DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund (CF)

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

MECHANISM	FY 2013 Actual		FY 2014 Enacted[2]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	299	$139,519	296	$138,125	343	$160,280	47	$22,155
Administrative Supplements	*(63)*	13,977	*(90)*	20,064	*(91)*	20,064	*(1)*	
Competing:								
Renewal	0	0	0	0	0	0		
New	132	149,160	140	158,488	150	169,297	10	10,809
Supplements	0	0	0	0	0	0		
Subtotal, Competing	132	$149,160	140	$158,488	150	$169,297	10	$10,809
Subtotal, RPGs	431	$302,656	436	$316,677	493	$349,641	57	$32,964
SBIR/STTR	0	0	0	0	0	0		
Research Project Grants	431	$302,656	436	$316,677	493	$349,641	57	$32,964
Research Centers:								
Specialized/Comprehensive	56	$79,374	60	$85,201	79	$112,658	19	$27,457
Clinical Research	0	0	0	0	0	0		
Biotechnology	1	2,964	1	2,964	1	2,964		
Comparative Medicine	3	6,062	3	6,062	3	6,249		187
Research Centers in Minority Institutions	0	0	0	0	0	0		
Research Centers	60	$88,399	64	$94,227	83	$121,871	19	$27,644
Other Research:								
Research Careers	10	$1,305	22	$2,822	26	$3,322	4	$500
Cancer Education	0	0	0	0	0	0		
Cooperative Clinical Research	0	0	0	0	0	0		
Biomedical Research Support	0	0	0	0	0	0		
Minority Biomedical Research Support	0	0	0	0	0	0		
Other	38	31,989	44	37,025	72	60,317	28	23,292
Other Research	48	$33,294	66	$39,847	98	$63,639	32	$23,792
Total Research Grants	539	$424,349	566	$450,751	674	$535,151	108	$84,400
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0		
Institutional Awards	0	0	0	0	0	0		
Total Research Training	0	$0	0	$0	0	$0		
Research & Develop. Contracts	0	$45,784	0	$45,784	0	$12,903		-$32,881
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*		
Intramural Research	0	30,718	0	20,316	0	20,519		203
Res. Management & Support	0	12,624	0	14,323	0	14,466		143
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*		
Construction		0		0		0		
Buildings and Facilities		0		0		0		
Total, Common Fund	0	$513,476	0	$533,039	0	$583,039		$50,000

[1] All items in italics and brackets are non-add entries. FY 2013 and FY 2014 levels are shown on a comparable basis to FY 2015.

[2] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

Major Changes in the Fiscal Year 2015 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 2015 President's Budget for the Common Fund, which is $50.000 million more than the FY 2014 Enacted level, for a total of $583.039 million.

Research Project Grants (+$32.964 million; total $349.641 million): The NIH Common Fund expects to support a total of 493 Research Project Grant (RPG) awards in FY 2015. Noncompeting RPGs will increase by 47 awards and $22.155 million. New RPGs will be awarded in Common Fund programs to be launched in FY 2015 as well as in new initiatives within ongoing Common Fund programs.

Research Centers (+$27.644 million; total $121.871 million): The NIH Common Fund plans to support a total of 83 Research Center Awards in FY 2015. The launch of NIH-initiated Centers of Excellence in Biomedical Big Data within the Big Data to Knowledge (BD2K) program accounts for most of the increase in funding.

Other Research (+$23.792 million; total $63.639 million): The estimated increase in Common Fund support for the Other Research mechanism includes a request to use $30.000 million in Other Transaction Authority (OTA). OTA funds will be used to support programs and activities that aim to achieve rapid technology development. One anticipated use for OTA funds in FY 2015 is a new program under consideration, Bioelectronic Medicines, a DARPA-like program that is a high risk, goal-driven endeavor.

Research and Development Contracts (-$32.881 million; total $12.903 million): The estimated decrease in Research and Development Contracts reflects a planned completion of tissue procurement activities supported via contracts within the Genotype-Tissue Expression (GTEx) program. In FY 2015, GTEx will shift focus to concentrate on data generation and analysis made possible through tissues procured by these contracts.

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

Title of Initiative	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
High-Risk Research			
NIH Director's Pioneer Award	32,722	27,906	21,158
NIH Director's New Innovator Award Program	86,638	91,301	80,300
Transformative R01's	78,352	61,650	53,915
NIH Director's Early Independence Award Program	12,421	16,747	20,388
Subtotal, High-Risk Research	210,133	197,604	175,761
Big Data to Knowledge (BD2K)			
Big Data to Knowledge (BD2K)	704	18,727	49,832
Enhancing the Diversity of the NIH-Funded Workforce			
BUILD Initiative	3,086	27,818	35,150
National Research Mentoring Network (NRMN)	880	2,731	2,375
Coordination and Evaluation Center (CEC)	96	1,958	1,900
Subtotal, Enhancing the Diversity of the NIH-Funded Workforce	4,062	32,507	39,425
Epigenomics			
Mapping Centers	335	2,172	0
Human Health and Disease	3,458	3,008	3,000
Data Management Center for the Mapping Centers	2,998	0	0
Technology Development in Epigenetics	3,494	3,870	0
Pharmacology	3,750	4,051	4,000
Subtotal, Epigenomics	14,035	13,101	7,000
Extracellular RNA Communication			
Data Management and Resource/Repository (DMRR)	2,595	2,722	2,438
Reference Profiles of Human Extracellular RNA	80	4,075	4,078
Extracellular RNA Biogenesis, Biodistribution, Uptake, and Effector Function	7,220	7,443	7,233
Clinical Utility of Extracellular RNAs as Biomarkers and Therapeutic Agents	7,831	8,808	14,132
Subtotal, Extracellular RNA Communication	17,726	23,048	27,881
Genotype-Tissue Expression (GTEx) Resources			
Genotype-Tissue Expression (GTEx) Resources	31,872	51,973	9,649
Health Care Systems Research Collaboratory			
NIH-HMORN Coordinating Center	2,694	2,505	1,733
Expansion Activities	0	9,760	10,755
Subtotal, Health Care Systems Research Collaboratory	2,694	12,265	12,488
Illuminating the Druggable Genome			
Knowledge Management Network	0	3,096	3,091
Technology Development	0	2,604	2,609
Subtotal, Illuminating the Druggable Genome	0	5,700	5,700
Strengthening the Biomedical Research Workforce			
Director's Workforce Innovation Award to Enhance Biomedical Research Training	3,727	6,750	6,750
Undiagnosed Disease Program			
Undiagnosed Diseases Program Network	10,341	18,770	28,800
Training in the Use of Contemporary Genomic Approaches to Rare Disease Diagnostics	300	980	900
Subtotal, Undiagnosed Disease Program	10,641	19,750	29,700

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

Title of Initiative	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Building Blocks, Biological Pathways and Networks			
National Technology Centers for Networks and Pathways (TCNPs)	9,762	110	0
Bioinformatics and Computational Biology			
National Centers for Biomedical Computing	3,436	0	0
Re-engineering the Clinical Research Enterprise			
Translational Research Core Services	4,972	0	0
Dynamic Assessment of Patient-Reported Chronic Disease Outcomes	4,143	319	0
Enhance Clinical Research Training via the National Multi-disciplinary CR Career Development Program and CRTP and MSTP Expansions	1,066	1,100	0
Subtotal, Re-engineering the Clinical Research Enterprise	10,181	1,419	0
Library of Integrated Network-Based Cellular Signatures (LINCS)			
Perturbation-Induced Data and Signature Generation Centers (U54)	5,303	10,000	10,000
New laboratory-based technology development	2,686	0	0
Computational Tool Development and Integrative Data Analysis	1,686	0	0
Data Integration	15	0	0
Subtotal, Library of Integrated Network-Based Cellular Signatures (LINCS)	9,690	10,000	10,000
Gulf Long-term Follow-up of Workers Study			
Gulf Long-term Follow-up of Workers Study	5,459	2,500	0
Global Health			
Medical Education Partnership Initiative (MEPI)	2,910	3,000	0
Human Heredity and Health in Africa (H3Africa)	6,710	9,302	9,102
Subtotal, Global Health	9,620	12,302	9,102
Health Economics			
Changing Incentives for Consumers, Insurers, and Providers	1,319	625	665
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	2,783	3,943	4,395
Economics of Prevention	3,689	3,648	3,197
Data Infrastructure to Enable Research on Health Reform	1,723	495	77
Subtotal, Health Economics	9,514	8,711	8,334
Human Microbiome			
Sequence a Reference Set of Genomes	0	1,958	0
Demonstration Projects	742	0	0
Evaluation of multi-'omic data in understanding the microbiome's role in health and disease	5,403	6,892	5,000
Subtotal, Human Microbiome	6,145	8,850	5,000
NIH Center for Regenerative Medicine (NCRM)			
NIH Center for Regenerative Medicine (NCRM)	2,351	1,210	1,000
Good Manufacturing Process (GMP)	250	250	250
Cell Therapy Projects	0	4,040	4,250
Cell-Based Screenings	0	2,500	2,500
Subtotal, NIH Center for Regenerative Medicine (NCRM)	2,601	8,000	8,000

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

Title of Initiative	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Metabolomics			
Comprehensive Metabolomics Research Cores	12,822	12,796	10,935
Interdisciplinary Training in Metabolomics	4,322	3,553	3,554
Metabolomics Technology Development	2,381	2,513	2,502
Metabolomics Reference Standards Synthesis	1,263	1,880	1,960
Metabolomics Data Sharing and Program Coordination Core	964	2,489	1,913
Subtotal, Metabolomics	21,752	23,231	20,864
Molecular Libraries and Imaging			
Creation of NIH Bioactive Small Molecule Library & Screening Centers	46,029	574	0
Cheminformatics	243	0	0
Technology Development	121	0	0
Subtotal, Molecular Libraries and Imaging	46,393	574	0
Knockout Mouse Phenotyping Program			
Production, Characterization, and Cryopreservation	6,264	9,711	6,449
Phenotyping and Data Release	7,814	6,501	6,701
Data Coordination	657	488	550
Subtotal, Knockout Mouse Phenotyping Program	14,735	16,700	13,700
Nanomedicine			
Nanomedicine Development Centers	12,000	12,000	0
Protein Capture			
Antigen Production	49	900	0
Production of anti-TF antibodies	4,144	4,054	4,875
New Reagent Technology Development and Piloting	4,842	6,046	6,125
Subtotal, Protein Capture	9,035	11,000	11,000
Regulatory Science			
Advancing Regulatory Science through novel research and science-based technologies	24	0	0
Microphysiological Systems for Drug Efficacy and Toxicity Testing	6,010	5,300	4,000
Drug Repurposing	12,878	0	0
Subtotal, Regulatory Science	18,912	5,300	4,000
Structural Biology			
Membrane Protein Production	7,792	368	0
Single Cell Analysis			
Pilot Studies to Evaluate Cellular Heterogeneity	5,439	7,797	5,882
Exceptionally Innovative Tools and Technologies for Single Cell Analysis	3,073	4,505	4,550
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	5,619	7,998	7,716
Single Cell Analysis Challenges	60	1,061	1,100
Subtotal, Single Cell Analysis	14,191	21,361	19,248
Science of Behavior Change			
Mechanisms of Change	4,233	3,775	0
Strategic Planning Funds	2,431	5,413	2,611
Subtotal Common Fund	513,476	533,039	476,045
New Initiatives in Common Fund	0	0	106,994
Total Common Fund	513,476	533,039	583,039

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 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 + /- FY 2014
BA	$513,475,595	$533,039,000	$583,039,000	$50,000,000
FTE	0	0	0	0

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

Director's Overview

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, Common Fund programs tackle major challenges in biomedical research that affect many diseases or conditions or that broadly relate to human health. 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. Many Common Fund programs support the NIH Director's priority themes for FY 2015:

1. Today's basic science for tomorrow's breakthroughs
2. Precision medicine
3. Big opportunities in big data
4. Nurturing talent and innovation

Additionally, the Common Fund's High-Risk High-Reward program supports four unique awards for exceptionally creative and innovative scientists at various career stages who propose highly innovative approaches to tackle the most pressing contemporary challenges in biomedical research.

Program Portrait: High-Risk High-Reward Research

FY 2014 Level: $197.6 million
FY 2015 Level: $175.8 million
Change: -$21.8 million

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, the High-Risk High-Reward program (http://commonfund.nih.gov/highrisk/index.aspx) supports four complementary initiatives that support exceptionally creative scientists proposing innovative and transformative research in a scientific area of their choosing. These initiatives include the Pioneer Awards, New Innovator Awards, Transformative Research Awards, and Early Independence Awards.

Since the CF HRHR program tests new ways of supporting innovation, the NIH commissioned a rigorous external evaluation of the most mature of these initiatives, the Pioneer Awards. Comparison of research from Pioneer Awards, R01s, and research funded by the Howard Hughes Medical Institute (HHMI) showed that the Pioneer program has been successful in attracting and supporting research that is more innovative and has greater impact than R01s, and it is comparable to HHMI-supported research. Based on the success of the High-Risk High-Reward program, ICs have embraced these funding mechanisms and have committed to their support. While the CF will provide the first year of support for new Pioneer and Transformative Research Awards, ICs will support outyear costs. The CF will continue to fully support New Innovator and Early Independence Awards. Through a combination of CF and IC support, the overall NIH investment in these initiatives is steady, demonstrating NIH's commitment to nurturing scientific talent and innovation.

Overall Budget Policy: The FY 2015 President's Budget Request for the Common Fund is $583.039 million, an increase of $50.000 million, or 9.4 percent above the FY 2014 Enacted level. The Common Fund will continue to support high priority research with trans-NIH relevance in FY 2015. 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 limited-term Common Fund investment can have a catalytic impact.

Selected Program Narratives

The Common Fund supports more than 25 programs, most of which 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. These programs span a wide range of biomedical research fields and encompass both basic and translational research. We highlight here programs that exemplify the science supported.

Big Data to Knowledge (BD2K)

As biomedical tools and technologies rapidly improve, researchers are producing and analyzing an ever-expanding amount of complex biological data called "Big Data." As one component of an NIH-wide strategy, the Common Fund, in concert with the NIH Institutes and Centers, is supporting the Big Data to Knowledge (BD2K) program (http://commonfund.nih.gov/bd2k/), which aims to facilitate broad use of biomedical big data, develop and disseminate analysis methods and software, enhance training in the science of big data, and establish a network of collaborating centers of excellence. Begun as a planning phase in FY 2013 and ramped up in FY 2014, the BD2K program will undergo further expansion in FY 2015 with the planned support of a data catalogue, frameworks for the development of community-based standards, software development, and establishment of NIH-initiated Centers of Excellence for biomedical big data.

Budget Policy: The FY 2015 President's Budget estimate is $49.832 million for the BD2K program, an increase of $31.105 million or 166.1 percent above the FY 2014 Enacted level. This estimated increase in funding will be used to support activities described above.

Enhancing the Diversity of the NIH-Funded Workforce

The Enhancing the Diversity of the NIH-Funded Workforce program (http://commonfund.nih.gov/diversity/) aims to develop and test innovative approaches to biomedical research training and mentoring. The impetus for the program is the recognition that current efforts in this arena over the past two decades have not resulted in significant change at a population level: individuals from racial and ethnic minorities, from economically disadvantaged backgrounds, and those with disabilities remain underrepresented in biomedical research. Although these individuals enter college and express an interest in science at the same rate as majority students, they do not persist in science training at the same rate. Social science research has tested interventions on a small scale that could alter this trend; the Common Fund program will provide funds to test these ideas and other innovative approaches on a large scale to determine what works and for whom. This program consists of three highly integrated initiatives: a National Research Mentoring Network (NRMN), which will develop and implement novel mentoring strategies nationwide; the Building Infrastructure Leading to Diversity (BUILD) initiative, which will develop novel training approaches, including the support of training infrastructure and faculty support; and the Coordination and Evaluation Center (CEC), which will bring the whole consortium together and develop methods of evaluating each new approach. The program was launched with six-month planning grants in FY 2013 for BUILD and the NRMN. Five year awards will be issued in FY 2014 for BUILD, NRMN, and the CEC. Awardee institutions, in partnership with the NIH, will develop and test hypotheses about how to best prepare people from diverse backgrounds for research careers, with the expectation that transformative models for training and mentoring will be developed and trainees will advance to successful careers in biomedical research. Proven approaches will be broadly disseminated to provide maximum impact for diverse trainees across the country. In FY 2015, the BUILD initiative will expand to incorporate additional trainees.

Program Portrait: Building Infrastructure Leading to Diversity (BUILD) initiative: one component of the Enhancing the Diversity of the NIH-Funded Research Workforce program

FY 2014 Level: $27.8 million
FY 2015 Level: $35.2 million
Change: + $7.4 million

Although several training programs have been developed which aim to support diverse student groups, BUILD is unique in its partnership with the CEC and NRMN. Several innovative training strategies will be tested through BUILD, but exposure to meaningful research experiences is expected to be a common component of these awards. Student exposure research at the undergraduate stage is one variable associated with improved academic performance and sustained interest in research careers in the basic and biomedical sciences. The Building Infrastructure Leading to Diversity (BUILD) initiative, one of three initiatives within the Enhancing the Diversity of the NIH-Funded Workforce program, will therefore emphasize research opportunities for students as one effective way to motivate students from diverse backgrounds to enter into and persist in biomedical research career paths . However, even within this aspect of BUILD awards, important questions of efficacy will be addressed to determine optimal practices for provision of scholarships, lab training methods, etc. To add to this approach, BUILD awardee institutions will develop additional highly creative and innovative methods to engage students in research, including those highly talented individuals who might otherwise not elect research careers. Flexibility to innovate is a hallmark of the BUILD initiative, and institutions are expected to develop transformative approaches that leverage and move beyond existing programs and paradigms. The CEC will monitor success of these approaches in real time, and adjustments will be made throughout the life of the awards to optimize success. Successful approaches are ultimately expected to supplant less effective practices and methods to have a broad and sustained impact.

The BUILD Primary (applicant) Institution eligibility criteria are intended to target funds to relatively under-resourced institutions (less than $7.5 million in annual NIH research project grant funding) with a demonstrated commitment to students from financially disadvantaged backgrounds (at least 25% of students must be Pell grant recipients). These institutions typically emphasize undergraduate training and may be ideally poised to encourage students from diverse backgrounds to enter research careers. BUILD Primary Institutions are encouraged to form partnerships to broaden the potential pool of participating students and maximize opportunities for research training and faculty and staff development. Potential partners include Graduate/Medical Partners (medical and graduate institutions that do not have undergraduate programs but do engage in research activities and that receive less than $7.5M annually in NIH research project grant funding), Pipeline Partners (two- or four-year undergraduate institutions that will expand the pool of students engaged in BUILD activities), and Research Partners (research-intensive institutions). Motivation for all partner institutions to participate is expected to be the recognition that diversity – in background, race, ethnicity, physical ability, disciplinary thought, etc. – drives innovation and that this is required for scientific progress.

Budget Policy: The FY 2015 President's Budget estimate is $39.425 million for the Enhancing the Diversity of the NIH-Funded Workforce program from the Common Fund, an increase of $6.918 million, or 21.3 percent above the FY 2014 Enacted level. The estimated increase in funding will be used to support additional trainees within the BUILD initiative.

Epigenomics

The Common Fund's Epigenomics program (http://commonfund.nih.gov/epigenomics/) is developing resources, tools, and technologies to enable investigations of the role of epigenomic

modifications (modifications to DNA that do not change gene sequence, but can alter gene expression) in human health and disease. The Epigenomics program has almost 90 reference maps of epigenomic modifications in healthy human cells and tissues, as well as numerous resources and tools that are being disseminated to and used by the biomedical research community. Researchers in the Epigenomics program have published landmark studies on the role of epigenomic modifications in normal development and disease, including recent papers that reveal important insights about the role of epigenomic changes during development as stem cells differentiate into specific cell types, such as heart, brain, and skin. In FY 2013, the Epigenomics program launched a Functional Epigenomics initiative, which aims to develop novel tools and technologies to enable manipulation of the epigenome in a tissue, cell, or gene-specific fashion, and/or with temporal control. Such tools and technologies are needed for precise manipulation of the epigenome in order to discover fundamental biological principles, as well as develop novel epigenomic therapeutics. In FY 2015, the Epigenomics program undergoes a planned decrease due to the completion of the Technology Development in Epigenetics initiative.

Budget Policy: The FY 2015 President's Budget estimate is $7.000 million for the Epigenomics program, a decrease of $6.101 million, or 46.6 percent below the FY 2014 Enacted level. This decrease reflects the planned completion of the Technology Development in Epigenetics initiative and the Epigenomics Mapping Centers.

Extracellular RNA Communication

Ribonucleic acid (RNA) was once thought to exist in a stable form only inside cells, where it served as an intermediate in the translation of proteins from genes. However, recent research indicates that RNAs can play a role in a variety of complex functions, including newly discovered mechanisms of cell-to-cell communication via RNAs that are exported from the cell. The impact of these extracellular RNAs, or exRNAs, is currently unknown. The Common Fund's Extracellular RNA Communication program (http://commonfund.nih.gov/exrna/) aims 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 Extracellular RNA Communication program is supporting awards with the following aims: 1) to determine the biological principles that guide exRNA generation, secretion, uptake, and function; 2) to develop a catalogue of exRNAs found in healthy human body fluids; 3) to identify exRNA biomarkers that can be used to diagnose and monitor disease progression and response to therapy; 4) to develop and demonstrate the potential for clinical utility of exRNAs as therapeutic agents; and 5) to develop a community-wide resource for exRNA standards, protocols, and data. In FY 2015, awards in the Clinical Utility of exRNAs for Biomarker and Therapy Development initiatives will expand from pilot studies to pre-clinical qualification and validation studies.

Budget Policy: The FY 2015 President's Budget estimate is $27.881 million for the Extracellular RNA Communications program, an increase of $4.833 million, or 21.0 percent above the FY 2014 Enacted level. The estimated increase in funding will be used to support expansion of successful pilot studies using exRNAs as biomarkers or therapeutics to pre-clinical studies.

Genotype-Tissue Expression (GTEx)

Some diseases result from sequence variation within the protein-coding region of specific genes; however, 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) program (http://commonfund.nih.gov/GTEx/) provides data on how human DNA variation correlates with variation in gene expression levels, which is often caused by changes in DNA that lie outside of the gene coding region. These data will strengthen the power of genome-wide association studies to identify potential new gene targets for therapies. Initiated in FY 2010 as a two-year pilot, and having met the milestones of the pilot phase, GTEx underwent an expansion in FY 2013 to build a comprehensive data and sample resource of genetic variation and gene expression profiles in multiple human tissues. The GTEx program has been highly successful in procuring samples, extracting high quality RNA from tissues, and obtaining data from gene expression array and RNA sequencing experiments. Additionally, a number of Standard Operating Procedures and best practices for specimen collection are in place and available for use by the biomedical research community. Data and biospecimens are being made available to the research community to support additional molecular analyses of GTEx samples that will add scientific value to the resource as a whole. In FY 2015, tissue procurement efforts will wind down, as the GTEx program focuses on data generation and analysis.

Budget Policy: The FY 2015 President's Budget estimate is $9.649 million for the GTEx program, a decrease of $42.324 million, or 81.4 percent below the FY 2014 Enacted level. The estimated decrease reflects the planned reduction in tissue procurement activities.

Health Care Systems (HCS) Research Collaboratory

The Health Care Systems (HCS) Research Collaboratory program (http://commonfund.nih.gov/hcscollaboratory/) aims to strengthen the national capacity to implement cost-effective large-scale research studies that engage health care delivery organizations as research partners. This program will 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 guidelines and best practices for the effective conduct of research studies in partnership with health care systems. The HCS Research Collaboratory also supports efficient, large-scale pragmatic clinical trials focused on the management of patients with multiple chronic health conditions. The pragmatic trials must address questions of major public health impact and test interventions that can be applied broadly to the patient population and are suitable for use in many health systems, with the broad goal of determining whether the interventions improve health outcomes of patients with multiple chronic conditions.

Budget Policy: The FY 2015 President's Budget estimate is $12.488 million for the HCS Research Collaboratory program, an increase of $0.223 million, or 1.8 percent above the FY

2014 Enacted level. This level of funding reflects the planned decrease in support for the coordinating center, and an increase in support to allow expansion of successful pragmatic clinical trials for multiple chronic conditions from a planning phase to an implementation phase.

Illuminating the Druggable Genome (New in FY 2014)

The Illuminating the Druggable Genome (IDG) program (http://commonfund.nih.gov/IDG/) aims to increase our understanding of the properties and functions of poorly understood proteins within four of the most commonly drug-targeted protein families: the G-protein coupled receptors (GPCRs), nuclear receptors (NRs), ion channels, and protein kinases. This program is expected to catalyze discovery of truly novel biology and identify proteins as candidates for further exploration as targets for therapeutic development. The IDG program will support the adaptation and development of scalable technologies to enable exploration of large numbers of proteins within the four protein classes that represent the druggable genome, using medium- to high-throughput approaches rather than repeating the "one at a time" approach that might otherwise be undertaken. A Knowledge Management Center will be established to develop an integrated informatics solution that encompasses data accrual, analysis, data-driven prioritizations, and abstraction that will help identify gaps in knowledge of these proteins, as well as a web portal to promote efficient and user-friendly query and browsing tools that will bring together information from multiple data sources.

Budget Policy: The FY 2015 President's Budget estimate is $5.700 million for the Illuminating the Druggable Genome program, no change from the FY 2014 Enacted level. The estimated funding level reflects ongoing support for the Knowledge Management Center and technology development.

Strengthening the Biomedical Research Workforce

The Strengthening the Biomedical Research Workforce program (http://commonfund.nih.gov/workforce/) aims to enhance training opportunities for early career scientists to prepare them for a variety of career options in the dynamic biomedical research workforce landscape. This program is supporting the Broadening Experiences in Scientific Training (BEST) awards to develop innovative approaches to complement traditional research training in biomedical sciences. Awardee institutions are collaborating with non-academic partners to ensure that experts from a broad spectrum of research and research-related careers contribute to coursework, rotations, internships, and other forms of exposure for trainees. Awardee institutions are working together to define needs and share best practices so that proven approaches can be broadly disseminated and adopted by the biomedical research training community. This program is expanding in FY 2014 to accommodate a second group of institutions; support for these awards will continue in FY 2015.

Budget Policy: The FY 2015 President's Budget estimate is $6.750 million for the Strengthening the Biomedical Research Workforce program, no change from the FY 2014 Enacted level. The estimated funding level reflects ongoing support for two cohorts of BEST awardees.

Undiagnosed Diseases Network

It is estimated that rare diseases affect 25 to 30 million Americans. Often times, because their diseases are so uncommon or have never been described before, these individuals go for long periods of time without a diagnosis, as do those with rare variants of common diseases. To aid in the diagnosis of rare and new diseases, the Common Fund's Undiagnosed Diseases Network (UDN) (http://commonfund.nih.gov/diseases/) is establishing clinical sites at academic centers across the country. The UDN builds upon the experience and expertise of the NIH intramural Undiagnosed Diseases Program, established in 2008, and its cross-disciplinary approach to diagnosing both rare and new diseases. This Network will catalyze the field of rare disease research by bringing state of the art medical and genomic approaches to bear on a myriad of diseases, bringing together basic and clinical researchers to elucidate underlying biological mechanisms to identify treatments and training the next generation of clinical researchers to use these approaches in disease diagnosis. 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. Furthermore, through the support of mechanistic studies, the Network hopes to aid in disease management strategies for patients. In FY 2015, the Network clinical sites and coordinating center will expand as the Network begins to increase patient recruitment.

Budget Policy: The FY 2015 President's Budget estimate is $29.700 million for the Undiagnosed Diseases Network, an increase of $9.950 million, or 50.4 percent above the FY 2014 Enacted level. The increased level of funding will support expansion of Network clinical sites, core laboratories, and the coordinating center as this program increases patient recruitment.

Strategic Planning and Evaluation

The Common Fund's ten year restriction on support for any given program is designed to create a churn of funds so that new challenges and opportunities may be addressed each year. Strategic Planning is therefore a critical activity for the Common Fund. Conducted annually, the Strategic Planning process allows the NIH to be nimble and adaptive to the changing scientific landscape. This process is a collaborative activity between the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)/Office of Strategic Coordination (OSC) and the ICs. Common Fund strategic planning encompasses both the identification of broadly relevant scientific challenges and opportunities for strategic investments using the Common Fund (Phase 1 planning), and the articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic identified in Phase 1 (Phase 2 planning). Phase 1 strategic planning involves gathering broad input from external stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Phase 2 strategic planning involves more specific consultations with external experts, analysis of the NIH and worldwide portfolios of research on the given topic, and literature reviews to articulate specific gaps and areas of research where opportunities for transformative progress are possible.

Since Common Fund programs are goal driven, evaluation is critical and increasingly important as more programs near the end of their support period. Evaluation is also conducted as a

partnership between DPCPSI/OSC and the ICs, and it includes both formal and informal evaluative activities. Informal evaluation involves convening grantees and NIH-wide teams to review progress, discuss new challenges, and develop strategies to adapt as part of routine program management. It also involves gathering input from external consultants and using their input, together with internal analysis, to help guide the implementation of the program. Formal evaluations involve the development of baseline data for new programs and the development of multiple metrics of outcomes. Utility of data, resources, technologies, etc. are assessed through surveys and the analysis of bibliometric data.

Budget Policy: The FY 2015 President's Budget estimate is $2.611 million, a decrease of $2.802 million, or 51.8 percent below the FY 2014 Enacted level. The 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. New programs for FY 2015 may address: 3-D Nucleome, Bioelectronic Medicines, Citizen Science, Glycomics, and/or Mechanisms Underlying Benefits from Physical Activity. These programs may change in nature or scope depending on scientific opportunities and/or available funding.

- 3D Nucleome: To study nuclear architecture and its relationship to gene expression and cellular function; to explore the role of epigenetic modifications and chromatin remodeling in nuclear architecture; to uncover mechanisms governing lineage specific 3D nuclear conformations and their perturbation in disease states; and to develop tools and databases to enable the study of the 3D nucleome.
- Bioelectronic Medicines: To establish precise and effective methods to stimulate the peripheral, autonomic, and enteric nervous systems and thereby control the function of physiologic systems and treat multiple diseases and conditions. This potential program, if implemented, will be DARPA-like in nature, representing a high risk, goal-driven endeavor to develop proof of concept for an entirely new class of neural control devices that have the potential to precisely treat a wide variety of diseases and conditions.
- Citizen Science: To assess the infrastructural and computational needs associated with direct engagement with the public in data collection, donation, and analysis; investigate the ethical, legal, and social implications of biomedical research using citizen science methods.
- Glycomics: To facilitate the functional analysis of sugar compounds which are attached to most proteins. Currently, such analyses require highly specialized expertise. This program, if implemented, would develop tools and methods that would extend the analysis to a wider group of scientists.
- Mechanisms Underlying Benefits from Physical Activity: To explore the molecular and cellular mechanisms that underlie benefits of physical activity; to identify functions of

genetic networks activated by physical activity; to determine common physiologic and biochemical mechanisms by which physical activity improves health and well-being, and the thresholds needed for benefits to occur; and to develop standardized protocols, tools, measures, etc. to allow for generalizability and meta-analyses.

Additionally, several Common Fund programs will be reaching the end of their first phase of support in FY 2014, and ongoing planning activities are assessing whether a second phase of funding is needed to reap maximum benefit from the program. The programs that may receive a second phase of funding beginning in FY 2015 are the Gulf Long-term Follow-up of Workers Study, Medical Education Partnership Initiative (within the Global Health program), and Science of Behavior Change.

Budget Policy: In the FY 2015 President's Budget estimate, the Common Fund has $106.994 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.