Common Fund Strategic Planning Report 2009

The National Institutes of Health (NIH) Reform Act of 2006 requires the Secretary of HHS, through the Director of NIH, to submit a report to Congress containing a strategic plan for funding research that, "…represents important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from conducting or supporting additional research that involves collaboration between 2 or more national research institutes or national centers, or would otherwise benefit from strategic coordination and planning.

To date, the Common Fund has been used to support research initiatives under the NIH Roadmap for Medical Research. The NIH Roadmap is an innovative approach to accelerate fundamental discovery and translation of that knowledge into effective prevention strategies and new treatments. The strategic initiatives to be funded under the NIH Roadmap will address critical roadblocks and knowledge gaps that currently constrain rapid progress in biomedical research. They will synergize the work of many NIH Institutes and Centers (ICs), and collectively represent a unique effort that no single or group of Institutes or Centers or other entity can do, but are the responsibility of the NIH as a whole.

Initiatives under the Roadmap programs are intended to be catalytic in nature and are not expected to receive long-term Common Fund support. The intent with Roadmap programs is to stimulate the development of tools or technologies, acquire fundamental knowledge and data sets, or build critical research resources. The continued use of the tools, data, and resources is to be funded through the ICs.

Although the Roadmap programs are currently the only programs funded by the Common Fund, this may not always be the case as new scientific opportunities emerge and the NIH determines how best to respond to new challenges. As the Common Fund grows, the NIH will maintain a continuous effort to be responsive to community needs while providing ongoing support for areas identified through strategic planning endeavors.

This report describes:

- The strategic planning processes undertaken to date to identify program areas currently supported by the Common Fund
- The current status of programs designed to meet the needs articulated through strategic planning
- The plans for future strategic planning efforts

I. Strategic Planning for the Common Fund, 2002-2008: the NIH Roadmap

As described in the Common Fund Strategic Plan Report of 2007, the NIH Roadmap is a series of cross-cutting programs designed to meet criteria established for pooled funds by the NIH Leadership before the Common Fund was established through the 2006 Reform Act. Since these programs were designed to address roadblocks to research, the chief criterion for Roadmap initiatives was that they should be expected to transform the way a broad spectrum of health research is conducted by overcoming specific hurdles or filling defined knowledge gaps. Specific diseases are not targeted through these programs; programs are expected to be relevant to several diseases.

The strategic planning process that was undertaken to identify these hurdles and knowledge gaps had four components:

- Brainstorming with expert panels
- Seeking input from the wider community of NIH stakeholders
- Analyzing the NIH portfolio and research conducted elsewhere to avoid redundancy
- Discussing priorities with the NIH Leadership based on criteria stated in Appendix 1

Ideas for new Roadmap programs have been generated through this process 3 times: in 2002, 2006, and 2008. In each case, roadblocks to research were articulated and programs were developed to overcome these hurdles. The following section describes the problems that have been defined, the goals of the programs that were developed as a response, and the current status of each.

II. Roadblocks addressed through the NIH Roadmap Programs and Current Status

The challenges addressed by the NIH Roadmap Programs are shown in Table 1. The budget for each program is provided in Table 2.

The first Roadmap programs were funded in September 2004. Because the immediate goals of most of the Roadmap programs involve development of novel technologies, generation of large datasets, or support of research, the impact of these programs will not likely be appreciated for some time. The real impact of these Roadmap programs will be seen in IC-funded research that uses the tools, technologies, and infrastructure built through the Roadmap.

The continuation of the earliest programs beyond the initial five years followed reviews by external expert panels that provided input on the continued need for the programs, their initial successes, and the continuing priority for the program as a Common Fund/Roadmap program. Each panel also provided input to the NIH about how the programs should be adapted in future years to meet changing needs in the community. The panels also advised the NIH on how the scientific community at large could be made more aware of the opportunities afforded them by the new technologies, tools, and data generated by the programs.

In the paragraphs below, the status of each program is summarized, as are future plans in each area.
Table 1: Roadblocks addressed by NIH Roadmap Programs

Roadblock:	Programs:
1. Clinical and Translational Research Lags Behind Basic Discoveries • Infrastructural support does not integrate necessary components for clinical and translational research. • Numbers of clinical investigators are inadequate. • Basic scientists lack the expertise necessary to move their discoveries beyond the bench. • Improved measures of clinical outcomes are needed. • Inter-agency regulatory hurdles are overwhelming.	• Clinical and Translational Science Awards (CTSA) • Clinical Research Training Program (CRTP), CTSAs • Rapid Access to Intervention Development (RAID) and CTSAs • Patient Reported Outcomes Measurement Information System (PROMIS) • Clinical Research Policy Analysis and Coordination (CRPAC)
2. Partnerships between NIH and private sector entities can be difficult to establish and cultivate.	Public-Private Partnerships
3. Traditional RO1 application and review process can hamper innovation.	High Risk High Reward
4. Interdisciplinary approaches to complex scientific problems can be difficult to develop	Interdisciplinary Research
5. Small molecular compounds are needed to explore functions of human genes and to serve as leads for therapeutic compounds that can modify activity	Molecular Libraries and Imaging
6. A scientific gulf exists between basic nanotechnology research and clinical applications	Nanomedicine
7. Limited technologies to analyze protein-protein Interactions and cellular pathways hinder therapeutic applications	Building Blocks, Biological Pathways, and Networks
8. Limited technologies for structural analysis of membrane proteins can limit drug development.	Structural Biology of Membrane Proteins
9. Computational tools that allow investigators to mine large datasets need to be developed and combined into an integrated network.	National Computational Biology Centers
10. Knowledge of the contribution of non-pathogenic microbes to human health is rudimentary.	Human Microbiome Project

11. Contributions of higher order DNA structure to human health and disease are poorly understood.	Epigenomics
12. Genome-Wide Association studies reveal genetic variations that associate with disease, but the molecular effects of the variations are difficult to unravel	Genotype/Tissue Expression Resource

Table 2: Common Fund/Roadmap Budget Data

Dollars in Millions	FY 2006 Actual B.A.	FY 2007 Actual B.A.	FY 2008 Actual B.A.	FY 2009 Enacted	2010 Request
Institute or Center Roadmap/ Common Fund Contribution	$247.3	$0.0	$0.0	$0.0	$0.0
OD Roadmap/Common Fund Contribution	$85.3	$483.0	$498.2	$541.1	$549.0
Roadmap/Common Fund	**$332.6**	**$483.0**	**$498.2**	**$541.1**	**$549.0**
Roadmap/Common Fund Percent of NIH Labor/HHS Budget Authority[1]	1.2%	1.7%	1.7%	1.8%	1.8%

[1] Adjusted for Type I Diabetes, Global Fund for AIDS, Superfund, Secretary's transfer authority for NLM.

Status of each of the programs is described in further detail below.

1. Roadblock: Clinical and translational research lags behind basic discoveries.

Programs designed to overcome this problem: Clinical and Translational Science Awards (CTSAs), Clinical Research Training Program (CRTP), Medical Scientist Training Program (MSTP), Rapid Access to Intervention Development (RAID), Patient-Reported Outcomes Measurement Information System (PROMIS), and Clinical Research Policy Analysis and Coordination (CRPAC).

A. Clinical and Translational Science Award Program (CTSAs)

Status: This program supports a national consortium that provides a foundation for clinical and translational science that will catalyze clinical and translational research and allow investigators to move more quickly toward improvements in health. The program is jointly supported by the Common Fund and the National Center for Research Resources. The CTSA program affords the provision of research services and facilities, development of information systems that link clinical research centers nationwide, expansion of the national clinical research enterprise to include community clinics, and training a new generation of clinical investigators. This program, begun in 2006, is transitioning out of the Roadmap to be supported solely by NCRR in 2015.

B. Clinical Research Training Program (CRTP)

Status: As part of the Roadmap's effort to bolster the pipeline of clinical investigators, NIH's CRTP immerses medical students in an intense 12-month research experience during which they acquire the skills necessary to become successful, independent investigators and clinicians. The training environment of the NIH campus fosters multidisciplinary approaches and provides access to unique patient populations via the largest hospital dedicated to clinical research in the world. This program, begun in FY 2004, is transitioning to full support by the NIH Clinical Center in FY 2014.

C. Rapid Access to Intervention Development (RAID)/Translational Research Core Services

Status: This program makes available, on a competitive basis, certain critical resources that are needed 1) for the development of therapeutic agents and 2) to bridge the gap between discovery and clinical testing to enable more efficient translation of promising discoveries. The RAID program is designed to reduce some of the common barriers

that block progress of therapeutic discoveries, especially in cases where efforts 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 provides the resources needed to facilitate development of promising new therapies for widespread clinical use. By providing investigators with access to drug development resources, as well as expertise in the planning and submission of documents to the Food and Drug Administration, the RAID Program plays an integral role in fostering the development of novel therapeutics. This program is expected to be continued by IC funds when it transitions out of the Common Fund in FY 2014.

D. Patient-Reported Outcomes Measurement Information System (PROMIS)

Status: PROMIS is a revolutionary effort to enhance the measurement of patient-reported symptoms and functions. In the first phase of the program (FY 2004 – 2008), PROMIS developed and tested a large survey for measuring patient-reported outcomes and created a computerized adaptive testing system which analyzes all the responses and cross checks them against each other to gain a better understanding of the patient's well being. By analyzing the answers to multiple questions, the computerized adaptive testing system arrives at a more robust, quantifiable measurement of the patient's condition. The PROMIS Program has also created a publicly available, continually updated, web-based system that allows clinical researchers to access PROMIS-validated items, domains, computerized adaptive testing, and survey forms. Preliminary results demonstrate that brief, 4-10 question surveys of symptoms and functional states administered by the computerized adaptive testing outperforms today's commonly used, paper-based, self-reporting assessment tools in common health conditions. These results are indicative of the anticipated clinical research advantage of the PROMIS tool, which yields better answers with fewer patients. This program will be supported by the Common Fund through FY 2012, after which it is expected to be supported largely through public-private partnerships in support of clinical studies.

E. Clinical Research Policy, Analysis, and Coordination (CRPAC)

Status: This program was established to help catalyze the harmonization of clinical research policies across U.S. government agencies. 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. The multiple and often inconsistent federal requirements governing biomedical research present a considerable challenge to the biomedical research community. To address this problem, CRPAC has led a major effort to enhance the consistency of regulatory requirements, facilitate compliance, and optimize the analysis and use of adverse event data. CRPAC has developed a Basal Adverse Event Report (BAER) tool, a single baseline set of medical information for reporting adverse events and unanticipated problems in clinical research that is acceptable to multiple federal agencies. The BAER includes both pre- and post-market reporting and complies with national and international standards for data transmission and vocabularies. This program, established through the Office of Science Policy (OSP) in the NIH Office of the Director, is transitioning out of the Roadmap to become a permanent activity within OSP in FY 2010.

2. Roadblock: Partnerships between NIH and private sector entities can be difficult to cultivate and maintain.

Program designed to overcome this problem: Public-Private Partnerships (PPP)

Status: This program was developed as part of NIH's efforts to facilitate new ways of conducting and supporting research, including the formation of collaborations with pharmaceutical and biotechnology industries, as well as other private entities. The program identifies appropriate partners inside and outside the NIH, as well as develops useful policies to oversee those partnerships. As part of this program, the NIH has established the Biomarkers Consortium, a complex group of related partnerships between the NIH, Food and Drug Administration, industry, and private entities that work to accelerate the development of new drugs by identifying, developing, and qualifying biomarkers, useful indicators of disease progression and effects of therapeutic interventions. This program, established through the Office of Science Policy in the NIH Office of the Director, is transitioning out of the Roadmap to become a permanent activity within OSP in FY 2010.

3. Roadblock: Traditional R01 application and review processes can hamper innovation.

Program designed to overcome this problem: High Risk High Reward Programs, including the NIH Director's Pioneer Program, NIH Director's New Innovator Program, and Transformative R01 Program.

Status: The High Risk High Reward component of the NIH Roadmap has been built with the intent of finding new ways to foster innovation by piloting new application and review processes. The Common Fund, through these programs, sets aside a small percentage of the overall NIH budget for transformative research without designating

specific funding levels for specific scientific areas. All areas compete, with the most innovative proposals receiving the funds.

A. NIH Director's Pioneer Awards

Status: This program provides funding for scientists who propose innovative approaches that have the potential to produce an unusually high impact on a broad area of biomedical or behavioral research. The awardees propose to use pioneering and transformative approaches to address major scientific problems and challenge existing paradigms. Since 2004, the program has supported 63 individual investigators. Information about this program, as well as links to awardees by year, can be found at http://nihroadmap.nih.gov/pioneer/. This program has proven to be successful at the identification of outstanding scientists and innovative projects and receives funds from both the Common Fund and various ICs. The NIH Director therefore decided to continue Common Fund support for the program for the foreseeable future.

B. NIH Director's New Innovator Awards

Status: This program supports new investigators who propose research ideas that are unusually creative and highly innovative but lack the preliminary data required to apply for an RO1 grant. Since 2007, this program has supported 61 individual investigators. Information about this program, as well as links to awardees by year, can be found at http://nihroadmap.nih.gov/newinnovator/. Launched in response to Congressional language, this program, like the NIH Director's Pioneer Program, is projected to continue with combined funding from the ICs and the Common Fund for the foreseeable future

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C. Transformative R01s

Status: A new program for 2009, this program will pilot a new way of encouraging very high impact research by removing as many administrative barriers as possible. This program provides funding for scientists who propose innovative and unconventional projects that have the potential to profoundly impact a broad area of biomedical or behavioral research. No budget cap is imposed, allowing maximum flexibility to investigators to develop complex approaches that may be beyond the budget of traditional R01s. Award decisions are made by the NIH Director based upon recommendations from a multidisciplinary group of outside experts. Areas of research have been identified that are especially "ripe" for transformation and represent areas of highlighted need, but these awards are open to all areas of investigation and no set-aside dollar figure has been established for any particular topic. If the areas of highlighted need are not adequately addressed through this program, future initiatives on these topics may be developed.

These areas include:

a) Understanding and Facilitating Human Behavior Change
b) Complex 3-Dimensional Tissue Models
c) Formulation of Novel Protein Capture Reagents
d) Providing an Evidence Base for Pharmacogenomics
e) Functional Variation in Mitochondria in Human Disease
f) Transitions from Acute to Chronic Pain

4. Roadblock: Interdisciplinary approaches to complex scientific problems can be difficult to develop.

Program designed to overcome this problem: Interdisciplinary Research (IR) Program

Status: This program overcomes barriers to interdisciplinary research by building research teams, training scientists in multiple disciplines, and changing academic research culture. The program includes initiatives to dissolve academic department boundaries within academic institutions and increase cooperation between institutions, train scientists to cultivate interdisciplinary efforts, and build bridges between the biological sciences and the behavioral and social sciences.

A total of nine IR consortia, managed by teams of NIH staff from multiple ICs, have been funded through this initiative which represents a new funding mechanism for interdisciplinary research. Through this mechanism, the NIH is piloting a new way to fund projects that cross IC missions and require cooperation among NIH staff to manage the programs. These consortia address complex problems that require novel, interdisciplinary approaches, including

aging, fertility in women who undergo cancer therapy, regenerative medicine, Fragile X Syndrome, neuropsychiatric disorders, obesity, genetic engineering strategies, stress and its effects on self control and addiction, and genomics based drug discovery. Funded in FY 2007, these consortia will be funded by the Common Fund through FY 2011. If the new funding mechanism proves worthwhile, it may continue to be utilized through IC funds for either new projects or for continuation of the existing Common Fund-initiated projects.

As part of the IR Program's efforts, the Interdisciplinary Health Research Training Program enables institutions to develop postdoctoral training programs that provide formal coursework and research training in a new interdisciplinary field to individuals holding advanced degrees in different disciplines. Another IR program, entitled Training for a New Interdisciplinary Workforce, supports scientists at the undergraduate, graduate, and post-doctoral levels by exposing them to both didactic and research experiences involving interdisciplinary and team approaches to address complex biomedical problems. These training programs, launched in FY 2004, will compete with IC-specific training programs beginning in FY 2009 for IC funds.

In an effort to help bridge the gap between medical researchers and behavioral or social scientists, the IR Program also provides exploratory/developmental grants through the Methodological and Technological Innovation in the Behavioral and Social Sciences Program to help facilitate the introduction of new methodologies and technologies to the behavioral and social sciences. These projects, funded in FY 2007, followed workshops held to foster team building in FY 2004 and FY 2006.

Finally, the IR Program encourages changes to administrative practices at NIH in ways that encourage teamwork through recognition and support of team leadership. Working with the NIH Office of Extramural Research, members of the trans-NIH IR Working Group helped design and implement the policy through which NIH now recognizes multiple principal investigators on individual projects. The recognition of multiple principal investigators represents a transformative step through which NIH seeks to foster collaboration and teamwork.

5. Roadblock: Small molecular compounds are needed to explore functions of human genes and to serve as leads for therapeutic compounds that can modify activity.

Program designed to overcome this problem: Molecular Libraries and Imaging Program

Status: This program establishes a national network of centers and supporting technologies for the discovery and development of small molecule probes to interrogate and modify biological pathways. The program currently supports a network of research centers that have identified new "probes" – molecules that are useful for research purposes and could be adapted for therapeutic use. Experts at the centers optimize and perform assays designed by academic researchers and peer-reviewed by the NIH. The centers use advanced technology to screen thousands of small molecules for their ability to bind to or inhibit a protein or protein-mediated activity of interest. In collaboration with the academic scientists who designed the assays, the center validates the "hits" and chooses a subset to improve by chemical modification. To date, the program has assembled a variety of screening assays designed to test small molecules for their ability to target proteins in critical cellular processes such as cellular transport, enzymatic reactions, and protein-protein interactions that become anomalous in multiple diseases. The screening center program moved from its pilot phase to its production phase in FY 2008 and will be funded by the Common Fund through FY2013, with co-funding from the ICs beginning in FY 2012. It is expected to transition exclusively to IC support beginning in FY 2014.

To support this large scale screening program, several support programs were developed as part of the pilot phase of the program and are continuing during the production phase. An assay development program, which funds investigators to develop high throughput screening assays for their biological area of interest, has been critical for enabling investigators to take advantage of the resources offered by the screening center. A technology development program enabled improvements to be made to the technical aspects of the high throughput screening process. In addition, an informatics component has been critical for the centralized collection of information about the molecules screened, their structures, and their activities in various assays; for allowing public access to this information; and for development of new informatics methodologies to mine the data. Finally, the library of compounds that the program has developed represents a truly unique and valuable component of the program as a whole. This collection is expected to grow from 300,000 to 500,000 compounds over the next 5 years. These components which support the screening endeavor are anticipated to transition to IC funding in FY 2014.

In addition to the small molecule screening effort, this program supports initiatives that are intended to develop novel imaging probes – in part, through adaptation of molecules that could be identified as probes through the screening centers. These initiatives have developed a database of imaging reagents and have supported the development of

novel imaging reagents. Common Fund support for the database continues through FY 2013, while future funding for the imaging probe synthesis facility will be determined later this year.

6. Roadblock: A scientific gulf exists between basic nanotechnology research and clinical applications.

Program designed to overcome this problem: Nanomedicine

Status: This program establishes a network of Nanomedicine Centers at academic institutions to help elucidate how molecular structures are constructed and how they function in order to facilitate the development of biomedical applications for nanobiology. The program seeks to determine how cellular machines operate at the nanoscale level and use these design principles to develop and engineer new technologies and devices for repairing tissue, as well as preventing and curing diseases. Designed as a 10-year program that began in fiscal year 2005, the program's first five years were intended to address fundamental basic science questions as a prerequisite to the development of therapeutic strategies. To achieve the targeted goals of this program, the NIH uses the Flexible Research Authority (FRA) provided by Congress to oversee and manage the research. The FRA facilitates the movement of funds to the most successful projects within the program. Approved for its second five-year funding period this past year, the program is now planned to continue with Common Fund support through FY 2014. This is a high risk program that expects the goals, if accomplishable, can be achieved within the overall 10 year timeframe of the program. Therefore, no IC funding beyond FY 2014 is planned.

7. Roadblock: Limited technologies to analyze protein-protein interactions and cellular pathways hinder therapeutic applications.

Program designed to overcome this problem: Building Blocks, Biological Pathways, and Networks

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Status: This program consists of two initiatives that are intended to catalyze basic studies of cellular functions by developing tools that will allow basic scientists to study protein-protein interactions and to analyze the consequences of cellular activities through examination of cellular metabolites.

The Technology Centers for Networks and Pathways develop and apply technologies to detect transient protein-protein-interactions that control the cellular functions. Five centers were established in FY 2005 to develop innovative tools to enable researchers to determine, in real time, the amounts, locations, and interactions of large numbers of individual proteins within a single cell. These fundamental needs are still pressing and unsolved, so these centers will receive additional support through the Common Fund through FY 2013.

The Metabolomics initiative was established in FY 2004 to support the development of technologies that will allow investigators to monitor cellular processes more accurately through analysis of by-products (metabolites) generated by the processes. This program was developed as a 5 year program that has been jointly funded by the Common Fund and the ICs. FY 2008 was the last year of Common Fund support for this initiative, as IC-funded investigators can now use the technologies developed, and further technical advances are being funded through the ICs.

8. Roadblock: Limited technologies for structural analysis of membrane proteins can limit drug development.

Program designed to overcome this problem: Structural Biology of Membrane Proteins
Status: This program establishes centers for Innovation in Membrane Protein Production as well as individual research projects that aim 1) to formulate new methods for producing ample quantities of cellular membrane proteins that are of a quality suitable for structural and functional studies and 2) to develop and improve technologies and methods for structural analysis. The program develops novel approaches for the production and stabilization of membrane proteins to enable determination of their structures at high resolution. These approaches are paying off, as increasing numbers of membrane-associated protein structures are being determined and facilitating drug development. The success of the protein and continued need for technology development in this area prompted the decision to fund this program for an additional 5 years through the Common Fund; funding is now expected to continue through FY 2013. After that point, the community at large is expected to use the new technologies to analyze membrane proteins and use this knowledge to design novel therapies.

9. Roadblock: Computational tools that allow investigators to mine large datasets need to be developed and combined into an integrated network.

Programs designed to overcome this problem: National Centers for Biomedical Computing (NCBCs)

Status: This program was established in 2004 to develop computational tools intended to catalyze research in the basic and clinical sciences. The centers create innovative software programs and other tools that arm the biomedical community with the methods needed to integrate, analyze, model, simulate, and share data relevant to human health and disease. Each center also works with members of the research community to develop informatics needs targeted toward specific disease areas. These "driving biological problems" include Huntington's Disease, Hypertension, Cardiovascular Disease, Alzheimer's Disease, Diabetes, Schizophrenia and Bipolar Disorder, HIV, Prostate Cancer, and heritable disorders. The set of disease areas targeted by these efforts is dynamic and responsive to needs of the community. The need for informatics is so broad and cross-cutting that this program is continuing with Common Fund support through FY 2014.

10. Roadblock: Knowledge of the contribution of non-pathogenic microbes to human health is rudimentary but could potentially transform our understanding of health and disease.

Programs designed to overcome this problem: Human Microbiome Project

Status: This program develops tools and generates resources to facilitate characterization of the human microbiome and analysis of its role in human health and disease. The program establishes links between the human microbiome and states of health and disease through several integrated initiatives.

The first was launched in FY 2007 to "jumpstart" the effort by sequencing a reference set of genomes from cultured microbes. These reference sequences will facilitate the analysis of complex mixtures of microbes to be obtained from human body sites. Beginning in FY 2009, samples from 5 body sites (skin, nose, mouth, gastrointestinal tract, and vagina) will begin to be collected from more than 100 individuals. By analyzing microbial populations at multiple body sites in normal, healthy individuals, the program builds the foundation for an advanced understanding of the degree of microbial diversity that may exist among individuals. A series of demonstration projects will build upon this foundation to analyze the microbiome in individuals with varying diseases or conditions to determine whether changes in our microbiome correlate with changes in health status.

In addition to the sequencing effort, this program supports the development of technological improvements that will enable the effort to proceed faster and with reduced costs. NIH is also working with researchers from several countries to establish the International Human Microbiome Consortium. This consortium will provide a forum for data sharing and information exchange relevant to the program. In addition, the vast amount of sequence data generated by this program will be deposited in a publicly accessible database and the sequences of the bacterial strains studied will be made available for future studies. Finally, the Ethical, Legal, and Social Implications (ELSI) of the microbiome project are being studied through a dedicated initiative.

The Human Microbiome Project will be funded by the Common Fund through FY 2012. During this timeframe for a foundation will be laid to allow the continued exploration of the human microbiome through investigator-initiated projects funded by the ICs.

11. Roadblock: Contributions of higher order DNA structure to human health and disease are poorly understood.

Program designed to overcome this problem: Epigenomics of Human Health and Disease

Status: This program seeks to help define the relationship between the modifications to DNA that alter its three dimensional structure (the epigenome) and human health and disease. Like the Human Microbiome Project, a series of integrated initiatives has been established to achieve this goal.

Studies in experimental animal models has established that diet, environmental exposures, and aging can significantly alter genetic activity by producing chemical modifications to DNA that alter the coiled structure that DNA assumes in different cell types. However, very little information is available about the way that DNA coils in normal, healthy human cells, so it is difficult to know the extent to which human disease may result from changes to this structure. To clarify this, the Epigenomics Program is enabling the development of comprehensive reference maps of the human epigenome from many different cell types. It also fosters new technologies for epigenomic analysis, an integrated Data Coordinating Center, and novel regulators of epigenomic structure.

An understanding of the human epigenome has the potential to transform knowledge about disease onset and progression, as well as to lead to novel therapeutic approaches. Together with several international partners, the NIH is working to establish an International Consortium to foster collaboration and information exchange worldwide in this endeavor. The fundamental knowledge obtained through this program will catalyze research in all areas of medicine

and increase our understanding of the genetic basis of health and disease. This program was launched with "jumpstart" funds in FY2007 but major funding began in FY 2008. It is slated to receive Common Fund support through FY 2015.

12. Roadblock: Genome-Wide Association studies reveal genetic variations that associate with disease, but the molecular effects of the variations is difficult to unravel.

Program designed to overcome this problem: Genotype/Tissue Expression (GTEx) Resource

Status: Genome-Wide Association Studies are revealing increasing numbers of genetic variations that result in susceptibility to disease. However, using this information to intercede before disease develops will require an understanding of the molecular consequences of the genetic variation. This is very difficult to unravel, since a change in DNA sequence may alter a part of the chromosome involved in regulating a gene (or genes) far removed from the sequence variant itself, and it could influence the regulation of genes in many tissues.

To overcome this problem, the GTEx program, to begin in FY 2010, will correlate genetic variability with variability in expression of many genes in many tissues. To do this, samples from 320 donors (either surgical donors or autopsy donors) will be acquired from several tissues, the genotypes determined for each, and then a gene expression profile obtained for each tissue. The genes expressed and the level at which they are expressed can then be correlated with genetic variations of the donors.

Common Fund support of this program will allow the feasibility of the approach to be determined through a two year period of support. Analysis of the data from the initial two years will determine whether further investment to scale up the approach is warranted.

III. Looking to the Future: Strategic Planning for the Common Fund

The Common Fund was established by the 2006 Reform Act to encourage strategic planning for research that crosses IC borders and coordination in program management. These core principles for the Common Fund are sufficiently broad that they provide the NIH with flexibility to determine the most pressing needs and to respond corporately to these challenges.

Through the Roadmap Programs, the NIH addresses fundamental, cross-cutting challenges that influence virtually every disease area and have potential for exceptionally high impact. Future planning for Roadmap programs will continue to involve heavy input from the public to identify common bottlenecks and to articulate cross-cutting areas of exceptional opportunity. However, as the Common Fund grows, additional types of programs may be supported that serve the stated mission of the Common Fund to encourage multi-IC planning and coordination but do not address the criteria established for the Roadmap.

While growth and diversification of Common Fund programs will depend on growth of the Fund itself, the planning strategies for all types of Common Fund programs will share the requirement that multiple ICs and their respective communities are served by each program. This will require staff from multiple ICs to interact, share information, and bring their communities together to identify gaps in knowledge, brainstorm, and articulate programmatic needs.

Facilitated by the Office of Strategic Coordination (OSC) within the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), these planning activities will involve gathering input at multiple levels to establish priorities for Common Fund dollars. Data concerning the NIH research portfolio, research conducted elsewhere, and the research needs vocalized by the community will also be used to help establish these priorities.