

NIH'S COMMON FUND AT 10

ALTERNATIVE FUNDING MECHANISM stimulates innovation, but ongoing support for some efforts is uncertain

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CURRENT AND PAST LEADERS of the National Institutes of Health recently celebrated 10 years of cross-cutting, transformative science supported by the Common Fund. This special fund was set up a decade ago by then-NIH director Elias A. Zerhouni to support biomedical research that cuts across scientific disciplines.

A festive, daylong symposium at NIH last month celebrating the fund and its achievements was complete with videos and songs. But beneath all of the accolades, concerns are rising about how to sustain innovative research programs when their time in the Common Fund comes to an end.

Each research program supported by the Common Fund is expected to achieve its defined goals within 10 years. After that, the program must rotate out of the fund, freeing money for other, new, potentially game-changing ideas, says NIH Director Francis S. Collins.

Initially called the NIH Roadmap for Medical Research, the Common Fund sup-

ports research that does not fit easily into any one of NIH's 27 institutes and centers, which are typically focused on specific diseases.

Programs supported by the Common Fund are expected to be groundbreaking, lead to the development of novel tools and technologies, or provide a fundamental foundation for research that can be broadly adopted.

In the beginning, Zerhouni and the directors of each of NIH's institutes and centers, with input from the biomedical community, settled on a list of 28 initiatives to support with the Common Fund. The initiatives were grouped according to three broad themes—new pathways to discovery, reengineering the clinical research enterprise, and research teams of the future. The themes are still reflected in the fund's portfolio today.

Many Common Fund proj-

ects have been successful, and some of them have even led to the creation of entirely new fields of science. For example, optogenetics was made possible because of research supported by the Common Fund, Collins says.

Optogenetics allows researchers to manipulate brain activity using light and neurons that are genetically sensitized to light. The field is an essential part of the \$100 million Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, announced by the White House last year. That effort aims to examine how individual cells and complex neural circuits interact in the human brain.

THE COMMON FUND receives a relatively small pot of money compared with the total NIH budget. When it was first announced as the Roadmap in fiscal 2004, each of the NIH institutes and centers contributed 1% of their budgets to the fund. That first year its budget totaled

\$132 million, or 0.5% of NIH's \$27.9 billion budget. Two years later, Congress gave the Common Fund its own dedicated appropriation under the NIH Reform Act of 2006.

At the time, lawmakers envisioned that the Common Fund would increase as the NIH budget grew. Congress capped the fund at 5.0% of NIH's total budget and stipulated that it could



Human Microbiome Project begins first phase.

A LOOK BACK AT THE DECADE The Common Fund celebrates 10 years of funding cross-discipline scientific research.

2004



Roadmap debuts NIH launches the Roadmap for Medical Research to fund high-risk, transformative research that cuts across scientific disciplines. Initial programs include molecular libraries and imaging, structural biology, bioinformatics and computational biology, nanomedicine, high-risk research (Pioneer Awards), interdisciplinary research, public-private partnerships, and clinical research. Francis S. Collins (right) and Elias A. Zerhouni are shown at a press conference for the launch.

2005

2006

Roadmap becomes Common Fund

Congress passes the NIH Reform Act. The Roadmap is renamed the Common Fund and is given its own separate appropriation.

2007

New Innovator Award

NIH creates this award for researchers in the early stage of their career.

2008

Epigenomics program starts.

2009

Director's Transformative Research Award created.

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Online version is available at <http://cenm.ag/nihcf10>.

NHGRI (ROADMAP DEBUTS)/USDA (HUMAN MICROBIOME PROJECT)/NOAA (GULF OIL SPILL HEALTH EFFECTS)/JONATHAN HIMMELFARB AND EDWARD KELLY/UC OF WASHINGTON (ORGAN ON A CHIP)/NIH (DRUGGABLE GENOME)

not go lower than 1.7%. But ever since, NIH's budget has been shrinking when inflation is factored in. As a result, the Common Fund has remained flat, hovering around 1.7% of NIH's total budget. For fiscal 2014 the Common Fund received \$533 million, or 1.8% of NIH's \$30.2 billion budget.

Because funds are limited, the Common Fund will support many programs for only five years, Collins says. "This is our venture capital space. This is where we try things out," he says. "If they are successful, then they should get adopted by other parts of the enterprise" at NIH.

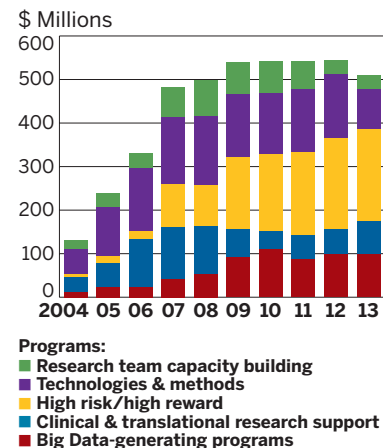
One of the more successful initiatives was the structural biology program, notes Jeremy M. Berg, a former director of the National Institute of General Medical Sciences (NIGMS) who is now at the University of Pittsburgh School of Medicine. That effort focused on membrane protein expression.

As a result, the majority of membrane protein classes now have one or more known structures, Berg says. This makes the field today quite different when compared with 10 years ago, he says.

Another successful example is the Human Microbiome Project, which was launched in 2007, Collins says. It brought together expertise across multiple institutes and disease categories. In the first

Stem cell therapy NIH establishes the Center for Regenerative Medicine to serve as a national resource for stem cell science and to accelerate the development of cell-based therapies.

A DECADE OF THE COMMON FUND High-risk, high-reward research has grown to nearly one-third of the fund's total budget.



SOURCE: NIH

phase, which lasted five years, researchers characterized the composition and diversity of microbial communities found on various sites of the human body. The project is now focused on creating a data set of microbiome properties and microbiome-associated diseases.

The effort has led to "a transformation in our understanding of the microbial environment that we are part of," Collins says. "We really are an ecosystem." The project

Big Data to Knowledge (BD2K) initiative begins.

has also generated a massive amount of data and lots of disease-oriented spin-off projects that various NIH institutions and centers are supporting, he says.

Other programs, however, haven't been as successful in finding support at NIH outside of the Common Fund. The poster child for this problem was the Interdisciplinary Research program, which was set up under the Common Fund to "cut across the grain of the NIH structure," Berg says. The program aimed to change the culture of academic research to reward interdisciplinary approaches and team science. When the program expired in 2012, many centers had been created, some of which were notably successful, Berg says. But by design, they didn't fit into any one of NIH's institutes or centers, he notes.

"It was a problem trying to find homes for them," he says. Some couldn't be continued and thus died.

Likewise, with the Molecular Libraries & Imaging program, the hope was that other institutes would step up with support, Berg says. But because of tight federal budgets, that did not happen.

The molecular libraries program was one of the first programs supported by the Common Fund. It was launched in 2004 under the Roadmap to empower the bio-

Druggable genome Illuminating the Druggable Genome program begins



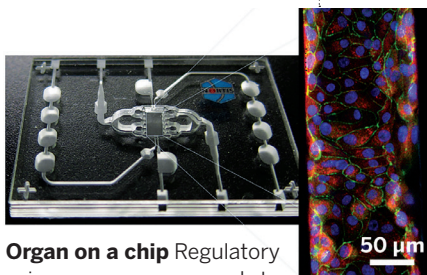
2010

Gulf oil spill health effects The Gulf Long-term Follow-up (GuLF) Study, an investigation of the potential health effects associated with the Gulf of Mexico oil spill, begins.



2011

Single Cell Analysis program commences.



Organ on a chip Regulatory science program expands to address a specific high-priority challenge to develop "human on a chip" microfluidic platforms that accurately model the structure and function of human organs.

2012

Metabolomics program starts.

2013

Diversity in the workforce NIH creates programs to strengthen and enhance the diversity of the biomedical research workforce.

2014

Ten-Year Commemoration The Common Fund celebrates 10 years.



“There will be no future of science in America unless we fund the new innovators, we fund the pioneers, and we fund them at greater levels than we do today.”

medical community to use small-molecule compounds in their research, Collins says. At the time, small-molecule screening was primarily the domain of biotech and pharmaceutical companies, he adds.

A handful of screening centers were created under the Molecular Libraries program, including one at NIH. As of this year, the library contained about 390,000 unique compounds, all of which have been studied using assays that were developed under the program, Collins says. The program “has really brought into the laboratories of many academic scientists a whole new set of tools and capabilities that simply were not there 10 years ago,” he says.

MUCH OF THE CURRENT excitement about the Common Fund is centered on a series of highly competitive awards for high-risk, high-reward research. About one-third of the Common Fund goes to support these awards. They are given to researchers for outside-of-the-box science ideas that don't have much preliminary data to back them up. One, the Pioneer Award, dates back to the start of the Roadmap.

NIH recently commissioned a study to compare the effects of Pioneer Awards with NIH's traditional funding mechanism for researchers, R01 grants. It scrutinized the impact and innovation of each. The study showed that Pioneer awardees outperformed and were more innovative than researchers funded via R01 grants. Because of those findings, various NIH institutes

are now considering the addition of this kind of award to their portfolios, given the evidence of its potential for inspiring innovative science, Collins says.

Although the Pioneer Award program has been hugely successful, that wasn't always the case, recalls Judith H. Greenberg, acting deputy director of NIGMS. The first year, the request for applications was issued quickly, and the applications were reviewed by panels that were also put together swiftly, Greenberg tells C&EN.

“It turned out, those panels contained almost no women,” she says. The first group of Pioneer Award recipients was composed of nine men, eight of whom were Caucasian. That lack of diversity raised a lot of eyebrows, Greenberg says.

At that time, Berg had just joined NIGMS as its new director. Berg went to Zerhouni and expressed disappointment to the NIH head about this lack of diversity. He also pointed out that most of the awardees were well established within the NIH grant system. Within two days, NIGMS was put in charge of the Pioneer Award program, Berg says.

Greenberg took the lead for the 2005 competition. She encouraged women and minorities to apply and made certain that these groups were represented on the review panels, she says. That seemed to make a significant difference—six of the 13 recipients that year were women.

The success of the Pioneer Award led NIH to create a similar award called the New Innovator Award in 2007. That award

is targeted at researchers in the early stage of their careers, a group of scientists who often find it difficult to get funding. That problem has long concerned Zerhouni, who believes more money should be invested in young investigators.

“There will be no future of science in America unless we fund the new innovators, we fund the pioneers, and we fund them at greater levels than we do today,” Zerhouni says. But assuming Congress does not increase NIH's budget, the money would have to come from some other part of NIH's budget.

“Frankly, this is a debate of special interests in the status quo versus the new model,” Zerhouni says. To scrutinize what is being spent with 1.7% of NIH's budget without examining the other 98.3% is not fair, he says.

Looking back over the past decade, the Common Fund has supported “an amazing portfolio of really exciting science that has brought a lot of investigators together across disciplinary boundaries to really change our view of how life works and how disease occurs,” Collins says.

Zerhouni says he is amazed at the number of Common Fund programs that have borne fruit, including a Nobel Prize in Chemistry in 2012. It went to Brian K. Kobilka, a professor at Stanford University School of Medicine and a grantee of the Common Fund Structural Biology program, for studies on a class of membrane proteins called G protein-coupled receptors.

Yet even more important, Zerhouni says, is that the Common Fund has been an agent of change. “It's been a catalyst of enabling science that would not have happened without it,” he says.

“Throughout the world people are trying to emulate the Roadmap process,” Zerhouni says. The prime minister of Japan, a country building its own NIH modeled after the U.S. institutes, recently asked Zerhouni to explain how the process works. “The international impact has been enormous,” Zerhouni says. “I think we've been a vanguard, an experiment, a pilot stage, an adventure stage, but also a new model of how to work across scientific fields and break barriers.” ■



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