Translation under one roof

By Steve Usdin, Senior Editor

NIH director Francis Collins is pushing to move more NIH research downstream, but he is facing opposition from academic groups concerned that focusing on translational research in a time of flat budgets poses a threat to basic science funding as well as skepticism that NIH has the resources or expertise to make a major impact on drug development.

Collins achieved a major victory earlier this month when NIH's Scientific Management Review Board endorsed creation of the National Center for Advancing Translational Sciences (NCATS). The board's action makes it possible for Collins to recommend the creation of NCATS to **U.S. Department of Health and Human Services** secretary Kathleen Sebelius, who is expected to notify Congress of the plan.

Barring opposition from Congress, NCATS will be launched next year, in time for it to be included in the fiscal 2012 budget.

Collins told *SciBX* that the new center is intended to help fill a growing chasm between advances in scientific understanding of disease and the availability of venture finance to turn new scientific insights into products.

Initially, the center will consist of existing translational programs—and their budgets—that are scattered around NIH's organizational chart (see **Table 1, "Consolidating translational science"**).

NCATS also will house the Cures Acceleration Network (CAN), a program authorized by the Patient Protection and Affordable Care Act that is intended to create a flexible, rapid pathway to fund translational research conducted in universities or industry.

Although the law authorizes Congress to provide up to \$500 million a year for CAN, a pending appropriations bill allocates a maximum of \$50 million for FY11.

Collins' enthusiasm for NCATS is not shared by some influential academic groups.

More than a dozen researchers who are concerned that they could lose funding as programs are folded into NCATS earlier this month asked the Scientific Management Review Board to delay its vote on establishing the new center.

The Federation of American Societies for Experimental Biology (FASEB) argued in a letter to the board that "creation of a new entity could delay translation by creating a new bureaucratic structure that is cut off from the research base" in NIH's established institutes and centers. FASEB asked the board to push back transmission of its report to Collins "to allow for a more substantive dialogue with all stakeholders and an analysis of the potential consequences of these changes."

Collins told *SciBX* that the organization's concerns are understandable but misplaced. "There is a great deal of anxiety because funding is very tight now," he said, adding that NCATS "will not have any impact on the pot of funds for FASEB members. The basic science budget at NIH is and will remain 60% of our portfolio."

In the long term, Collins said he hopes NCATS receives substantial funding, but he contended that bringing diverse translational programs together in a single, integrated organization will have a substantial impact even without new money.

Researchers funded by smaller institutes will get access to technologies and capabilities for drug development that previously were limited to the **National Cancer Institute** and the **National Institute of Allergy and Infectious Diseases**, Collins said. In addition, there will be a systematic effort to look at NIH's research portfolio to find and exploit opportunities to get science from the lab to the clinic.

Much of NIH's research leads to "discoveries that are in many ways pointers to new drug targets, and many of these targets are not being exploited, either because there is not enough economic incentive or because the target seems a little too risky," Collins said. The new center will "allow academic researchers funded by NIH to fill those gaps."

Table 1. Consolidating translational science. The proposed National Center for Advancing Translational Sciences would bring together existing NIH translational programs, which had a combined budget of over \$590 million in the fiscal year that ended Sept. 30. It would also include Cures Acceleration Network, which was authorized in the Patient Protection and Affordable Care Act but has not yet received appropriations.

Source: NIH

Component	FY10 budget (\$M)
The Clinical and Translational Science Awards (CTSAs), which support a national consortium of medical research institutions.	~\$450
The Molecular Libraries and Imaging program, which includes a consortium that performs high throughput screening against a collection of 300,000 small molecules.	\$107
The Therapeutics for Rare and Neglected Diseases (TRND) program, which performs preclinical and early clinical development of new drugs.	\$24
The Rapid Access to Interventional Development (RAID) program, which assists translational research, including synthesis and scale up production of small molecules, peptides, oligonucleotides, gene vectors, recombinant proteins and mAbs.	\$8
The NIH-FDA Regulatory Science Initiative, which is a collaborative effort to conduct and fund regulatory science research.	~\$3
The Cures Acceleration Network, which will fund collaborations between government agencies and companies to speed product development.	Not applicable

NIH's translational research efforts "are not an attempt to duplicate projects the private sector would want to undertake but rather to de-risk projects the private sector is not doing," said Collins.

NIH plans to take drug development "just far enough to develop commercial interest," he said. "As soon as a company says it wants it, we would hand it over. In some instances this might happen early in the development of a compound, and in other instances, if the market is not compelling, NIH might go to an IND or conduct Phase I or II trials."

Collins cited schistosomiasis as an example of a huge unmet medical need that the private sector has neglected because of lack of a market. "There hasn't been a new drug for schistosomiasis for 50 years and the current drug is showing resistance," he said. "NIH has already been able, using high throughput screening, to come up with a promising lead compound. It has been moved to the preclinical arena and we hope for an IND in the next year or two."

Collins also referenced NIH's collaboration, announced in November, to take an investigational sickle cell therapeutic developed by **AesRx LLC** through preclinical development and initial clinical trials. NIH's Therapeutics for Rare and Neglected Diseases (TRND) program, slated to become part of NCATS, is funding and conducting the preclinical work needed to file an IND for Aes-103, and an investigator at the **National Heart, Lung, and Blood Institute** plans to conduct clinical trials.

Aes-103 is an "example of the classic biotech 'valley of death,'" AesRx CEO and founder Stephen Seiler told *SciBX*. "Preclinical funding is increasingly hard to come by. VCs want some human clinical data."

Seiler added: "It is entirely possible this project would not have gone forward but for TRND" and collaborations with other NIH programs.

Although some projects may yield results relatively quickly, Collins said it is important to manage expectations. "Enthusiasm needs to be

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**—Francis Collins,
National Institutes of Health**

modified on the basis of reality when it comes to what can be done in a short period" with NIH's approximately \$500 million budget for translational research.

Metrics for judging NCATS should include how many projects enter the development pipeline, how many are out-licensed to companies

and "how many partnerships NIH enters into for projects that might have floundered for lack of venture capital," he said.

Although he doesn't expect quick results in general from translational research, Collins said there may be one exception: repurposing. TRND hopes to get access to compounds that have gone through sufficient testing to demonstrate safety in humans but were dropped either because they failed to demonstrate efficacy or for commercial reasons.

"We will meet in the new year with leaders in the pharmaceutical industry," Collins reported. "We hope to get access to hundreds and hundreds of compounds being stored in freezers and do a cross-reference with what we know of the molecular basis of rare diseases. There could be a match that hasn't been apparent before."

Although many not-for-profit disease organizations are doing this, as well as some biotechs, Collins said NIH's effort will be on a larger scale and conducted more systematically than previous attempts to repurpose failed or abandoned drug candidates.

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COMPANIES AND INSTITUTIONS MENTIONED

AesRx LLC, Newton, Mass.

The Federation of American Societies for Experimental Biology, Bethesda, Md.

U.S. Department of Health and Human Services, Washington, D.C.

National Cancer Institute, Bethesda, Md.

National Heart, Lung, and Blood Institute, Bethesda, Md.

National Institute of Allergy and Infectious Diseases, Bethesda, Md.

National Institutes of Health, Bethesda, Md.