

IN brief

NCATS launches

In December, President Barack Obama signed an appropriations bill authorizing the new National Center for Advancing Translational Science (NCATS) at the National Institutes of Health (NIH) and setting its first budget at \$576.5 million for fiscal year (FY) 2012. The new Center, proposed in 2010 by NIH director Francis Collins to support translational efforts has been controversial among scientists in academia and industry from the start. However, Biotechnology Industry Organization (BIO) president Jim Greenwood calls it “potentially a good thing” for the biotech industry in terms of its avowed goal of moving therapeutic products more rapidly into the hands of doctors and their patients. “It’s a work in progress—a good idea,” he says, but must be “done in the right way.” Ramping up federal support for translational research is “very important,” says H. Thomas Watkins, president and CEO of Human Genome Sciences in Rockville, Maryland, who now chairs the BIO board of directors. Although the bulk of funding for NCATS in FY 2012 is carved from established NIH programs, \$10 million in new funds are allocated to its Cures Acceleration Network (CAN). The CAN program was established in 2010 to help bridge the so-called ‘valley of death’, between basic and clinical research. It is situated within NCATS and is authorized to issue grants to biotech companies. *Jeffrey L. Fox*

BASF moves GM crop research to US

BASF Plant Science is relocating from its European headquarters to the US, a move prompted by the European public’s hostility to genetically modified (GM) crops, its president Peter Eckes said. The German company is also cancelling the development and commercialization of all projects destined solely for the European market and in future will concentrate on markets in America and Asia. “The political and regulatory climate in Europe is unwelcoming at this moment—this is a political failure,” says Carel du Marchie Sarvaas, director of advocacy group EuropaBio in Brussels. In 2010, the European Commission approved BASF’s Amflora, a GM blight-resistant potato for industrial use. The road to approval took 13 years, during which the company had to deal with protestors and sabotage to test sites in Germany. BASF will continue the regulatory process for three breeds of potato already in the European pipeline but will halt work on a wheat variety resistant to fungal disease. Despite moving its Limburgerhof headquarters in Germany, BASF is not pulling out of Europe completely and will retain offices in Ghent, Belgium, and in Berlin. Another GM crop developer, Bayer CropScience of Monheim, Germany, has no plans to leave Europe and will retain an active research program in Ghent. Julian Little, Bayer’s UK spokesperson in Cambridge, says that Europe “remains an excellent place to do research but commercialization of such technology in Europe remains problematic.” *Lucas Laursen*

HIV neutralizing antibodies reignite interest in vaccine

Patient stratification of the results of the 16,000-participant RV144 trial of a prime boost HIV vaccine in Thailand has revealed the binding antibody linked to protection against the lentivirus in a proportion of participants. Taken together with several broadly HIV-neutralizing antibodies that have recently been identified, interest is growing in exploiting the epitopes that elicit such antibodies as the basis for new vaccine opportunities. As yet, however, companies are waiting to see whether public efforts can provide more clinical evidence of potency before reentering the HIV vaccine space.

At the AIDS Vaccine Conference in Bangkok last September, scientists from the US Military HIV Research Program released the results of their analysis of RV144. In 2009, the trial had caused a stir by showing that a prime-boost regimen of two recombinant vaccine candidates—a canarypox vector-based primer ALVAC-HIV vCP1521 from Sanofi Pasteur of Lyon, France, followed by a protein boost with AIDSVAX B/E, a bivalent recombinant version of HIV’s gp120 surface protein from VaxGen (now part of diaDexus of Brisbane, California)—lowered the rate for HIV infection by ~31%, but did not affect viral load. The aim of the new analysis was to determine how the vaccine regimen provided its modest level of protection against HIV to certain individuals.

After analyzing blood samples collected from volunteers in the trial, the researchers identified two antibody responses: one correlated with a reduced risk of HIV infection, and the other with an increased risk. In the first case, vaccinated trial participants whose blood contained an IgG antibody that recognizes a portion of HIV’s outer envelope—the V2 loop—were 43% less likely to acquire HIV than volunteers whose immune systems did not generate this antibody response. In the second, vaccinated volunteers in the trial who developed IgA antibodies that targeted the HIV envelope were 54% more likely to become HIV infected, suggesting that these antibodies reduced the protective effect of the vaccines.

The clues—correlates of risk, rather than correlates of immunity—are starting points for further basic research, rather than validated targets for biotech companies. “Right now scientists are trying to work out if they can get any hint of what the correlate of immunity was in those people who were protected,” says Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, which oversees HIV research for the US National Institutes of Health (NIH). “When that gets worked out, the approach is going to be developing immunogens that will induce that type of an immunogenic response,” he says. “That’s where biotech companies would come in.”



Protective responses found in some patients taking part in the Thai phase 3 trials for RV144 have yielded molecular clues that could be further exploited.

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Two companies, Sanofi Pasteur and Novartis, are involved in the clinical side of the Thai trial follow-up, working on components of vaccine combinations to be tested in follow-up trials.

The protective antibody identified in patient analysis of the RV144 trial joins several broadly neutralizing antibodies, isolated from HIV-infected people around the world, which are highly potent against HIV. They are also capable of blocking a broad range of HIV variants—a key to vaccine development, as HIV is wildly mutable. In addition to the virus-neutralizing antibodies PG9, PG16 and VRC01 reported in *Science* (326, 285–289, 2009; 329, 811–817, 2010), 17 novel broadly neutralizing antibodies (some of which were 10–100 times more potent than PG9, PG16 and VRC01) were reported in *Nature* last August (*Nature* 477, 466–470, 2011). This discovery was a result of a collaboration between the International AIDS Vaccine Initiative (IAVI), university laboratories and biotech companies, such as Seattle-based Theraclone Sciences, which contributed its process for isolating the antibodies, and S. San Francisco, California-based

Monogram Biosciences, which contributed its neutralization assays.

Now researchers are trying to delineate the nature of the epitopes on the HIV envelope to which broadly neutralizing antibodies bind. “It’s very basic [research],” says Fauci. “They’re still trying to develop the right conformational structure of what these epitopes are.” But eventually there will be a need for the private sector, he says. “You’re going to need companies to come along and partner with the basic scientists to develop these immunogenic epitopes—how do you scaffold them, how do you present them to the body—so that they would induce an immune response.” But getting to that point won’t be easy. “How to translate that into a vaccine—it’s not trivial,” says Jaap Goudsmit, CSO at vaccine developer Crucell in Leiden, The Netherlands.

The few existing private sector vaccine developers have been funded by government and charitable sources, such as NIH, IAVI in New York, and the Bill and Melinda Gates Foundation in Seattle. Those organizations tend to direct the course of the research and supply nearly 97% of the global investment

in preventive HIV vaccine research, according to the HIV Vaccines and Microbicides Resource Tracking Working Group. “VCs [venture capitalist] are simply not investing in the area,” says David Cook, COO at IAVI. “Living on grants is a very uncertain way of living.”

With large public and philanthropic funding organizations controlling the direction of research, and those funders forced to pool diminishing resources, the field could use more independent voices from the private sector, say some scientists. “One of the biggest problems in the field is the lack of diversity of opinions and approaches,” says Bruce Walker, director of the Ragon Institute in Charlestown, Massachusetts. “NIH, Gates Foundation, IAVI, et cetera, are aligning around specific products to take forward,” particularly in pursuing Thai trial repeat studies, he says. Some scientists are questioning the wisdom of concentrating resources on a single approach, he says. “Most funders agree that multiple concepts merit testing, but there is just not enough funding to do that.”

Emily Waltz, Nashville

Around the world in a month

