triggers production of the antibody.

Maxygen has begun to hunt for this elusive protein. Its scientists plan to shuffle envelope genes from several different isolates of HIV and test whether any of the proteins expressed by these reshuffled genes bind to Burton's antibody. They will then inject the most promising genes into mice to see whether they produce a strong antibody response. This strategy, Burton notes, differs markedly from rational gene design, which aims to fashion new HIV envelopes by deleting parts of the known structure. "One strategy says you work everything out and design a change in the protein," says Burton. "Here, you just randomize and select. And that's what nature does. It doesn't design."

In February, Maxygen's AIDS vaccine project received a boost when the nonprofit International AIDS Vaccine Initiative, in collaboration with the Rockefeller Foundation, both of in New York City, agreed to fund the work in exchange for a royalty-free license to distribute any resulting vaccine to poor countries. David Ho of the Aaron Diamond AIDS Research Center in New York City became a part of this collaboration, too, providing envelope genes from Asian isolates of HIV. "The concept is obviously novel," says Ho. "It's a fishing expedition: The more you toss the line out, the more chances you have."

Novel as the HIV vaccine project is, it also has a serious constraint: Maxygen's screening assays currently ignore cellular immunity. And that's true for all of their vaccines under development. "They've got a ways to go before they maximally exploit the technology," says Burke of Johns Hopkins. Maxygen's Howard agrees. "If we have an inferior assay, we're going to get inferior products," he says. And he says they eventually plan to develop assays for cellular immunity.

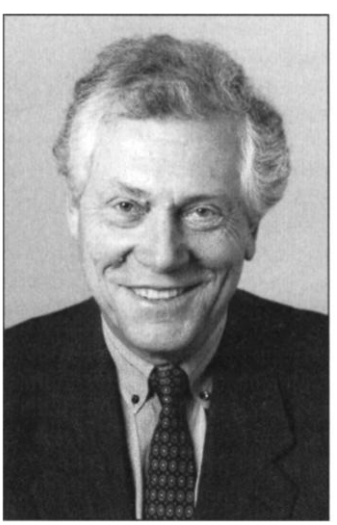
Whether Maxygen's experiments lead to new and improved vaccines remains to be seen. But already it's clear that they are introducing vaccine researchers to a sexy new technology. **–JON COHEN**

NEWS

Closing of Basel Institute Scatters Immunologists

Hoffmann–La Roche's celebrated center—an experiment originally run by basic researchers—experiences a traumatic change

BASEL, SWITZERLAND—Hoffmann–La Roche shocked Europe's immunology community last year when it pulled the plug on its renowned Basel Institute of Immunology (BII). For more than 30 years, the drug manufacturer had supported the institute's self-directed program of basic immunology research. In return, the institute gave Roche access to first-rate science and talented biologists. It was an idyllic relationship, but it came to an end on 5 June 2000 when Roche announced that it was converting the institute into a center for medical genomics. The BII's board of directors voted to dissolve itself, and Roche took direct control.



Paterfamilias. Fritz Melchers, the institute's former chief.

The institute has been slowly dispersing since then. Fritz Melchers, the BII's director for 20 years, retired this past April. Twenty-seven of the 48 members of the scientific staff have left, reportedly with generous severance deals. More are expected to leave by the end of July, when additional contracts expire, and a few who have longer contracts will depart over the next 18 months.

Roche's publicly stated rationale for the transition was that it needed to position itself at the "cutting edge of the biosciences." But employees paint a more complicated picture. Some BII alumni worry that the institute's demise indicates that Europe is losing interest in basic biology that doesn't involve genomics. Others say it has long been in a precarious position. It seemed as though the BII "was always closing," says Christopher Paige, who spent 8 years there in the 1980s and now directs research at the Ontario Cancer Institute. "Even when I left," says Brigitte Askonas, an immunologist at Imperial College, London, who was at the institute for a short period in the early 1970s, "there was uncertainty about the longer term future of the BII." The company's ambivalent support diminished, some say, following the death in 1999 of Paul Sacher, a Swiss conductor and avid patron of the arts and sciences who married into the Roche family. Observers say the BII was Sacher's pet project and that his departure tipped the balance.

The transition has been bruising for some, particularly researchers past middle age like Louis Du Pasquier, whose early retirement means an end to 31 years of studying amphibian immunology. Yet by and large the institute is "successful even in its death," says Melchers, pointing to the number of employees who have found good jobs. The big loss, say the people who knew the institute well, is the closing of an extraordinary opportunity for young scientists. Du Pasquier says it was "a paradise for creativity at the single-person level"—one that's not likely to be replaced.

The Valium windfall

Roche conceived the idea of an independent academic institute in the late 1960s, flush with money from sales of benzodiazepines. The company hired Niels Jerne, then almost 60, to direct the new center and gave him $22 million a year and a free hand in planning it. Although Roche got a first look at research coming out of the institute, by all accounts, commercial payback was never the focus. Askonas remembers how Jerne called several meetings of the new institute's first recruits, and "we had a wonderful time discussing how an institute should be run to encourage original research."

The structure that emerged was simple but unique. Administration was nominal. Groups were kept small to discourage empire building. Although the BII hired a handful of researchers on a permanent basis, most scientists came on 2-year, rolling contracts. "It was not a place to stay," says Du Pasquier, adding that the turnover kept it young. According to Polly Matzinger, an immunologist at the National Institutes of Health who spent 6 years at the BII, the advantage was the freedom and support for researchers to do what they wanted without any questions and without having to write grants. "The only limitation was your own brain," says Michael Julius, a one-time member of the institute and now vice president for research at the Sunnybrook and Women's Health Sciences Center in Toronto.

Jerne tried to encourage interaction by connecting the labs with a famous network of spiral staircases and putting the cafeteria in a central location. "We were forced to

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communicate," says Matzinger. The sum of these small groups collaborating was greater than its parts, says Fred Alt, an immunologist at Harvard Medical School in Boston, who served as an adviser to the BII in its final years.

The institute became home to 50 scientists and 25,000 model organisms, mostly mice, but also worms, chickens, frogs, and trout. Researchers were backed by a corps of superbly trained technicians. Hundreds of scientific visitors contributed to a knowledge base that made the institute a mecca for immunology. "Everybody stopped in Basel," says Alt. Large parts of the canon of immunology were hammered out at the BII. Just as important, it served as a breeding ground for immunologists. A map fills a wall in the conference room on the second floor, pasted over with photos of many of the 500 scientists who worked there. "There are metastases from the institute all over the world," says Klaus Karjalainen, a member for 17 years. Julius points out that the department of immunology at the University of Toronto has "filled up with ex–BII members."

"It was a great place to establish the seeds of new research," says Susumu Tonegawa, director of the Center for Learning and Memory at the Massachusetts Institute of Technology in Cambridge. Tonegawa's work at the BII on antibody diversity garnered him one of the three Nobel Prizes awarded to members within the institute's first 11 years of operation. (Georges Köhler and Jerne, together with César Milstein, snagged the other two.) But he and others eventually began to chafe at the limits on group size. "Some research does go on better in factories," admits Paige. Pressure to perform and the peculiar social situation of the institute—50 foreign scientists isolated in a small Swiss city—also exacted a toll.

Icon of immunology. Jean Tinguely's iron sculpture of a helix towered over the entrance to the Basel Institute for 30 years.

Melchers likens it to going into a monastery for a few years. "You hurt by the time you left," observes Matzinger.

Jerne retired in 1980 and was succeeded by Melchers. The staff gives Melchers credit for maintaining Jerne's singular vision, but by the 1990s, something had changed. Melchers himself volunteers freely that after 20 years, it was time for him to go. But there was no scientific reason to close the institute, he says.

The BII's shutdown, some observers say, coincides with a decline in support for basic research in Europe. People feel that European leaders are emphasizing science as a means of stimulating the economy "as opposed to discovering novel principles in biology," says Harald von Boehmer, a permanent member who left in 1996 and now heads a group at the Dana-Farber Cancer Institute in Boston. That's one reason, he says, why several leading immunologists have moved to the United States, "where funding for basic research ... is by comparison enormous."

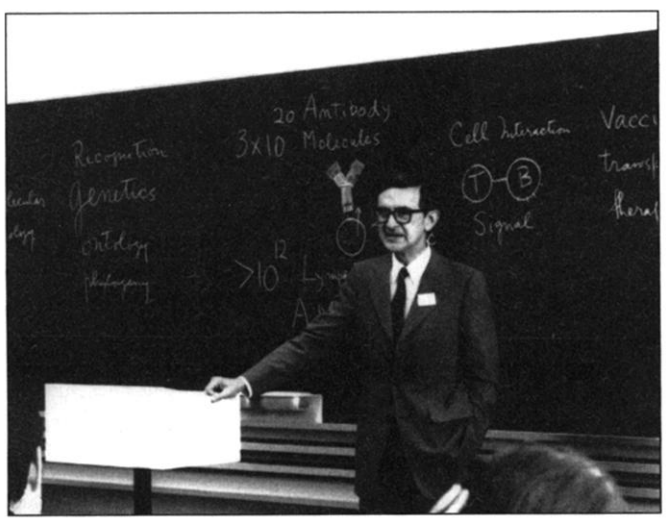
Nearby universities have snapped up several BII scientists. Other members of the BII staff are heading for the Swiss Federal Institute of Technology in Zurich, Washington University in St. Louis, and the European Institute of Oncology in Milan, to name just a few. Karjalainen will join the Institute of Research in Biomedicine recently started in southern Switzerland by Antonio Lanzavecchia, who left the BII the year before it closed. In accepting a chair endowed by Roche for $6.7 million at the University of Basel, Ton Rolink, who was with the BII since 1983, will become the university's first professor of immunology.

The new Roche Center for Medical Genomics, meanwhile, has yet to take shape. Signs for the center and the BII face off outside the building, but inside, there's little sign of new life. The institute's library was dismantled months ago to make way for a department of bioinformatics that Roche's media office confirms has been staffed with a department head and several other people. Detailed drawings for renovating the cafeteria have gone up and come down from the announcement board, fueling speculation that Roche may be rethinking its commitment to the center. But the company maintains that its plans are "right on track."

For many immunologists who grew up at the BII, there can be no successor. "There is no place that I know of on this planet where a bright young person can go and just do what they want to do," says Matzinger, who fears that without the institute, immunology will become more mainstream. Indeed, muses Askonas, "the BII provided the opportunity for young investigators to develop into independent scientists."

No one disputes Roche's right to disband the institute. What people do regret is the abrupt way it was done. Still, many express wonder that the BII continued for as long as it did. "It was a remarkable experiment," says Julius. **–GISELLE WEISS**

Giselle Weiss is a writer in Allschwil, Switzerland.



Founder. Niels Jerne, the first director, had a free hand to design a center for basic research in immunology.

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