding reflects a scale up from pilot projects to larger awards that support research with the highest potential to move iPSC- based therapies closer to clinical use.

Re-engineering the Clinical Research Enterprise

Begun in FY 2004, this program has sought 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 one of the initiatives have ended or transitioned to other sources of support.

Enhance Clinical Research Training via the National Multi-Disciplinary CR Career Development Program and MRSP Expansion

In FY 2014 NIH will start a new program, the Medical Research Scholars Program (MRSP), to serve up to 70 fellows per year. This program aims to attract the most creative, research-oriented medical and dental students, called "fellows," to the intramural NIH campus in Bethesda, Maryland. The fellows will be engaged in a mentored clinical or translational research project in areas that match their personal research interests and career goals. Until 2011, a similar program the Clinical Research Training Program (CRTP) had been supported by the Common Fund. The CRTP was conducted in parallel with a program of similar goals funded by the Howard Hughes Medical Institute (HHMI). Upon the HHMI decision to terminate their program, the CRTP was enlarged from 30 to 45 fellows in 2012 through support from the Foundation for the NIH (FNIH). The new MRSP program will build upon

lessons learned from the HHMI and CRTP programs. MRSP will be supported from the Common Fund through FY 2014. This will facilitate the transition of the program to a public-private partnership model for continued support.

Budget Policy: The FY 2014 President's Budget estimate is $1.1 million, a decrease of $19.840 million, or 94.7 percent below FY 2012 Actual levels. The estimated decrease in funding reflects the planned completion of several initiatives, including the Patient Reported Outcomes Measurement Information System (PROMIS) and Bridging Intervential Development Gaps (BrIDGs). Funds requested in FY 2014 will continue to support the MRSP.

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 interdisciplinary area of biomedical research that serves to generate new knowledge and tools for assessing experimental therapies, devices, 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 address 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. This initiative, Microphysiological Systems for Drug Efficacy and Toxicity Testing, involves a new inter-agency collaboration between the NIH, FDA, and the Defense Advanced Research Projects Agency (DARPA). In an ongoing effort to pilot new approaches to regulatory science, the Common Fund launched a new initiative in drug repurposing in FY 2013, designed to discover new therapeutic uses for existing molecules that have already been developed by the pharmaceutical industry. This initiative, begun as a partnership between the Common Fund and NCATS, will transition to NCATS support in FY 2014.

Budget Policy: The FY 2014 President's Budget estimate is $0.0 million, a decrease of $6.802 million, or 100.0 percent below the FY 2012 Actual level. This estimated decrease in funding reflects the planned transition of several initiatives within the Regulatory Science program. Emerging scientific opportunities within the scope of the Regulatory Science program may be supported in FY 2014 using funds for new initiatives.

Undiagnosed Diseases Program (New in FY 2013)

To aid individuals with rare and difficult to diagnose diseases, and to also make progress in uncovering, understanding, and treating these disorders, 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 in FY 2013 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 this type of program in an extramural environment. It will assist patients with unknown disorders in reaching an accurate diagnosis, and 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.

Budget Policy: The FY 2014 President's Budget estimate is $17.650 million, an increase equal to the total request for the program, which was not supported in FY 2012. This new program will establish a network of academic medical centers to advance rare disease diagnosis and treatment, thereby enhancing collaboration among laboratory and clinical researchers at multiple locations and sharing data and approaches broadly throughout the scientific community.

Program Portrait: Undiagnosed Diseases Program

FY 2012 level: $0.0 million
FY 2014 level: $17.7 million
Change: +$17.7 million

In the United States, it has been estimated that approximately 6 percent of the general population suffers from a rare disorder. Often times, these individuals go for long periods of time without a diagnosis. Established in 2008 to address this critical need, the NIH intramural research program in undiagnosed diseases has made over 100 diagnoses, and has identified two new diseases and 15 new disease genes.

The Common Fund Undiagnosed Disease program, launched in FY 2013, aims to build upon the success of the intramural program and pilot by expanding the reach of the original program to include a network of both intramural and extramural sites. This expansion will catalyze the field of rare disease research by bringing contemporary genetic approaches to bear on a myriad of different, rare and new diseases, and training the next generation of clinical researchers to use these approaches in disease diagnosis. This program will bring together clinical and basic researchers to elucidate biological mechanisms underlying rare diseases so that treatments may be identified. The insights gained from understanding rare diseases may provide important clues about the pathology and potential treatments of a host of common diseases as well.

Theme 3: Recruiting and Retaining Diverse Scientific Talent and Creativity

The entire biomedical research enterprise relies on the creativity, innovation, and dedication of the scientific workforce. The Common Fund supports a number of programs that aim to train and nurture the best and brightest scientists of all career stages, to ensure a robust workforce for the future. New Common Fund programs, including Increasing the Diversity of the NIH-Funded Workforce and Strengthening the Biomedical Research Workforce, were launched in FY 2013 as components of a broad, high priority, trans-NIH effort to enhance the diversity of the NIH-supported biomedical workforce.

Increasing the Diversity of the NIH-Funded Workforce (New in FY 2013)

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 Working Group on Diversity in the Biomedical Research Workforce provided concrete recommendations toward improving the recruitment and retention of underrepresented minorities (URM), people with disabilities, and people from disadvantaged backgrounds 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, NIH established the Increasing the Diversity of the NIH-Funded Workforce Program to unify and strengthen institutions and faculty that are dedicated to the recruitment and retention of diverse scientists. This program, to be launched and piloted through the NIH Common Fund, will build off of 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, building networks, and ensuring that under-represented scientists and relatively under-resourced institutions that support them are not marginalized.

Budget Policy: The FY 2014 President's Budget estimate is $32.3 million, an increase equal to the total request for the program, which was not supported in FY 2012. The requested funds will be used to support initiatives to strengthen the infrastructure of comparatively under-resourced institutions, build mentoring networks, and support coordination and resource sharing efforts to facilitate the dissemination of best practices.

Program Portrait: Increasing the Diversity of the NIH-Funded Workforce

FY 2012 level: $0.0 million
FY 2014 level: $32.3 million
Change: +$32.3 million

Despite longstanding efforts from the NIH and other entities to increase the number of scientists from underrepresented groups, participation in biomedical research by minority groups remains unacceptably low. As one component of a broader NIH strategy address these issues, the Common Fund's Increasing the Diversity of the NIH-Funded Workforce is supporting the following initiatives:

- NIH Building Infrastructure Leading to Diversity (BUILD): this initiative aims to strengthen the infrastructure of comparatively under-resourced institutions 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 is establishing and solidifying 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.
- National Research Mentoring Network (NRMN): NRMN coordinates pairings of students and faculty from all biomedical and behavioral disciplines into a nation-wide consortium to develop standards for good mentorship and providing training opportunities for both mentors and mentees.
- BUILD and NRMN Coordinating and Evaluation Center: To enhance career development, networking opportunities, and resource sharing between BUILD and NRNM, a Coordinating and Evaluation Center is developing and maintaining 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.

The Common Fund is soliciting applications for planning grants for BUILD and NRMN in FY 2013. Future awards for implementation of BUILD and NRMN are anticipated in FY 2014.

Strengthening the Biomedical Research Workforce (New in FY 2013)

NIH shares concern with the broader biomedical community that the long training time and the declining percentage of PhD 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 PhD graduates can meaningfully contribute to the biomedical research enterprise.

Based on recommendations from the Advisory Committee to the Director Working Group on Biomedical Workforce (http://acd.od.nih.gov/Biomedical_research_wgreport.pdf), the Common Fund launched a new program in FY 2013, called Strengthening the Biomedical Research Workforce, 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 known as 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.

The first awards for this program are being issued in FY 2013, and additional awards are anticipated in FY 2014.

Budget Policy: The FY 2014 President's Budget estimate is $6.939 million, an increase equal to the total request for the program, which was not supported in FY 2012. Requested funds will be used to support BEST awards, which aim to develop innovative approaches to train students for a broad landscape of careers in support of the biomedical research enterprise.

Global Health

The Common Fund Global Health Program supports two initiatives that will expand research capacity in Africa, largely through infrastructure development and the support of training and career development. Expansion of research capacity on the African continent will facilitate research conducted there through many IC-supported efforts. Both communicable and non-communicable diseases and conditions are being addressed through these initiatives.

The Medical Education Partnership Initiative (MEPI) was funded beginning in FY 2010 in partnership with the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). MEPI is developing and strengthening models of medical education, and building research and clinical capacity in countries of Sub-Saharan Africa. While PEPFAR investments necessarily have an AIDS focus, the Common Fund investments train healthcare providers and researchers in non-AIDS areas of research.

The Human Heredity and Health in Africa (H3Africa) initiative was funded through planning activities beginning in FY 2010 and involves collaboration with the Wellcome Trust to build genomic research capacity in Africa. The first awards were issued in FY 2012 to support career development and training; infrastructure improvement, specifically bioinformatics and biorepository capacity; and to support researchers studying the genetic and environmental contributions to health and disease.

The Global Health program is expanding in FY 2014 to provide additional support if the pilots are successful for the scale-up of the biorepositories funded through the H3Africa initiative.

Budget Policy: The FY 2014 President's Budget estimate is $10.652 million represents an increase of $1.709 million, or 19.1 percent above the FY 2012 Actual level. The estimated increase in funding will be used to support additional biorepositories within the H3Africa initiative, as well as scale-up of existing biorepositories that meet criteria established by the program. Studies on the ethical, legal, and societal issues of genomics research within the H3Africa program will also be supported.

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. 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 or approaches. 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 Award initiative, the NIH Director's New Innovator Award initiative, the Transformative Research Award initiative, and the NIH Director's Early Independence Award initiative. These initiatives represent complementary approaches to foster innovation and promote transformation across the broad mission of NIH.

- The Pioneer Award initiative supports outstanding individual investigators at any career stage who have demonstrated exceptional creativity and who propose highly innovative research projects that have the potential for far-reaching impact.

- The New Innovator Award initiative supports exceptional new investigators who propose highly innovative projects with the potential for high impact, but who may lack the preliminary data required to fare well in the traditional NIH peer review system.

- The Transformative Research Award initiative provides unique opportunities for unconventional research projects that involve more risk than traditional NIH research projects or that require unusually large budgets to support potentially high pay-off questions.

- The Early Independence Awards initiative provides a mechanism for exceptional early career scientists to move rapidly into independent research positions by omitting the traditional post-doctoral training period. Spurred by recommendations from the Advisory Committee to the Director on Biomedical Workforce, the number of these awards each year is anticipated to increase, with the number of awards to be determined by the number of outstanding candidates.

Budget Policy: The FY 2014 President's Budget estimate is $210.187 million, a net increase of $1.596 million, or 0.8 percent above the FY 2012 Actual level. The requested funds will be used to support new cohorts of exceptional scientists proposing creative and innovative research through the High-Risk High-Reward initiatives. The estimated increase in funding will be used to support an expansion of the Early Independence Awards, as recommended by the Advisory Committee to the Director on Biomedical Workforce.

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. These planning efforts are being supported through the Common Fund Strategic Planning and Evaluation Funds. FY 2014 Strategic Planning and Evaluation Funds will be used to identify research areas that address key roadblocks in biomedical research or that represent emerging scientific areas ripe for Common Fund investment, to form the basis of potential new Common Fund programs that will begin in FY 2015 or FY 2016. Strategic planning for the Common Fund takes place yearly, and while the specific process undertaken varies from year-to-year, several core activities underlie all the planning activities. Phase 1 of strategic planning identifies broad program areas nominated by external and internal experts, public and private sector partners, and stakeholders. Phase 2 of strategic planning refines these broad areas into a series of well-defined programs and initiatives. Each potential Common Fund program is evaluated on the basis of defined criteria, chief of which are the requirements that the programs be relevant to multiple NIH ICs; have the potential to have a transformative, catalytic impact on research; and are capable of achieving a defined set of goals within defined period of time.

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 2014 President's Budget estimate is $2.594 million, an increase of $1.082 million, or 71.6 percent above the FY 2012 Actual level. These funds will be used to implement a strategic planning process to identify areas of scientific opportunity that are ripe for short-term, catalytic support from the Common Fund. Funds will also be used to evaluate the outputs and outcomes of both 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 strategic planning process described above has produced new potential program areas where Common Fund investment could have a broad, transformative impact. In FY 2014 the Common Fund is undertaking planning activities to identify and understand ongoing work related to the druggable genome and to determine whether opportunities exist for the Common Fund to have a significant impact.

- *Illuminating the Druggable Genome*: The vast majority of drugs target proteins in one of four protein classes: G-protein coupled receptors (GPCRs), nuclear hormone receptors, ion channels, or kinases. However, hundreds of human proteins in these groups are completely uncharacterized, and are therefore referred to as "orphan" proteins. Planning activities for this topic will consider the opportunities to characterize these genes as a large group, rather than the "one at a time" approach that might otherwise be undertaken, potentially enabling the identification of small molecules that target proteins with a role in disease-relevant processes. This effort will be undertaken in close collaboration with the private sector, in order to ensure

that NIH-supported work is complementary and not competitive with programs in biotech and pharma.

Budget Policy: In the FY 2014 President's Budget estimate, the Common Fund has $52.237 million available for new initiatives. Potential new initiatives will be selected through strategic planning activities designed to identify and understand ongoing work in each scientific area and to determine what opportunities exist for the Common Fund to have a significant impact.