

FUNDING TRANSDISCIPLINARY RESEARCH

NIH Roadmap/Common Fund at 10 years

A mechanism for funding biomedical research at NIH that transcends Institute and Center boundaries is bearing fruit

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A fundamental challenge facing all institutions of science, including the National Institutes of Health (NIH), is whether their structures and disciplines, inherited from the past, continue to reflect the reality of current science and the needs of future science. Without an explicit process of adaptation to changes that often transcend established scientific structures and disciplines, the risk of missing emerging opportunities grows. This is why, 10 years ago, NIH launched an approach to the support of science that transcended all Institutes and Centers, known as the “NIH Roadmap” (1). The

POLICY NIH Director and the Director of each of the NIH Institutes engaged in a broad priority-setting exercise, informed by extramural and intramural NIH scientists, public representatives, and leaders from other government agencies and the private sector. We asked three questions: What are today’s most pressing scientific challenges? What are the roadblocks to progress and what must be done to overcome them? Which efforts are beyond the mandate of one or a few institutes, but are the responsibility of NIH as a whole? Each of the initial Roadmap programs that emerged was designed to achieve defined goals or transition to other sources of support within 10 years. As we have reached the 10th anniversary of these programs, a look back is in order.

All Institutes and Centers contributed 1% of their budgets to a common pool, and criteria were established to prioritize the many ideas that came from the consultation sessions; these criteria have changed little during the past 10 years (see the first table). With the 2006 NIH Reform Act, Congress established the NIH Common Fund within the Office of the Director, and it was authorized as a line item in the NIH budget; in fiscal year (FY) 2007, \$483 million was appropriated (1.7% of the NIH budget). The Act stipulated that the Fund could not drop to a lower percentage, and anticipated a rise to 5%. As of 2014, the budget is \$531 million (1.8% of

NIH total appropriation) (see the first figure and second table) (Fig. 1). Fig. 1

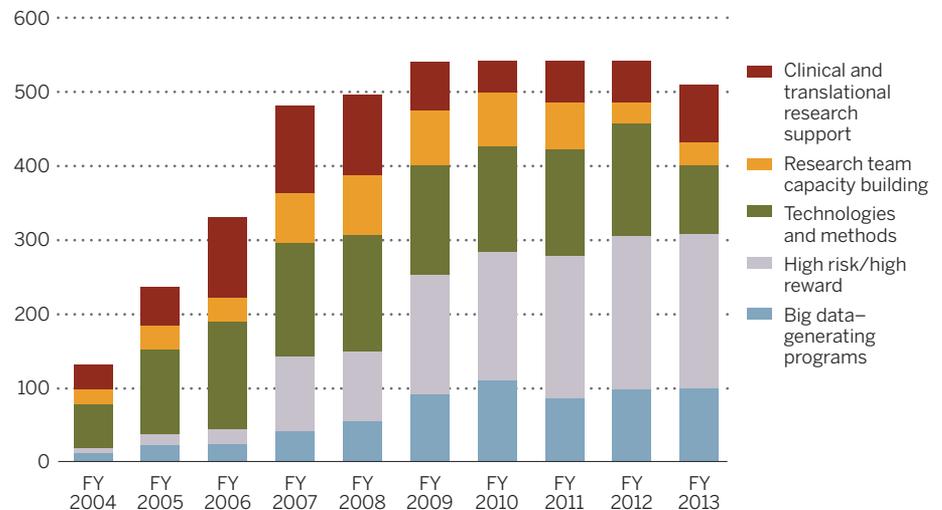
As many of the initial programs conclude this year, final outcome assessments have not been completed, but regular external scientific panel reviews and informal assessments indicate that most of the programs have had positive outcomes. The vision-setting process for the NIH as a whole has thus delivered new technologies, research tools, experimental approaches, and large data sets that are enabling investigator-initiated research across the NIH. New ways of supporting high-risk and high-reward research have been tested. We believe that it is unlikely that these goals could have been achieved without the Common Fund.

CREATION OF INNOVATIVE TOOLS AND TECHNOLOGIES. The lack of adequate tools, methods, and technologies is a challenge that has been articulated frequently during consultations with the research community. Although some NIH R01’s support tool and/or technology development, this type of research fits the transformative, catalytic requirement of Common Fund programs.

Here are a few examples: As a method to control neural activity with light, optogenetics was developed with support from Common Fund “Pioneer” and “New Innovator” Awards to Karl Deisseroth and Ed Boyden, respectively. It has revolutionized neuroscience by providing the ability to characterize neural circuits and offers potential approaches for treatment of neural disorders (2, 3). Over the past decade, investigators supported by “Structural Biology of Membrane Proteins” have developed methods and tools that have contributed to an exponentially growing number of eukaryotic membrane proteins that have been structurally analyzed (4). “Patient-Reported Outcomes Measurement Information System” (“PROMIS”) was designed to enable clinicians to obtain reproducible and quantitative feedback from patients about aspects of their health such as fatigue, anxiety, depression, social participation, and well-being. Through advances in information technology, psychometrics, and health survey research, PROMIS has generated a robust computer adaptive testing system based on item response theory that is being

Common Fund allocation by category of program

Millions (\$)



Funding by categories. Roadmap/Common Fund programs were assigned to one of five categories (12), and funds allocated to each category are shown. Some programs have relevance to more than one category, but each program was assigned to only one category.

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used to assess treatment efficacy in diverse situations (5, 6). The emphasis on developing transformative tools can also be seen in the “Knock-Out Mouse Phenotyping” Program, which provides broad, standardized phenotyping of a genome-wide collection of mouse knockouts generated by the International Knockout Mouse Consortium (7).

LARGE DATA SETS. The development of massive, publicly available data sets is perhaps the clearest example of “Common Fund-able” research: It benefits every avenue of biomedical research and would be impossible for individual investigators to achieve. The Roadmap/Common Fund has enabled large, complex data sets, such as those related to the human microbiome and the epigenome, to be provided to the entire community. End users serve as consultants to ensure that computational tools are user-friendly and meet community needs. Demonstration projects are also often included in programs that generate large data sets, (i) to provide evidence that the data are applicable to a wide spectrum of the NIH mission, (ii) to enhance the data resource, and (iii) to provide feedback to the data developers to increase the utility of the program.

ENCOURAGING RISK-TAKING. The “High Risk/High Reward” program was established in 2004 with the Pioneer Awards, which recognize and reward investigators who have demonstrated innovation in prior work and provide a mechanism for them to go in entirely new, high-impact research directions. The requirement for strong preliminary data in R01 applications was felt by many to inhibit creativity and innovation. Recently, we commissioned an independent evaluation comparing impact and innovation achieved through Pioneer, R01, and Howard Hughes Medical Institute (HHMI) funding (8). When controlled for funding, the Pioneer awardees, as a group, performed comparably to HHMI investigators, and their research was deemed more innovative, with higher impact than R01 investigators working in similar areas who had similar backgrounds and resources. The success of the Pioneer awards led to the expansion of the High Risk/High Reward program to include the “New Innovator,” “Early Independence,” and “Transformative Research” awards. The Pioneers’ success also led to the distinction of the High Risk/High Reward program as the only Common Fund program without an established end date; each individual project, however, is restricted to 5 years of support. Broader implementation of similar programs is being considered across the NIH.

CHALLENGES FOR THE COMMON FUND APPROACH. For the Common Fund to take on a steady stream of new projects, it has been essential that funded programs be completed or adopted by other funding sources after a certain period of time. One issue that has become apparent is that programs that work toward broad, long-term goals, rather than aiming to achieve a specific set of goals in 5 to 10 years, do not align well with the directives of the Common Fund. Although the broad, stimulatory goals are critical to advancing science, if an end point—a deliverable—is not envisioned in advance, it becomes difficult to assess impact. Continued funding to achieve the long-term goals may also be problematic for investigators to secure.

The “Interdisciplinary Research” program included an emphasis on recognizing and rewarding team-led science, and it contributed to the development of the multiple-Princi-

Sustainability of infrastructure also proved to be a challenge. Although future support of some of the infrastructure was built into the design of the program (10), the sustainability of other programs was to be determined by requirements at the time of transition. For example, the Roadmap “Molecular Libraries” program, aimed to provide pharmaceutical-quality small-molecule screening capacity to academic investigators, enabling them to develop screening assays for diverse cellular functions and to put screening data into publicly accessible databanks with computational tools to enable wide use. The team of investigators, external consultants, and NIH staff who contributed to the management of this program established a consortium through which innovation in assay development, screening, and computational methods is combined. Although the core infrastructure continues to evolve within the National Center for Advancing Translational

Characteristics of Common Fund programs

Transformative: Must have high potential to dramatically affect biomedical and/or behavioral research over the next decade

Catalytic: Must achieve a defined set of high-impact goals within 5 to 10 years

Synergistic: Outcomes must synergistically promote and advance individual missions of NIH Institutes and Centers

Cross-cutting: Program areas must cut across missions of multiple NIH Institutes and Centers, be relevant to multiple diseases or conditions, and be sufficiently complex to require a coordinated, trans-NIH approach

Unique: Must be something no other entity is likely or able to do

pal Investigator policy at the NIH. Although an evaluation of the program indicated that the emphasis that the program placed on interdisciplinary research did have an impact on barriers to team science at research institutions (9) and that valuable research was conducted, the success in establishing new inter-disciplines is difficult to assess. Individual consortia and training programs that were launched ultimately faced a substantial challenge in continuation. As large, investigator-initiated projects that crossed boundaries of several NIH Institutes and Centers, they did not fit easily within the traditional funding schemes of the NIH. The research was ultimately pursued via smaller awards, but the synergies of interdisciplinary teams working together were likely compromised.

With this lesson in hand, new Common Fund programs continue to support interdisciplinary teams, but specific, short-term goals for the teams are articulated. Continuation of the science happens via uptake and use of the Common Fund deliverables rather than sustained funding for the specific projects initiated by the Common Fund.

Sciences, the need for an integrated network of centers dissipated as additional screening facilities were developed by institutions across the country. Transition from central management and funding to decentralized partnerships between screening facilities and assay providers presented challenges. Today, we emphasize sustainability from the outset and work with awardees to establish a plan for the future.

The “National Centers for Biomedical Computing” (NCBCs) program aimed to develop software and data management tools to facilitate computational analysis of diverse biological problems. Each Center was established to tackle a core set of computational challenges but also collaborated with a series of partners. Although Centers interacted to develop training opportunities, the computational approaches developed through the program were largely developed by individual Centers. In an internal review of this program, it was recognized that, despite the many successes of the NCBC program (11), tighter coordination between projects—with increased expert and user

feedback obtained on a regular basis—would be necessary as the program moves forward. That experience is now being used to inform plans for the “Big Data to Knowledge” (“BD2K”) initiative.

The scientific accomplishments of the Roadmap/Common Fund have required unprecedented levels of coordination and collaboration among the leadership and staff across the NIH. Although we have had anecdotal feedback that this effort has enabled the success of the programs and has worked well, we have engaged the NIH Council of Councils to evaluate the planning and management processes used for the Common Fund. Their final report is expected later this month.

LOOKING FORWARD. As mature programs come to a close, we have the opportunity to address new, emerging challenges and opportunities. We reserve ~30% of the Common Fund for the investigator-initiated, High Risk/High Reward initiatives, but otherwise, the definition and scope of new program areas are determined by the challenges and opportunities that emerge through strategic planning activities each year. Community input continues to be fundamental to the process.

We use both virtual and in-person approaches to reach out to the entire community. One lesson learned through these discussions is that, although it is easy to identify research challenges and exciting new areas, it is more difficult to identify those where recent advances—perhaps in unrelated fields—create an opportunity to overcome the challenges within 5 to 10 years and where a coordinated, goal-driven, trans-NIH approach is required. As a result, we have launched new programs that build on lessons learned from the earlier programs. New paradigms for intercellular control of gene expression and cellular function may emerge from the “Extracellular RNA” program. New methods and models for clinical research partnerships between academic centers and health care providers are being developed by the “Health Care Systems Collaboratory” pro-

Current Common Fund programs

Big Data to Knowledge (BD2K)
Enhancing the Diversity of the NIH-Funded Workforce
Epigenomics
Extracellular RNA Communication
4D Nucleome
Genotype-Tissue Expression (GTEx)
Global Health
Glycoscience: Enabling Tools and Methods
Gulf Long Term Follow-Up Study
Health Care Systems Research Collaboratory
Health Economics
High-Risk/High-Reward Research: Early Independence Award (EIA) New Innovator Award Pioneer Award Transformative Research Awards
Human Microbiome Project
Illuminating the Druggable Genome
Knockout Mouse Phenotyping
Library of Integrated Network-Based Cellular Signatures (LINCS)
Metabolomics
Nanomedicine
NIH Center for Regenerative Medicine
NIH Medical Research Scholars Program
Protein Capture Reagents
Regulatory Science
Science of Behavior Change
Single Cell Analysis
Strengthening the Biomedical Research Workforce
Undiagnosed Diseases

gram. More recently, we have established plans to launch the “4D Nucleome.” A “Glycoscience” program to develop methods to simplify the functional analysis of glycans in diverse contexts is also under way.

The Common Fund also continues to develop new ways to enhance innovation and support the workforce by developing and testing novel methods for training and mentoring young scientists and for supporting early career stages. One new program is beginning with the recognition that the NIH mission requires participation of scientists from all sectors of our population, yet measures to diversify the biomedical workforce have not yielded the desired outcomes. Emerging opportunities from social science research provide the basis for

the Common Fund’s “Enhancing Diversity of the NIH-Funded Workforce” program: Understanding the factors that contribute to decisions by students from underrepresented groups to leave biomedical research career paths provides the opportunity to develop and test new training and mentoring methods.

CONCLUSION. Although investigator-initiated research funded through individual Institutes and Centers remains the lifeblood of the NIH, the Roadmap/Common Fund has established a tradition of bringing the biomedical research community together for coordinated, transdisciplinary collaboration when such effort is required. Although not every program has been completely successful, the synergies created by the Common Fund are inspiring, and the catalytic nature of these programs ensures that their impact will continue to grow. ■

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12. Roadmap/Common Fund programs were assigned to the categories in the figure as follows: **Big Data–Generating Programs:** National Centers for Biomedical Computing, Human Microbiome Project, Epigenomics, Genotype-Tissue Expression (GTEx), Knockout Mouse Phenotyping, Library of Integrated Network-based Cellular Signatures (LINCS), BD2K, Extracellular RNA Communications. **High Risk/High Reward program:** Pioneer, New Innovator, Transformative Research Awards, Early Independence Awards. **Technologies and Methods:** Molecular Libraries, Structural Biology of Membrane Proteins, Building Blocks/Biological Pathways/Networks, PROMIS, Protein Capture Reagents, Single-Cell Analysis. **Research Team Capacity Building:** Interdisciplinary Research, Nanomedicine, Public-Private Partnerships, Strengthening the Biomedical Workforce, Enhancing Diversity of the NIH-Funded Workforce, Global Health. **Clinical and Translational Research Support:** Clinical and Translational Science Awards and related initiatives, Clinical Research Training Program, Rapid Access to Intervention Development, Metabolomics, Health Care Systems Collaboratory, Health Economics, Gulf Long Term Follow-Up Study, NIH Center for Regenerative Medicine, Undiagnosed Diseases Network.

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