DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund

FY 2010 Budget Page No.

NATIONAL INSTITUTES OF HEALTH

Common Fund

(Dollars in Thousands)

Budget Mechanism - Total

MECHANISM	FY 2008 Actual		FY 2009 Estimate		FY 2010 PB		Change	
Research Grants:	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	154	$77,465	191	$84,006	252	$121,485	61	$37,479
Administrative supplements	(41)	2,301	(45)	2,500	(45)	2,500	(0)	0
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	152	103,210	247	172,983	242	172,983	(5)	0
Supplements	0	0	0	0	0	0	0	0
Subtotal, competing	152	103,210	247	172,983	242	172,983	(5)	0
Subtotal, RPGs	306	182,976	438	259,489	494	296,968	56	37,479
SBIR/STTR	0	0	0	0	0	0	0	0
Subtotal, RPGs	306	182,976	438	259,489	494	296,968	56	37,479
Research Centers:								
Specialized/comprehensive	39	114,155	44	128,607	45	130,536	1	1,929
Clinical research	16	44,162	2	6,443	1	3,549	(1)	-2,894
Biotechnology	21	7,992	13	5,133	13	5,210	0	77
Comparative medicine	0	0	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Subtotal, Centers	76	166,309	59	140,183	59	139,295	0	-888
Other Research:								
Research careers	48	55,505	41	47,367	15	17,367	(26)	-30,000
Cancer education	0	0	0	0		0	0	0
Cooperative clinical research	0	0	0	0		0	0	0
Biomedical research support	0	0	0	0		0	0	0
Minority biomedical research support	0	0	0	0		0	0	0
Other	34	28,052	33	27,446	33	27,858	0	412
Subtotal, Other Research	82	83,557	74	74,813	48	45,225	(26)	-29,588
Total Research Grants	464	432,842	571	474,485	601	481,488	30	7,003
Research Training:	FTTPs		FTTPs		FTTPs			
Individual awards	0	0	0	0	0	0	0	0
Institutional awards	491	19,816	496	20,014	501	20,214	5	200
Total, Training	491	19,816	496	20,014	501	20,214	5	200
Research & development contracts	0	13,186	0	13,489	0	13,691	0	202
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs		FTEs	
Intramural research	0	20,433	0	20,903	0	21,217	0	314
Research management and support	0	11,967	0	12,242	0	12,456	0	214
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	0	498,244	0	541,133	0	549,066	0	7,933

Includes FTEs which are reimbursed from the NIH Common Fund

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

Title of Initiative	FY 2008 Actual (B.A.)	FY 2009 Enacted	FY 2010 PB	Change
Molecular Libraries and Imaging				
Creation of NIH Bioactive Small Molecule Library & Screening	$85,136	$80,550	$80,200	-$350
Cheminformatics	4,038	4,100	4,100	0
Technology Development	21,494	23,300	22,000	-1,300
Development of High-Specificity/High-Sensitivity Imaging Probes	3,572	0	0	0
Imaging Probe Database	700	700	700	0
Core Synthesis Facility to Produce Imaging Probes	3,000	3,000	0	-3,000
Subtotal, Molecular Libraries and Imaging	117,939	111,650	107,000	-4,650
Building Blocks, Biological Pathways and Networks				
National Technology Centers & Metabolomics Development	16,269	11,600	11,600	0
Metabolomics Technology Development	3,915	0	0	0
Subtotal, Building Blocks, Biological Pathways and Networks	20,184	11,600	11,600	0
Structural Biology				
Membrane Protein Production	9,892	9,880	10,000	120
Bioinformatics and Computational Biology				
National Centers for Biomedical Computing	23,010	26,970	24,500	-2,470
Nanomedicine				
Nanomedicine Development Centers	25,000	25,000	25,000	0
Human Microbiome				
Sequence a Reference Set of Genomes	2,931	13,840	12,523	-1,317
Demonstration Projects	37	13,669	8,733	-4,936
New Tools and Technologies for Metagenomic Analyses	3,774	5,500	10,000	4,500
Data Coordination	2,235	2,263	2,236	-27
Resource Repository for Materials & Reagents	225	400	400	0
ELSI Studies Unique to HMP	237	500	500	0
HMP Workshops	575	635	635	0
Subtotal, Human Microbiome	10,015	36,807	35,027	-1,780
Epigenomics				
Mapping Centers	10,070	10,000	10,000	0
Human Health and Disease	163	4,000	8,000	4,000
Data Management Center for the Mapping Centers	2,997	3,000	3,000	0
Technology Development in Epigenetics	3,500	3,500	7,000	3,500
NIH International Committee on Epigenomics (NICE)	0	0	0	0
Discovery of Novel Epigenetic Marks in Mammalian Cells	3,451	3,500	4,000	500
Subtotal, Epigenomics	20,181	24,000	32,000	8,000
Connectivity Map				
Workshops	100	0	0	0
Genotype-Tissue Expression (GTEx) Resources				
Genotype-Tissue Expression (GTEx) Resources	0	0	11,127	11,127
Interdisciplinary Research				
Interdisciplinary Research Centers	42,975	39,563	39,563	0
Interdisciplinary Research Training Initiative	10,847	6,242	0	-6,242
Innovation in Interdisciplinary Technology and Methods	2,966	2,968	2,968	0
Subtotal, Interdisciplinary Research	56,789	48,773	42,531	-6,242
High-risk Research				
NIH Director's Pioneer Awards	33,801	40,600	40,600	0
NIH Director's New Innovator Awards	61,755	80,000	80,000	0
Transformative R01's	0	35,000	70,000	35,000
Subtotal, High-Risk Research	95,556	155,600	190,600	35,000
Public-Private Partnerships				
Public-Private Partnerships	641	593	0	-593
Re-engineering the Clinical Research Enterprise				
Clinical Research Policy Analysis and Coordination	1,664	11,000	0	-11,000
Feasibility of Integrating and Expanding Clinical Research Networks	700	0	0	0
Translational Research Core Services	2,569	8,000	8,000	0
Dynamic Assessment of Patient-Reported Chronic Disease Outcomes	9,436	8,190	8,190	0
Enhance Clinical Research Training via the National Multi-disciplinary CR Career Development Program and CRTP and MSTP Expansions	8,744	4,193	1,100	-3,093
Clinical and Translational Science Awards	95,652	53,224	25,245	-27,979
Subtotal, Re-engineering the Clinical Research Enterprise	118,764	84,607	42,535	-42,072
Strategic Planning Funds	171	5,653	5,463	-190
Subtotal Common Fund	498,244	541,133	537,383	-3,750
New Initiatives in Common Fund	**0**	**0**	**11,683**	**11,683**
Total Common Fund	**498,244**	**541,133**	**549,066**	**7,933**

Office of the Director
Justification
Common Fund

	FY 2008 Appropriation	FY 2009 Omnibus	FY 2009 Recovery Act	FY 2010 President's Budget	FY 2010 +/- 2009 Omnibus
BA	$498,244,000	$541,133,000	$136,837,000	$549,066,000	$+7,933,000
FTE	0	0	0	0	0

In FY 2009, a total of $136,837,000 American Recovery and Reinvestment Act (ARRA) funds were transferred from the Office of the Director. These funds will be used to support scientific research opportunities that help support the goals of the ARRA and are described in more detail below. The ARRA allows NIH to execute these funds via any NIH funding mechanism. Funds are available until September 30, 2010. These funds are not included in the FY 2009 Omnibus amounts reflected in this document.

Overview

The NIH Common Fund was enacted into law by Congress through the 2006 NIH Reform Act to support important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from conducting or supporting additional research that involves collaboration between two or more national research institutes or national centers, or would otherwise benefit from strategic coordination and planning. The Common Fund serves to encourage collaboration across the Institutes and Centers (ICs). Common Fund program priorities are determined through iterative processes that involve NIH stakeholders and NIH Leadership.

The Common Fund currently supports only those programs that collectively compose the NIH Roadmap for Medical Research. However, beginning in FY 2009 with funds made available through the Recovery Act, the Common Fund will also support trans-NIH strategic research that is not part of the Roadmap. The Roadmap will continue to be a major component of the Common Fund, encompassing programs that meet the needs of NIH as a whole, identified through a defined strategic planning process that will occur every 3-5 years. In the interim years, as new opportunities and challenges surface, the NIH Director will need to have the flexibility to respond by developing additional initiatives or funding cross-cutting, investigator-initiated projects that address strategic needs. In addition, the Common Fund may be used to foster collaborative efforts involving multiple ICs but perhaps not as broad in scope as Roadmap programs. Encouragement of such efforts was provided in the language accompanying the 2006 Reform Act, and this remains a goal for the Common Fund. Criteria for these initiatives or projects will be defined by the NIH Director.

Criteria for Roadmap programs are well established and include relevance to multiple ICs, an expectation that the program will transform the way science is conducted, little likelihood that the program will be conducted by other entities, and the expectation that the science will synergize with, or catalyze, research supported by the ICs. Roadmap programs are expected to have exceptionally high impact and are often accompanied by exceptionally high risk. A key operational expectation for Roadmap programs is that they are expected to be completed within a 5-10 year timeframe or to transition to the ICs for continued funding after that time.

Although Common Fund programs have broad, overarching goals, and do not specifically focus on individual diseases, the individual projects that make up each program oftentimes have a disease-specific relevance. For instance, there are numerous projects throughout the various Common Fund programs that support autism and cancer research.

The National Computational Biology Centers (NCBC) Program, for example, aims to support the development of innovative computation tools that support disease research in a number of areas. One of these centers has developed tools to improve genetic analyses of neurodevelopmental disorders such as autism. The Interdisciplinary Research Program has supported the development of training programs that provide investigators with training in multiple disciplines, so they can bring unique perspectives to intractable problems. One of the projects supported through this program trains postdoctoral investigators to take an interdisciplinary approach to autism, combining training in neuroanatomy, genetics, immunology, human behavior, epidemiology, and pharmacology. The Pioneer Program has also contributed to autism research through projects that address the social determinants of autism, the cognitive impact of early life epilepsy, and the use of stem cells to study the cellular basis of autism.

There are many Common Fund programs that have individual research projects focused on cancer. An example is a consortium within the Interdisciplinary Research program in which an interdisciplinary team seeks to preserve fertility in women who have a cancer diagnosis. The National Computational Biology Centers (NCBC) program also supports a center that develops computational tools to facilitate analysis of the massive data sets available to disease researchers, with an emphasis on prostate cancer data sets. The NIH Director's Pioneer Award Program, the Molecular Libraries Program, the Nanomedicine Program, the Epigenomics Program, and the Human Microbiome Program also support individual projects that address the causes of cancer as well as potential new therapies.

Plans for Common Funds provided by ARRA

Funds provided to the Common Fund through ARRA will be used to support and expand existing Roadmap programs but will also be used to address cross-cutting emerging needs and opportunities outside the Roadmap. Existing Roadmap program

areas will be supported through Challenge Grants, in which challenges that relate to the Roadmap Program areas have been articulated. They will also be supported through administrative supplements and competitive revisions to existing projects. Finally, ARRA will allow the NIH to pay additional awards through Roadmap initiatives that had been planned for FY 2008, FY 2009, or FY 2010 funding. This includes the New Innovator Program, through which the Common Fund ARRA funds will support an additional 10 investigators in FY09 and another 10 in FY 2010. ARRA funds will not be used to fund additional Pioneer Awards, since these are five year awards, and the Common Fund budget in FY 2011 cannot accommodate the commitments that would be incurred.

The Common Fund ARRA funds will also be used to support emerging needs and opportunities that are outside the areas addressed by the Roadmap. Through the Challenge Grant Program, the NIH Director has launched a Common Fund program in Science, Technology, Engineering, and Math (STEM) Education. The challenges articulated in STEM Ed that the Common Fund ARRA funds will address the development of novel educational tools, curricula, and programs, and efforts to determine which tools, curricula, and educational approaches are most effective.

The Grand Opportunity Common Fund grants will allow the community to address emerging needs and opportunities that span the missions of multiple ICs. Common Fund GO grants are expected to develop resources, methods, and tools that can later be used by a wide spectrum of the community or to address inter-IC research areas.

Major Changes in the Fiscal Year 2010 Budget Request

The Transformative R01 program (TRO1), a high risk/high reward initiative designed as a result of strategic planning to fund ground breaking research opportunities will be expanded in FY 2010. Strategic planning within the Common Fund has also resulted in a new program entitled, The Genotype/Tissue Expression Resources, or GTEx, which will begin in FY 2010. It will allow investigators to correlate changes in genetic sequence with global changes in gene expression across many tissues.

Significant increases in existing Common Fund projects over FY 2009 levels will occur in the following areas:

Human Microbiome New Tools and Technologies:	(+$4.500M; total $10.000M)
Epigenomics in Human Health and Disease:	(+$4.000M; total $8.000M)
Technology Development in Epigenetics:	(+$3.500M; total $7.000M)
Genotype-Tissue Expression (GTEx) Resources:	(+11.000M; total $11.000M)
Transformative R01s Program:	(+$35.000M; total $70.000M)

Major decreases in existing Common Fund projects will occur in several programs as detailed below:

Most of these programs are transitioning to the ICs for continued support as planned via the incubator space concept for Common Fund Programs. The reduction in Microbial Sequencing costs was planned through the Human Microbiome Project, since large scale sequencing efforts early in the program were to be followed by later analysis. Similarly, the Demonstration Projects provide funding in FY 2009 to many pilot efforts, only some of which will demonstrate success and be continued in FY 2010.

The increased support to the Clinical and Translation Science Awards program provided by the National Center for Research Resources (NCRR) results in a substantial decrease in Common Fund support to the program. The declining Common Fund support to this program results in a decrease to the overall estimated funding for research centers and research careers.

Intramural Imaging Probe Development Center	(-$3.000M; total $0)
Molecular Libraries Technology Development	(-$1.300M; total $22.000M)
National Centers for Biomedical Computing	(-$2.500M; total $24.500M)
Sequence a Reference Set of Microbial Genomes	(-$1.300M; total $12.5M)
Human Microbiome Demonstration Projects	(-$5.000M; total $8.7M)
Interdisciplinary Research Training Initiative	(-$6.000M; total $0)
Clinical Research Policy Analysis and Coordination	(-$11.000M; total $0)
Enhance Clinical Research Training	(-$3.000M; total $1.100M)
Clinical and Translational Science Awards:	(-$28.000M; total $25.000M)

Portrait of a Program: New Common Fund Initiatives for FY 2010

FY 2008 level: $ 0.000 million
FY 2009 level: $12.000 million
Change: +$12.000 million

In FY 2010, the NIH Common Fund will spend $12.000M on programs to be determined in consultation with the new NIH Director. The core goals of the Common Fund (CF), as expressed in the 2006 NIH Reform Act, are to support cross-cutting, trans-NIH programs that require participation by at least two NIH Institutes or Centers (ICs) or that would otherwise benefit from strategic planning and coordination. These goals leave the NIH Director flexibility to select program areas based on input from the broad community, the IC Directors, and his/her own scientific judgment. The new Director will have input from the community gathered during the CF strategic planning process of 2007 and 2008; many more important and cross-cutting needs were identified during that process than the CF has been able to address to date. In addition, the IC Directors, through constant interaction with their communities are aware of emerging needs and scientific opportunities. With this input, the new NIH Director will establish priorities for the CF in FY 2010 that is both timely and responsive to the needs of NIH stakeholders.

Highlights and Progress of the NIH Common Fund Areas

Molecular Libraries and Molecular Imaging
Most drugs for the treatment of disease are small organic molecules that bind

specifically to one protein, which then modifies the behavior of that protein and its ability to interact with other cellular entities. In the pharmaceutical industry, a critical initial research and development step in drug development is to screen large libraries of small molecules in order to find those that bind to a protein of interest and has the desired properties for a suitable drug candidate. However, such extensive small molecule databases have historically not been readily available to researchers in the public sector. A publicly available repository of small molecules is important for understanding and developing cures for diseases that do not receive much attention by private pharmaceutical companies. Additionally, having a large, well-characterized database of small molecules will make it possible to understand cellular pathways with greater accuracy and precision.

The main contribution of Molecular Libraries and Molecular Imaging is the establishment of a national network of screening centers known as the Molecular Libraries Probe Production Center Network (MLPCN). In collaboration with the broad scientific community, these centers are focusing on high throughput screens (HTS), an automated procedure for simultaneously analyzing many compounds. By submitting assays to a member Center, the scientific community gains access to a large and complex repository containing the small molecules. All data from these screens are deposited in the free, online database, PubChem (http://pubchem.ncbi.nlm.nih.gov/), which was designed and implemented by Molecular Libraries and Molecular Imaging program. This public access database contains information on the available small molecules, including structural information and biological activity profiles. In addition, for each small molecule in PubChem, there are links to related databases such as scientific literature (PubMed) and the 3D Structure Database, all of which have been developed and supported by NIH researchers. In FY 2010, the Molecular Libraries and Molecular Imaging production phase will screen at least 300,000 different chemicals in at least 100 assays provided by the scientific community. Approximately $70.000M will be spent on Probe Production Centers and $8.000M will be spent on Assay Technology Development. New grants will be funded in FY 2010 to continue to increase the size and diversity of the Small Molecule Repository.

Building Blocks, Pathways, and Networks

In the human body, all biological components – from individual genes to entire organs – work together to promote normal development and sustain health. This amazing feature of biological systems is accomplished through dynamic interactions between molecules in cells, such as proteins and metabolites, which make up biological pathways. Understanding how these molecules and pathways are integrated and maintained, how they can become disturbed, and what might be done to restore disturbed pathways to their normal function is key to understanding health and disease. Although scientists can currently study interactions between molecules within cells, their ability to do is equivalent to taking a snapshot – looking at a single, isolated moment in time. To address the need for improved tools to study the dynamic nature of molecular building blocks, the NIH Common Fund launched two initiatives: the Metabolomics Initiative and the National Technology Centers for Networks and Pathways (TCNP).

The Metabolomics Initiative was conceived as a 5-year program, starting in FY 2005, aimed at development of novel technologies to study the dynamic activities and interactions of metabolites in cells. A battery of new tools, including fluorescent sensors and cellular imaging tools, has been made available to the research community through this initiative. The goal of the TCNP program was to support the development of new technologies to help researchers detect dynamic molecular events, such as protein-protein interactions, in cells. Technologies developed through these centers have enabled researchers to better understand these processes under normal conditions and under conditions where pathways are disturbed, often leading to disease. Due to its success, the program is beginning a second funding phase in FY 2009. The centers serve as an important overall resource for NIH-supported investigators by promoting collaboration with and education of biomedical researchers, as well as the transfer of technologies to other laboratories. In FY 2010, the NIH anticipates spending $12.000M on technology development and dissemination at the TCNP centers.

Structural Biology

One of the most important classes of proteins for maintaining cellular integrity and overall health is membrane-bound proteins. In order to understand better how membrane-bound proteins function, one needs to produce sufficient quantities for study in a laboratory setting; this is very difficult and is frequently the rate limiting step in any experiment using membrane proteins. The Structural Biology initiatives aim to formulate new methods and techniques for producing ample quantities of these proteins that are of a quality suitable for structural and functional studies. This is an area that has long stymied biologists and the ability to produce membrane proteins for further study would lead to major breakthroughs throughout the biological sciences. The first funds directed to support the Structural Biology initiatives were used to establish Centers for Innovation in Membrane Protein Production. In FY 2009, the Centers competed for a second phase of support by the Common Fund. In FY 2010, R01s funded through the Structural Biology program will re-compete for a second term of funding.

Bioinformatics and Computational Biology

In an age where the ability to manage and organize large amounts of varied data is necessary for research, the need for informatics tools is critical. These tools must be tailored to handle the large amount of scientific data that is generated and use engineering systems that are adapted for data analysis in the context of biological systems. The Bioinformatics and Computational Biology program, which funds the National Centers for Biomedical Computing (NCBCs) was funded beginning in 2003-2004 and began a second five-year phase of Common Fund support in FY 2009.

Nanomedicine

Nanotechnology, the study and manipulation of molecules less than 100 nanometers in size, holds tremendous promise for medical innovation. Molecules at this size have unique electronic and chemical properties that make them suitable for interacting with and reporting on physiological processes. Nanotechnology products are currently being

developed to deliver drugs to specific locations in the body, for diagnostic purposes, as sensors to measure levels of cellular components, and for imaging. The Common Fund Nanomedicine program takes things one step further. The goal of this program is to understand the mechanics of, and be able to manipulate, nanoscale biological components in a cell for specific medical purposes. For example, investigators within the Nanomedicine program are developing nanoscale protein folding machines that work within cells to manipulate proteins that control the folding of other proteins. If successful, these machines could be useful in the treatment of diseases such as Alzheimer's and Huntington's, where misfolded proteins are thought to play a role. In FY 2005, a network of eight Nanomedicine Centers at academic institutions across the country was established. The Centers will re-compete in FY 2010 for an anticipated additional five years of Common Fund support. This program is implemented through the Flexible Research Authority, which provides NIH staff with an unusually high level of flexibility in determining how funds are distributed among centers within the network. This allows funding to flow to those projects with greatest potential for clinical utility.

Human Microbiome Project

The number of microbial cells residing on or in the human body outnumbers the human cells by a factor of 100. Many of the microbes are beneficial whereas others cause disease. Bacteria have been implicated in conditions as diverse as asthma, cancer and obesity, yet the great majority of bacteria and viruses that reside on people are unidentified and uncharacterized. The Common Fund Human Microbiome Project was launched to leverage advances in high throughput genomic technologies to identify and characterize approximately 600 new human microbes and to establish precedence for a definitive, causal link between certain bacteria and disease. It will also determine whether a core microbiome is shared by all people or whether each person has a unique spectrum of microbes by sampling microbes from several body sites from multiple people. In FY 2010, $13.000M will support sequencing and cataloging efforts of these samples. In addition, $9.000M will fund grants designed to establish the link between the microbiome and disease.

Epigenomics

The completion of the Human Genome Project in 2003 provided a wealth of information about the sequence of the estimated 25,000 human genes that control normal physiology and that, if mutated, can cause disease. However, the sequence of DNA in a gene is only one level of regulation of the genetic information. Epigenetics is an emerging frontier of science that involves the study of changes in the regulation of gene activity and expression that are not dependent on gene sequence. The human epigenome is the collection of all stable modifications of the human genome structure that do not change the DNA sequence. Some human diseases, such as cancer, are known to be associated with epigenetic changes, but these changes have been difficult to study in the vast majority of human diseases. Researchers need more sophisticated tools to efficiently detect and correlate them to specific diseases or health conditions.

The Common Fund Epigenomics program includes a series of complementary initiatives, launched in FY 2008, to provide the research tools, technologies and infrastructure needed to accelerate research on the role of epigenomics in human health and disease. The Reference Epigenome Mapping Centers are developing reference epigenomes—a "map" of all epigenetic changes—in a variety of cell types that can serve as comparative normal or healthy cells in disease-specific studies. The scientific community will be able to use these maps to identify therapeutic targets and gain insights into normal biology as well as disease mechanisms. An Epigenomics Data Analysis and Coordination Center (EDACC) will analyze and coordinate data from the Mapping Centers and other epigenomics research efforts. The EDACC is creating a database of standardized datasets that will be accessible to the public. Two other initiatives launched in FY 2008 support individual investigator projects on the topics Technology Development in Epigenetics and Discovery of Novel Epigenetic Marks in Mammalian Cells. A fourth initiative, the Epigenomics of Human Health and Disease, was launched in FY 2009. In FY 2010, the Technology Development, Novel Epigenetic Marks, and Health and Disease initiatives are expected to be re-announced for Common Fund support.

Interdisciplinary Research Consortia

A major focus of the NIH Common Fund is to foster new modes of conducting research. Today, the complexities of the biological problems being examined require a range of expertise. In the past, scientists were trained in one field or technique or they focused on one type of biological system. Current biological problems and questions require that researchers access a range of techniques and expertise. This requires scientists to work with scientists whose area of expertise differs from their own. In FY 2007, the NIH awarded nine Interdisciplinary Research Consortia. These consortia are exploring new ways to integrate different scientific disciplines to address critical health challenges.

Genotype-Tissue Expression (GTEx)

The Genotype-Tissue Expression (GTEx) project aims to provide the scientific community a resource with which to study more comprehensively the relationship between genetic variation and human disease. The NIH plans to commit $11.000 million to this program in FY 2010.

Portrait of a Program: Genotype-Tissue Expression (GTEx)
FY 2009 Level: $ 0.000 million
FY 2010 Level: $11.000 million
Change: +$11.000 million

Despite the rapid progress achieved using genome-wide association studies to identify genetic changes associated with common human diseases, such as heart disease, cancer, diabetes, asthma, and stroke, a large majority of these genetic changes lie outside of the protein-coding regions of genes and often even outside of the genes themselves, making it difficult to discern which genes are affected and by what mechanism. The GTEx program will help to identify genes whose expression are affected by genetic variation, and will provide a valuable basis on which to study the mechanism of that gene regulation.

The GTEx project is a two-year pilot with the primary goal of testing the feasibility of collecting high-quality RNA and DNA from multiple tissues from approximately 160 donors identified through low post-mortem

interval autopsy or organ transplant settings. For a small subset of tissues, collection from living surgery patients will also be performed to compare to the autopsy-derived tissues. If the pilot phase proves successful, the project will be scaled up to involve approximately 1000 donors.

The project will also involve consultation and research into the ethical, legal, and social issues raised by the research, support for statistical methods development, and creation of a database to house existing and GTEx-generated data. The database will allow users to view and download computed eQTL results and provide a controlled access system for de-identified individual-level genotype, expression, and clinical data. The associated tissue repository will also serve as a resource for many additional kinds of analyses.

High-Risk High-Reward Research

Research that aims to transform science is inherently difficult – if it was either obvious or easy, the need for transformation would not exist. The difficulty associated with it brings considerable risk, but without risk, science will merely creep forward or come to a stop when roadblocks occur. A primary goal of the Common Fund is to provide opportunities for investigators to take risks when the potential impact is high, to think outside the box, and to try things that may not fare well in standard peer review which relies on solid preliminary data to support proposed hypotheses.

The Common Fund developed complementary approaches to foster innovation and promote transformation which have resulted in three separate initiatives within the High Risk/High Reward Program.

NIH Director's Pioneer Award

The NIH Director's Pioneer Award recognizes visionary scientists. In FY 2010, the NIH will fund the seventh round of the Director's Pioneer Award. Traditionally, most NIH grants to individuals are awarded to individual investigators for specific research proposals. In contrast, the highly prestigious Pioneer Awards support specific researchers and are designed to allow the researcher to conduct extensive, high-risk, highly innovative research. Awardees perform research that is broad in scope and may contribute to a transformation of new, fundamental principles within that research niche. These unique awards provide $500,000 each year in direct costs for a total of 5 years. From FY 2004 through FY 2008, 62 scientists have received this award through a combination of funds from ICs and the Common Fund. Recent publications from awardees have demonstrated progress on topics as diverse as stem cells deterioration during aging and the function of sleep.

NIH Director's New Innovator Award

The Director's New Innovator Award was launched in FY 2007 for the dual purposes of stimulating highly innovative research that has a potential to make a significant contribution to biomedical or behavioral research and supporting extraordinary new investigators. The New Innovator Awards provide up to $1.500 million in direct costs over 5 years. New investigators who have never held one of NIH's traditional investigator-initiated research project grants (often referred to as "R01s") or equivalent

NIH grant are eligible to apply for this award. From FY 2007 through FY 2008, New Innovator Awards have been given to 31 promising new investigators on the basis of their creativity and potential for innovation, funded through a combination of Common Fund and IC monies. The budget for this program in FY 2010 will support 34-35 additional investigators.

Portrait of a Program: Transformative R01s (T-R01s)

FY 2009 level: $35.000 million
FY 2010 level: $70.000 million
Change: +$35.000 million

The Transformative R01 (T-R01) program has been specifically created in the Common Fund to support exceptionally innovative, high-risk, original and/or unconventional research projects that have the potential to profoundly impact a broad area of biomedical or behavioral research. To facilitate submission and review of the boldest, most creative and high-impact proposals, the T-R01 program will pilot novel approaches to peer review and program management. A high degree of risk in these proposals is expected and welcome.

Transformative applications in any area of NIH interest were encouraged for submission. Areas of highlighted need were also emphasized in the request for applications. These areas of highlighted need were identified through a strategic planning process and included:

- Understanding and Facilitating Human Behavior Change
- Complex 3-Dimentional Tissue Models
- Functional Variation in Mitochondria in Human Disease
- Transitions from acute to Chronic Pain
- Formulation of Novel Protein Capture Reagents
- Providing an Evidence Base for Pharmacogenomics

More than 700 applications were received in 2009. There is no budgetary restriction for T-R01 applications, therefore we expect to award grants of varying size and scope.

Re-engineering the Clinical Research Enterprise

This Program seeks to enhance the efficiency and effectiveness of clinical research. The initiatives within Re-engineering the Clinical Research Enterprise strive to transform the entire system of clinical research in order to fulfill the potential of modern medicine. These initiatives will 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.

Clinical Research Policy Analysis and Coordination (CRpac)

As part of Re-Engineering the Clinical Research Enterprise Program, the Clinical Research Policy Analysis and Coordinator Program (CRpac) was formed to work toward the harmonization of clinical research policies across Government. CRpac engages relevant Federal agencies as well as private sector stakeholders to coordinate, streamline, and optimize policies and requirements for the conduct and oversight of clinical research. Among the group's specific achievements is the development of a Basal Adverse Event Report, a single baseline set of

information for reporting adverse events and unanticipated problems that is acceptable to multiple Federal agencies that includes data elements needed for adverse event and unanticipated event reporting across all types of clinical research and complies with national and international standards for data transmission and vocabularies. The Common Fund has also supported the development of a web-based portal to provide a seamless online method to submit adverse event reports. Funding is also enabling the development of a data gateway that will allow receipt of clinical trial safety data from the federal-wide adverse event portal. Achieving harmony and consistency among Federal clinical research policies is an ambitious goal that will require a sustained, long-term program. For this reason, the CRpac office is transitioning in FY 2010 to the NIH Office of the Director appropriation for continued support.

Translational Research Core Services: NIH Rapid Access to Intervention Development (RAID)

Many promising new therapeutics encounter roadblocks during clinical development. Especially vulnerable are therapeutic approaches that involve high risk ideas or therapies for uncommon disorders that cannot attract private sector investment. Where private sector capacity for drug development is limited or not available, the NIH can help to bridge the gap by providing the resources needed to facilitate development of promising new therapies for widespread clinical use.

The NIH Rapid Access to Intervention Development Pilot program (NIH-RAID) is designed to reduce some of the common barriers that block progress of therapeutic discoveries from the bench to the bedside. By providing investigators with access to drug development resources to perform scale-up synthesis, development of analytic methods, formulation, pharmacodynamics studies, and toxicology analysis, as well as expertise in the planning and submission of documents to the Food and Drug Administration, the NIH-RAID Pilot program plays an integral role in fostering the development of novel therapeutics. The NIH-RAID program currently supports eight active protocols and anticipates an additional seven projects may be added to the program by the end of FY 2009.

The NIH RAID program is expanding through the provision of supplements to existing grants that will enable investigators who have developed relevant animal models of disease to test efficacy of potential new drugs. These supplements will partner investigators with a potential new drug with those who have developed the animal models. NIH RAID is also expanding to include small businesses as eligible applicants. These expansions of the program have been implemented as a result of a review of the program by a panel of experts and are expected to result in several additional projects being funded through RAID in FY 2010.

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

PROMIS is a revolutionary effort to enhance the precision of measures of patient-reported symptoms and function. The value of many treatments is best determined by asking patients themselves about their pain, fatigue, depression, physical functioning, social function, and other important outcomes of medical care, but these parameters have often been difficult to measure reliably, PROMIS employs internet and other electronic media to gather patient input, and to report scores that are referenced to the U.S. general population.

Modern statistical methods allow for more efficient assessment, tailored to the individual, by selecting the best questions from item banks that have been previously validated and calibrated. Data from PROMIS will help to better inform clinical practice at the individual level, at lower cost, in a shorter time frame, with less patient burden and with greater precision than any existing methods. In addition, short versions of PROMIS tests can be developed and standardized from available item banks to enable customized testing of specific patient groups with multiple co-morbid disorders, something which has previously been difficult to study systematically. In the first phase of the PROMIS initiative, seven Primary Research Sites (PRS) developed survey questions and data compilation methods. Each PRS pursued independent objectives but also comprises an essential part of an integrated national effort. The success of the first phase of PROMIS reinforces the high potential of this initiative to transform the conduct of clinical research in a way that is beyond what a single institute or center could have achieved independently. The goals of the second phase of PROMIS are to validate the PROMIS domains in the context of large scale clinical trials and to develop the PROMIS system to facilitate adoption by clinical researchers. In FY 2010, the Common Fund will provide $8.200M to the PROMIS network of investigators to reach these goals.

Clinical and Translational Science Awards (CTSAs)

The CTSA program is a unique and bold venture that meets the NIH Common Fund objective to restructure and improve the clinical research enterprise. The CTSA program will transform how clinical and translational research is conducted, enabling researchers to provide new treatments more efficiently and quickly to patients. To better address the needs of the clinical research community, the longstanding General Clinical Research Centers program (GCRC), administered by NCRR are being transitioned into the CTSA program. Currently, the CTSA program is administered and funded by both the NIH Common Fund and NCRR. As the program expands, its management and function will transition solely to NCRR. It is anticipated that the Common Fund will provide $25.245 million towards the CTSA program in FY 2010.

Through the CTSAs, academic health centers (AHCs) will work as a national consortium. The CTSA infrastructure will enable institutions to enhance the research capacity developed through the General Clinical Research Center program, train a cadre of multi- and inter-disciplinary investigators, and

collaborate to translate laboratory discoveries into improved therapies for patients. To date, 24 CTSAs have been funded at AHCs throughout the country. When fully implemented in 2012, approximately 60 CTSAs will be linked together to energize the discipline of clinical and translational science.

NIH Strategic Planning Funds

The Core Mission of the NIH Common Fund is to foster collaboration, coordination, and strategic planning activities across the NIH. To facilitate these efforts, the Common Fund began supporting trans-NIH workshops and planning activities in FY 2008 in areas related specifically to NIH Common Fund supported programs. This effort is now being expanded to all areas of research that span the missions of individual ICs, and the funds provided for these activities are being re-named NIH Strategic Planning Funds. Planning and coordinating activities funded through the Common Fund Strategic Planning Funds are expected to result in multi-IC funded research programs. These funds also contribute to costs associated with the planning and review of Common Fund programs. Approximately $5.000M/year has been allotted to this fund for FY 2010.