universities to select some of their own students, and thereby compete for talent, instead of the centralized system now used—a change Baden-Württemberg also hopes to bring in under its new law. Another hot topic is academic career structure: Researchers rarely get a professorship, or scientific independence, before about age 40—and in today's dismal market, many survive on temporary jobs paid from highly competitive grants. As professors, however, they are tenured from day one—and utterly unaccountable for the rest of their academic lives. According to Michael Daxner, president of the University of Oldenburg, a Science Council committee is now looking at the problem and will issue recommendations, possibly including a tenure-track system, later this year.

Perhaps the most contentious issue is funding: If Germany is to stay near the top of world science and technology, say many, it cannot continue dropping the proportion of national income spent on universities, where it is now low on the list of major industrial nations. Some quick first aid will come from a just-approved federal program, which replaces an expired one, to help pay for crucial needs like graduate training. Tuition fees, which some states hope to introduce, and interest from certain government loans to students may also inject some funds. But what is really needed, says the DFG's Frühwald, is a shift of priorities: Merely building 50 kilometers less new highway each year and investing the money in science and universities would solve the problems nicely, he says. Adds Science Council Chair Dagmar Schipanski: "We simply cannot afford to let our universities starve."

–Patricia Kahn

IMANISHI-KARI CASE

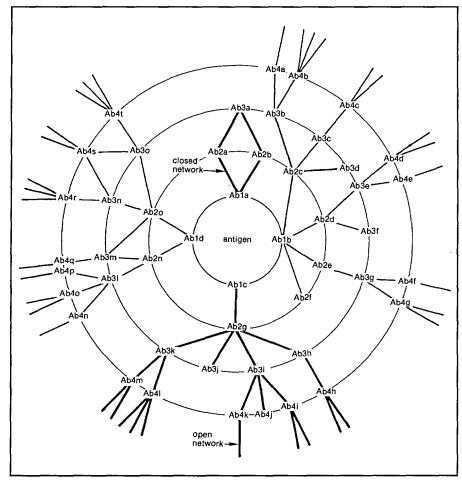
Disputed Results Now Just a Footnote

Perhaps no paper in biology has been as intensively analyzed, dissected, and argued over as the publication by Thereza Imanishi-Kari *et al.* in the 25 April 1986 issue of the journal *Cell*. It's been examined by two university committees, a squad of federal investigators, a congressional subcommittee, the Secret Service, a government appeals board, and countless lawyers—all of whom have focused on whether Imanishi-Kari committed scientific misconduct. Yet, in the decade that this infamous paper has been in the spotlight, the research topic on which it was based has slipped from one of the hot fields of immunology to, at best, a quiet backwater.

Thus, when an appeals board dismissed misconduct charges against Imanishi-Kari last month with a withering indictment of the case against her, the ruling spoke volumes about the way misconduct cases are handled. For Imanishi-Kari and her co-author, biologist David Baltimore, the decision ended a decade-long nightmare and, they said, helped correct an injustice (*Science*, 28 June, p. 1864). But many immunologists contacted by *Science* said that for the field of immunology itself, any verdict on the integrity of the *Cell* paper has turned out, in strict scientific terms, to be largely irrelevant.

When the *Cell* paper came out, says immunologist Hugh McDevitt of Stanford University, it demonstrated an "amazing" and "unexpected" fact: that inserting a new immune system gene into a mouse triggered changes in the antibodies expressed by the mouse's endogenous genes. Since then, he says, other immunologists have confirmed that the phenomenon is real. But it has come to seem less than earthshaking, in part because the theory it seemed to bolster—the idea that interacting antibodies form a "network" that regulates the immune system—has lost its luster. As one senior immunologist put it, people have decided "there isn't any pay dirt" in the concept. Moreover, immunologists have concluded that there are other ways to explain Imanishi-Kari's observation without assuming a network.

The network theory was proposed in 1974 by Niels Jerne, former director of the Basel Institute of Immunology, and it helped to earn him the 1984 Nobel Prize. This theory held that as the immune system develops, the new antibodies it creates (idiotypes) trigger the creation of complementary antibodies (anti-idiotypes), which form an interlocking network of structures that encompass the complete "repertoire" of the individual's immune system. This ever-adjusting network, according to the theory, regulates the immune system. At the time Imanishi-Kari and her colleagues began their work, the theory lacked solid experimental support, in part because it was horrendously difficult to verify.



HOOD *ET AL.*, *IMMUNOLOGY*, 2ND ED., BENJAMIN CUMMINGS PUB. CO., 1984

Textbook model. Depiction of Jerne's theory of an expanding network of idiotypes.

The *Cell* paper seemed to give the network hypothesis its strongest boost to date. The authors' broad claim was that their evidence "strongly implies" that immunoglobulin molecules detected in a transgenic mouse were "selected by idiotype-specific regulation," a process stipulated by Jerne's philosophy. Imanishi-Kari and her colleagues reported that, after inserting a new gene into an experimental mouse, the functioning of the animal's endogenous genes were altered so that they expressed antibodies containing the idiotype of the new gene. The authors tentatively concluded that they had evidence of idiotype mimicry supporting Jerne's idea.

Many immunologists were skeptical at the time because the science was so murky. Leonore Herzenberg, another Stanford immunologist, recalls that she was intrigued by Imanishi-Kari's work when it came out and tried to replicate it. "I had a major argument with Thereza about those mice [in the 1986 paper]," she says. "The work we did ... basically showed that the original assumptions about the mice were incorrect." Later, Herzenberg and her postdoc Alan Stall, now at Columbia University, found that hybridoma cells upon which Imanishi-Kari based her data didn't behave as Imanishi-Kari had assumed: They were abnormal, producing two, not just one, idiotypes. Imanishi-Kari challenged this finding; Herzenberg and her colleagues conducted new experiments confirming that "double-producer" cells existed, but they also learned that the cells evolved so rapidly into single producers that this probably hadn't affected Imanishi-Kari's results. Now Herzenberg concedes that "everything that [Imanishi-Kari] said—with the exception of the idiotype, which we couldn't check—everything else was correct." Herzenberg says, however, that she still has qualms about the reliability of some of the reagents Imanishi-Kari used.

But even while some of the *Cell* paper's findings have held up, says McDevitt, who sat on a panel sponsored by the National Institutes of Health (NIH) that examined Imanishi-Kari's claims in great detail, they may amount to no more than an immunological footnote. "Nobody today—or 99% of immunologists don't believe the network theory, because there are about 10 other ways you can explain" events in the immune system that "make more sense" than the one Imanishi-Kari chose, he says.

Herzenberg confirms that "it is absolutely true" that 99% of immunologists today are not interested in Jerne's theory or the data in the 1986 *Cell* paper. But she thinks McDevitt

may be too dismissive. She remains intrigued by Jerne's theory, which she describes as a "seminal bit of thinking" and adds that at one time, "99% of physicists would have told you they were uninterested in Einstein's theory." Imanishi-Kari herself says that her peers seem to regard idiotype mimicry as a "taboo" subject: "People don't like to talk about it. ... Today, in the 1990s, we talk about selection," she says. "It's semantics."

Ronald Germain of NIH says, "Science has trends just as any aspect of life does," and the terminology of idiotype networks "doesn't catch people's imagination" any longer. Instead, the bandwagon has moved on to genetics—identifying and cloning genes of the immune system, which many researchers now assume are the "predominant structures" that control immune responses. Imanishi-Kari agrees that the boom in molecular biology in the '80s attracted "lots of people who thought that everything was dictated by the structure of the genes."

Today a few researchers are still exploring the implications of Jerne's theory. Some—including Mark Greene and colleagues at the University of Pennsylvania—say they have been inspired by Jerne's ideas to study antibody structures in the hope of designing new drugs. And John Kearney at the University of Alabama continues to rely on Jerne's ideas in exploring the neonatal immune system. But—in the United States, at least—they are in the minority.

Immunologists on Immunology

Advances in immunology spawn an ever-growing range of potential applications in medicine, but how are the prospects shaping up? As part of a special issue on the field (5 April 1996), *Science* asked immunologists to give us their views in an on-line questionnaire. Find out the results in the analysis on *Science*'s Web site at http://www.aaas.org/science/immunology/analysis96.htm.

European immunologists, however, have remained more enamored of Jerne's general ideas, notes Germain. "Europeans like models," he says, and Jerne's theory provides a framework for what is now called "connectivity" in the immune system. Immunologist Martin Weigert of Princeton University notes, for example, that Antonio Coutinho at the Pasteur Institute is applying a version of Jerne's concept to show how idiotype interactions may expand the immune system in newborns. Coutinho and others are developing a "second generation of network theories," says Weigert: "We are asking more specific questions, looking at interactions between antibodies in unique and special circumstances." In contrast, Germain says, most U.S. scientists tend to be "pragmatic. ... They want to know, 'What does this gene do?' " Because Jerne's model has yielded few physiological results, Germain says, Americans have turned away from it.

Indeed, they have turned so far that concepts such as "idiotypy" and "network regulation," so pivotal 10 years ago, could vanish from the immunologists' lexicon. Charles Janeway, the Yale University researcher who co-edits the popular textbook *Immunobiology*, says he's losing interest himself. The first edition of his book had three sections on Jerne's theory of idiotypes; his second edition had one section. The third edition, which will come out next year, Janeway says, "will have nothing." That deletion, more than any decree from Washington, may convey the scientific community's judgment on the topic of idiotypic mimicry. While armies of lawyers in Washington were poring over the data, scientists simply lost interest in the science behind them.

–Eliot Marshall

NASA LIFE SCIENCES

Panel Backs Joint Bion Mission

An independent task force recommended last week that NASA continue to participate in a space life sciences program with Russia that has drawn fire from animal-rights activists and some members of Congress. The panel praised the quality of the research in this fall's Bion mission and dismissed accusations that the effort mistreats rhesus monkeys and is of dubious scientific value. At the same time, it suggested that NASA look at the ethical issues raised by the use of animals in all its life sciences research before participating in a second Bion flight in 1998.

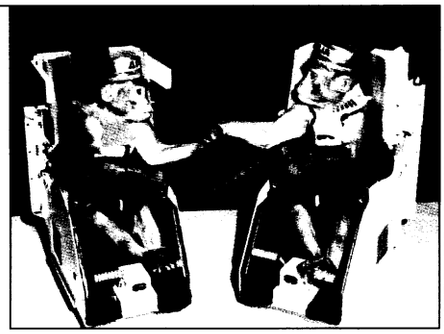
Although the panel, led by Ronald Merrell, chair of Yale University's surgery department, gave Bion a green light, Congress is sending a very different signal. On 26 June the House voted to ban 1997 funding for the project (*Science*, 5 July, p. 25). NASA officials say that step, if endorsed by the Senate, would cripple their ability to analyze data from the Bion 11 flight, scheduled for this fall, and would force NASA to abandon work on Bion 12. "We have to see if we can turn this around in Congress," says Ken Souza, associate director for life sciences at Ames Research Center in California. "If not, it will kill" U.S. participation in Bion.

The program is a joint U.S., French, and Russian endeavor to gather physiological data from monkeys on the effects of weightlessness that could prove useful to astronauts on long missions. Russia has flown eight capsules with rhesus monkeys since 1973. "There are now courses ... and textbooks on space biology, none of which would have been the case without Bion," Souza told the panel. The Merrell panel backed his analysis. "The science integrity [of the project] is unquestioned," said Merrell at the end of the day-long deliberations. "It is solid and of high caliber, and is highly likely to produce useful results."

Animal-rights activists maintain, however, that the experiments could be done on humans rather than monkeys and that Bion has yielded few results that benefit astronauts. "This is garbage science," says Mary Beth Sweetland, director of research, investigations, and rescue at People for the Ethical Treatment of Animals (PETA), who testified at the panel meeting. "We've learned about all we can from these animals. The data will be stored in cardboard boxes, and no one is going to give a damn."

PETA also has argued that restraining the two monkeys aboard Bion for 14 days following three sets of surgeries to implant medical devices such as a skull cap is cruel and unethical. But the panel disagreed. Franklin Loew, a panel member and dean of veterinary medicine at Cornell University, led a subcommittee that concluded that "NASA standards meet existing requirements."

The one loud note of dissension came from Tom Beauchamp, a philosophy professor and senior research scholar at Georgetown University. He criticized NASA for failing to provide evidence that it conducted a serious review of the ethical issues associated with using monkeys for the Bion experiments. At his urging, the panel recommended a broad study of NASA's entire life sciences research program, including a look at the care and treatment of animals.



INSTITUTE FOR BIOMEDICAL PROBLEMS, MOSCOW

Thumbs up. Two rhesus monkeys after a Bion mission, which won praise from NASA panel.

In the meantime, the countdown to Bion 11 continues. The first surgeries for the 10 October launch were conducted last month, according to Eugene Ilyin, who heads the program at the Institute for Biomedical Problems in Moscow and sat in on the Merrell panel meeting. Ilyin is clearly worried, however, about the fate of Bion 12. Given Russia's cash-strapped space program, he says, "if any partner pulled out, it would pose a serious problem."

–Andrew Lawler