

cine to stimulate the immune system (like the Bristol-Myers Squibb vac/env vaccine) and then follow up with a coat protein vaccine, do generate some T-cell responses, but is that enough? No one knows.

In most areas of medicine, these issues would be resolved with an animal model, but for AIDS, there isn't one that precisely mimics the human disease state. Recent work with pigtail macaques, and with hybrids of the simian AIDS virus, SIV, and HIV, suggests these might ultimately fill that void. But work with these systems is only just getting under way (*Science*, 19 June, p. 1630 & 14 July, p. 478). Other animal models have provided some answers, but not many. For example, several labs have now shown that a vaccinated chimp can be protected from infection when both virus and vaccine have been made from the same HIV strain. So far, however, no one has done the "heterologous" challenge, with vaccine made from one strain challenged with another.

Some researchers are arguing, however, that it's not necessary to answer all these questions before starting efficacy trials. Donald Burke of the Walter Reed Army Institute for Research says he would be prepared to move a vaccine into efficacy trials so long as it was safe, capable of inducing some kind of immune response, and able to demonstrate protection in at least some animal model. Burke is quite upbeat in part because some candidate vaccines—including one made by Genentech and based on the HIV coat protein known as gp120 from the LAI strain—already meets those minimal criteria. In fact, Burke is widely reported to be planning a trial of just such a vaccine among Thai soldiers.

Once large-scale trials do finally get under way, researchers will then have to grapple with a new set of issues: How do you decide when a vaccine has proved itself good enough to be released to the public? Some researchers argue that it isn't necessary to wait to develop an almost-perfect vaccine, because one that is far less than optimal would go a long way toward stemming the AIDS epidemic. NIAID's Vermund, for example, presented results of a simple model showing that even a 60% effective vaccine could save thousands of lives. And that, he argues, is realistic: "It's unlikely that the first efficacy trial will be a grand slam [success]."

The public message coming out of last week's meeting was, therefore, don't expect a magic bullet. Indeed, researchers were eager to get across the idea that it's going to be tough even to produce a less than ideal vaccine. "Efficacy testing is going to be a long and difficult exercise," says Jose Esparza of the WHO Global Program on AIDS. And, whatever their approaches, that was a message that all involved at last week's meeting could agree on.

—Joseph Palca

## BIOTECHNOLOGY

# Lithuanian Biochemist Builds Enzyme Empire

VILNIUS—If you like to browse through laboratory catalogs looking for the latest equipment and reagents, you might have come across a surprising entry in the most recent offering from New England Biolabs. There, on page 46, you'll find a whole set of new restriction enzymes—the enzymes that chop up DNA and are a vital part of every molecular biologist's toolbox. The surprise: The enzymes are all labeled "Made in Lithuania."

Lithuania? How could a small Baltic state, independent for less than a year, compete with hot shot Western biotech companies in supplying enzymes to the United States? Ask Rich Roberts, the former Cold Spring Harbor Laboratory molecular biologist who is now director of research for New England Biolabs and he will answer in a word: "Janulaitis." Vidas Janulaitis (pronounced Yanoo-LITEis), he will tell you, is professor of biochemistry at the University of Vilnius, head of the Institute of Applied Enzymology—and creator of one of the world's largest collections of restriction enzymes, with more than 100 on offer. He also appears to be the first successful biotechnology entrepreneur to emerge from the former Soviet Union—and New England Biolabs' competitors are well aware of his talents. "Formidable," is how Jeremy Walker of Amersham International describes Janulaitis' contribution to the number of new restriction enzymes marketed each year.

The interesting question, of course, is how Janulaitis managed to rise above the chaos that has accompanied the dismantlement of the Soviet Union to become one of the world's top suppliers of new restriction enzymes—especially given that the venture capitalists who rushed off to make deals with Moscow labs in the early days of perestroika mostly came back disappointed. To find out, *Science* visited Janulaitis earlier this year at his institute on the outskirts of the 17th-century city of Vilnius.

As you approach the institute, it is hard to believe that you're about to meet a prime mover in the world of restriction enzymes. The road out of Vilnius passes clusters of old wooden farm huts with sagging roofs; hay wagons pulled by mules creak along the dirt roads; and in the surrounding potato fields, farmers trudge along behind horse and plow. Janulaitis, a stocky man who looks more like a Chicago Bears linebacker than a biochemist, sits down in his laboratory, lights the first

of a chain of strong Russian cigarettes, and gives a rapid-fire discourse on the difficulties of dealing with the Soviet bureaucracy.

Contrary to what most Westerners think, he explains, the Soviet Union invested immense amounts in biotechnology—including in his own solid redbrick institute. In 1975, the Ministry of Microbiological Industry in Moscow built and staffed four huge institutes—two in or near Moscow, one in Novosibirsk, and the Vilnius institute. All



**Beating the system.** Against all the odds, Vidas Janulaitis made Fermentas a world leader.

were given huge budgets and massive numbers of researchers to make enzymes. The institute in Vilnius, which was one of the smallest, was allotted a total staff of 730.

The problem was that the research administrators had no idea how to create products. The Soviet government, says Janulaitis, poured "thousands and thousands of people and billions and billions of rubles" into biotechnology and wound up, at best, with "some pretty good basic research but virtually no worthwhile industry." Individual scientists were not to blame, he adds quickly. "Even if the scientists had been willing to come up with what was really needed, they would have had a nearly impossible time persuading industry to produce the new products—the communist system simply provided no incentives for such innovative production."

Janulaitis, who traces his own Lithuanian ancestry back to one of the original tribes that have lived on this territory since at least the 8th century, says he believed Moscow's orders to develop and produce bulk industrial enzymes would give Lithuania little advantage: The work was easy and could be done anywhere. Instead, as he rose through the ranks in the institute, becoming director in

1989, he switched resources to restriction enzymes. Finding new restriction enzymes, Janulaitis reasoned at the time, would require lots of ingenuity and hard work but little costly equipment. And if they could be successfully made, they could be sold in small quantities and easily shipped—just the product for a small state with aspirations of independence from Moscow.

Institute researchers on holiday in far corners of the Soviet Union, as far as Kamchatka and Siberia, were asked to collect soil samples from hot springs, high mountains, and other unusual environments in the hopes of finding unusual strains of bacteria that produced unique enzymes. Janulaitis also asked friends at other research institutions and hospitals to send samples they had collected from all over the Soviet Union. And extensive searches were made close to home—paying off nicely when his colleagues found two unique strains in a garden near the institute.

As early as 1976, Janulaitis recalls that his first restriction enzymes were ready to sell to Soviet laboratories. Then came his first bruising encounter with Soviet bureaucracy. For just one sale to one institute, “You needed a stack of paper this big,” says Janulaitis, holding his hands a foot and a half apart. But Janulaitis came up with a solution that still makes him smile—he gave his enzymes away. “This required no paperwork,” he says, laughing. “That is how we made friends all over the Soviet Union—within a few months, everyone knew my name.” Friends helped him put pressure on Moscow and 4 years later—fast progress in those days—he was able to get enough foreign exchange to buy fermenting equipment from Germany.

By 1983, Janulaitis says he was ready to ask Moscow for permission to contact Western companies to try selling them restriction enzymes in bulk that they could then resell under their own brand names. “My co-workers told me I was crazy. ‘Why create all that extra work?’ they said. ‘The money will all go to Moscow anyway,’” recounts Janulaitis. But he persisted—and soon found that his friends were right. He won orders from a Japanese company but, he says, “once we began sales, we never saw a penny of the profits.” Why continue? “I used to think of it as my hobby,” says Janulaitis. But there was one other reason. “I wanted to get experience in dealing with foreigners.”

The experience paid off a few years later, when perestroika arrived. By 1987, Janulaitis was able to register his institute’s production facility as a semi-independent company, now called “Institute of Biotechnology Fermentas,” and in 1988 the Politburo in Moscow gave the new company permission to sell directly to Western clients and keep the profits. Then came the breakup of the Soviet Union, with independence granted to Lithuania in September last year.

These developments—joyous though they were—didn’t immediately make business easy. Contacts he had built up with the West from his “hobby,” plus a newfound freedom to travel, paid off in orders for a list of enzymes that by then was larger and more diverse than any other in the world. But Janulaitis still had to contend with the Soviet banking system. “We had to use the one bank in the entire country that was allowed to make foreign transfers,” recalls Janulaitis. “But the bank was usually insolvent. Even though we had money in our account, we had to go to Moscow to get the payments made. But at the bank headquarters in Moscow, you couldn’t get in the door—the doorway was always filled with people trying to get access to their money. It got to the point where they would keep the doors locked all the time.”

Janulaitis tried to cross this final hurdle the old-fashioned way but found himself back in a situation straight out of a Russian fairy tale. “Our person had to find a back door to the bank and actually bribe somebody to get in. Then, he found the person responsible for our transaction. He was sitting in a large room filled to the ceiling with huge boxes of receipts. He offered to help us, but only if we could find our receipt in one of those boxes.” That was the end of the fairy tale, however—Janulaitis’ people couldn’t find their re-

ceipt and had to go away empty-handed.

The business environment has since improved—when independence came, Lithuania finally set up its own bank, which completes transactions for the company within hours or days. And after several years of frequent trips to the West, Janulaitis is selling his enzymes through 15 companies in 12 countries. Success achieved, this year Janulaitis will resign as director and his colleague, biochemist Viktoras Butkus, will take over. In 1991, according to Butkus, the company earned about \$340,000 in foreign sales.

The biggest problem Fermentas now faces is the terrible image of the former Soviet Union. “Nobody trusts us,” says Janulaitis. Potential distributors of Fermentas enzymes often ask if they can remove the “Made in Lithuania” tag from the label. “We realize that most products [from the former Soviet Union] are worse than bad,” says Janulaitis. But he insists, “Our quality control is better than [that of Western companies].” Janulaitis says he is going to keep his “Made in Lithuania” labels no matter what. That way, he says, he will have done his part to win Lithuania a reputation for inventiveness and high quality.

—Steven Dickman

*Steven Dickman, a free-lance science writer, is a Knight Science Journalism Fellow at MIT.*

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## CRIME CONFERENCE

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### Back to the Drawing Board, Says NIH

The National Institutes of Health (NIH) has notified the University of Maryland that it will have to start all over with a new proposal if it wants to get funds for a controversial conference on “Genetic Factors in Crime.” The university, claiming that NIH has infringed its academic freedom, has indefinitely postponed the conference, which was to be held on 9 October.

In late July, NIH Director Bernadine Healy suspended a grant of \$78,000 that had been awarded the university for the conference after a number of critics, in particular a group that included Howard University political scientist Ronald Walters, complained that the topic of the conference was racist in its implications (*Science*, 7 August, p. 739). David Wasserman, a lawyer and researcher at the university’s Institute for Philosophy and Public Policy, who organized the original program, says he subsequently met with a group from the NIH Human Genome Center to try to modify the design of the conference. He told *Science* that he rewrote the conference brochure and added some nonacademics to the list of participants. Based on these changes, Jacob Goldhaber, acting vice president for academic affairs and provost at the university, wrote to John Diggs, deputy director for NIH intramural research, saying

Wasserman had addressed NIH concerns about the conference and asking that the funding freeze be lifted by 4 September.

Diggs replied on 4 September saying that Healy’s block on the funds was “fueled by legitimate concerns” that it would be “irresponsible” for NIH to ignore. He stated that NIH “will not” release funds for the conference “as currently constituted.” Diggs went on to say that the conference needed to be rethought because the original brochure advertising it “diverges radically from that approved by peer review....” He referred specifically to statements that genetic research offers “the prospect of identifying individuals who may be predisposed” to criminal behavior and of “treating some predispositions with drugs and unintrusive therapies.” Wasserman claims that these were contained “word for word” in the proposal that was approved.

Diggs hasn’t ruled out funding entirely, however. His letter says NIH “will accept a revised proposal for review by an ad hoc peer-review group.” Goldhaber, Wasserman, and university lawyers are now at work drafting a response, says Wasserman, who adds: “We’re optimistic, despite the rhetoric and smoke screen, that there’s a willingness to fund the conference at a later date.”

—Constance Holden