

For biomedical researchers, the nail-biting will continue for a while. Only after the Boundaries Panel completes its final Phase 1 report, which will propose the lineup of IRGs, will officials begin the hard part—drawing the boundaries of individual study sections within those IRGs and testing the system to see how it would work. That is expected to take at least another 2 years, and additional changes to the blueprint seem inevitable. “We’re feeling our way,” Alberts cautions. “We’re scientists who are doing experiments.”

—BRUCE AGNEW

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INDIA

Cyclone Wrecks Rice, Botanical Centers

NEW DELHI—Two major Indian laboratories are struggling to recover from a powerful cyclone that swept across parts of eastern India late last month. The storm, which packed winds of up to 280 kilometers an hour, caused extensive damage to the Central Rice Research Institute (CRR) in Cuttack and its



River of ruin. A killer cyclone in eastern India washed away roads and homes and uprooted millions.

germ-plasm stocks as well as destroying much of the collection of rare and exotic plants at the Regional Plant Resource Center (RPRC) in Bhubaneswar.

More than 8000 people have died and 15 million have been left homeless in the eastern state of Orissa, which was cut off from the rest of the country for 3 days after the storm struck on 29 to 30 October. The storm surge drove seawater as much as 15 kilometers inland in what has been described as the worst cyclone of the century.

The cyclone has “ravaged the entire campus” of India’s premier rice research center, CRR director Shanti Bhushan Lodh reported last week. All windows facing north were shattered, and the biotechnology, biochemistry, and engineering departments were filled knee-deep with water. Indian Council

of Agricultural Research officials this week announced a \$500,000 emergency grant to help in the rebuilding of the 53-year-old institute, which remains without electricity and water.

The 70 hectares of rice in experimental plots at the center have also been devastated. Lodh estimates that only a third of the 10,000 rice varieties being grown survived the gale-force winds and subsequent flooding that swept across the region. “The green fields of rice have now turned gray,” he says. Gurdev Khush, chief of rice breeding at the International Rice Research Institute in Los Baños, Philippines, says the devastation will be “a major setback for India’s rice research program” and a “tremendous loss” for scientists around the world.

Probably the worst affected will be the rice germ-plasm collection, which had its roof blown away and its refrigeration units flooded. The 22,000-strong varietal collection, one of the world’s largest, is a medium-term storage facility accessed by researchers around the world. Fortunately, most of its collection is duplicated at the National Gene Bank in New Delhi, a long-term repository for the seeds. In addition, a quick-thinking

scientist reportedly salvaged much of the lab’s supply of temperature-sensitive enzymes and reagents by taking the materials with him on a flight to Chennai a few days after the cyclone.

The damage was even heavier at the RPRC, one of the largest botanical gardens in the world. Created 20 years ago, the center is spread over 197 hectares on the outskirts of the state capital and bore the brunt of the cyclone’s fury. Most of its

valuable collection of rare trees, palms, bamboos, and medicinal and aromatic plants appears to have been destroyed. Director P. Das estimates overall damage at more than \$2 million; in addition to the destruction of labs, stores, and other structures, many roads and paths have been washed away. “It’s the only center of its kind in India,” says H. Y. Mohan Ram, an economic botanist at the Department of Environmental Biology of the University of Delhi.

Lodh is thankful that none of his 140 scientists lost their lives in the storm, but notes that “morale is very low.” A visit last week from a government team resulted in the emergency grant and a backup generator, but Lodh says that the center needs “maximum help” to recover from the devastation.

—PALLAVA BAGLA

AIDS VACCINE

Chimps and Lethal Strain a Bad Mix

BETHESDA, MARYLAND—For the first time in the history of the AIDS epidemic, the National Institutes of Health (NIH) convened a public meeting to discuss a proposed HIV vaccine experiment in chimpanzees. The reason for the extra scrutiny: The test involves giving the animals a strain of the virus that quickly destroys their immune systems and possibly even causes disease.

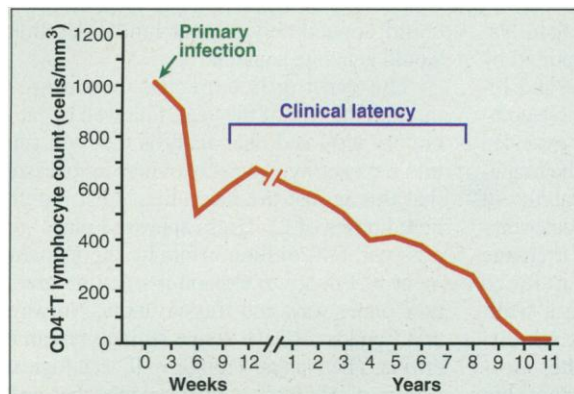
For 2 years, researchers have debated the science and ethics of injecting chimps with a potentially lethal HIV strain to test whether the immune response triggered by experimental AIDS vaccines can block infection or prevent disease (*Science*, 19 February, p. 1090). But what was a simmering academic dispute has now become a real-world dilemma. The National Cancer Institute’s Marjorie Robert-Guroff has proposed just such a test of a vaccine her lab has been developing with the drug company Wyeth-Lederle. A successful experiment, she argued, would help convince colleagues—and Wyeth—that her vaccine approach deserves more support than it’s been receiving.

Billed as a “consultation” to help NIH decide whether it should back Robert-Guroff’s trial, the 5 November meeting triggered impassioned debate over the role that animal “models” should play in the search for a vaccine. It also revealed that anyone who wants to use a lethal HIV strain in chimps first must build a compelling case—something Robert-Guroff failed to do, as the assembled researchers were unenthusiastic about her proposal, apparently leaving it dead in the water. “We recognize this is a complex issue,” said Peggy Johnston, who convened the meeting and heads the AIDS vaccine program at NIH’s National Institute of Allergy and Infectious Diseases. “This consultation is the first step, not the only step.”

Robert-Guroff’s vaccine is now in small-scale human trials to test its safety and ability to trigger an immune response. As her group described in the June 1997 issue of *Nature Medicine*, they had first tested the vaccine—consisting of HIV genes stitched into a harmless adenovirus—in chimps. In the most impressive study, they vaccinated four chimps and then “challenged” them with an injection of an HIV strain that doesn’t appear to harm the animals. More than 10 months later, none had detectable HIV in the blood, while the lone control was infected. “We were pretty encouraged by this study,” Robert-Guroff said. However, she admits that the results drew a tepid reaction from colleagues. “They said we really didn’t show anything, as the [challenge] virus was too wimpy.”

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The concerns underscore the serious limitations of any animal model used to test a potential AIDS vaccine. Monkeys, the most commonly used animal for such tests, usually can only be infected with SIV (a cousin of HIV) or a hybrid virus known as SHIV; they also cannot be infected easily with the adenovirus used in Robert-Guroff's vaccine. Although chimps exposed to HIV can become infected, they generally do not become sick. It was not until 1996 that a disease-causing strain hit the press, when a group led by Frank Novembre at the Yerkes Regional Primate Research Center in Atlanta, Georgia, reported that an HIV-infected chimp named Jerom had developed an AIDS-like disease.



Slippery slope. Typically it takes years (above) for HIV to deplete enough CD4 cells and bring on disabling AIDS symptoms in people. Some strains in chimps, on the other hand, nearly wipe out CD4s within weeks, raising doubts about their suitability as a model for testing AIDS vaccines.

Robert-Guroff and others hoped that this apparently lethal strain would make the chimp challenge model more persuasive. But as the meeting revealed, researchers are divided over how useful this strain might prove to be. For one, the virus is not as devastating as some had expected. Novembre described here how his team has used derivatives of Jerom's virus to infect seven more chimps, some of which now have fewer than 200 CD4 cells—the white blood cells that HIV destroys—per cubic millimeter of blood; one animal's count is down to zero. (For humans, a CD4 count below 200 defines AIDS.) Unlike Jerom, however, none of these animals has yet developed AIDS-like symptoms. This virus “isn't as virulent as I thought it was when I first read about it,” said the New York Blood Center's Alfred Prince, who opposes using lethal HIV in chimps. Still, he said, the strain's diminished reputation doesn't rule out the possibility that it might kill chimps; using it in a challenge experiment would entail unnecessary risks to the animals, he argued, as the goal of a vaccine should be to prevent chronic infection. “Disease is quite irrelevant,” he said.

Others disagreed. Patricia Fultz of the

University of Alabama, Birmingham, dismissed Prince's argument, contending that all chronic infections will, eventually, cause disease. She said the goal is to find a strain that more closely matches a human HIV infection. Although Fultz has tested several strains in chimps—many of which now have low CD4 counts—none duplicates a human infection, in which the virus replicates furiously for prolonged periods while steadily eroding CD4 levels. Ones derived from Jerom have the same shortcoming, she said, depleting CD4 cells more rapidly than is seen in a typical human infection. Finding a strain that behaves in chimps similarly to HIV in humans, Fultz said, is “important for evaluating those vaccine candidates that go into [large-scale efficacy] trials.”

A few scientists question whether the chimp model holds any promise at all. When HIV first infects people, it enters cells using a surface protein called CCR-5. Over time, the virus develops a preference for another receptor, CXCR-4. The Jerom-derived strains, by contrast, rely on CXCR-4 from the outset; thus they do not mimic the initial infection in humans, said Jonathan Allan of the Southwest Foundation for Biomedical Research in San Antonio, Texas. Indeed, he knew of no CCR-5 dependent HIV that could reliably infect chimps. “I don't think vaccine studies are going to go forward based on the chimpanzee model,” said Allan.

Scientific qualms aside, Robert-Guroff's own corporate partner has expressed surprisingly little interest in conducting another chimp challenge. Instead, said Wyeth's Zimra Israel, the company will decide how to proceed based on the immune responses seen in the ongoing clinical trials. Robert-Guroff maintained that positive results from a chimp challenge might build excitement at Wyeth. “If they were convinced by an experiment that this approach was really worthwhile in following, perhaps they would come back into the arena in a forceful way and help out,” she says.

Summing up the feelings of many participants, Norman Letvin of Harvard's Beth Israel Deaconess Medical Center in Boston said he did not think Robert-Guroff's proposal was “a crucial experiment.” Yet he stressed that a pathogenic HIV challenge would be “ethically defensible” for the right experiment, urging his colleagues “not to consign a possible very powerful model ... to the trash heap of history.”

—JON COHEN

ScienceScope

Genentech Settles One of the longest patent fights in biotech history may at last be over. On 16 November, the *Los Angeles Times* reported that Genentech Inc. of South San Francisco had agreed to pay the University of California (UC) \$200 million for having infringed UC's patent on a genetically engineered human growth hormone.

A trial on the decade-old infringement case ended with a hung jury in June (*Science*, 11 June, p. 1752). Now, a scheduled January retrial appears to have been averted. According to the *Times*, nearly half of the settlement will be split among the five scientists named as co-discoverers on the patent, and the remainder will go to UC San Francisco, with \$50 million earmarked to fund a new research building. As *Science* went to press, UC and Genentech were staying silent on the deal until the UC Regents had a chance to review it at a meeting earlier this week.

My Way Arguing that academic quality is paramount, the National Science Foundation (NSF) has reshaped a congressional plan to give out 10,000 scholarships a year to low-income college and graduate students pursuing degrees in computer science, engineering, and mathematics. And even more scholarships may be on the way.

Last year Congress levied a \$500 fee on employers who hire foreign workers for high-tech jobs and gave NSF about a third of the money to provide 2-year, \$2500 scholarships (*Science*, 4 December 1998, p. 1796). But NSF says it is better for institutions—not individuals—to compete for the funds, which total \$21 million in the first round of a 3-year program. The switch “allows us to ensure that the surrounding program is of high quality,” says Norm Fortenberry, NSF's head of undergraduate education. “It's better than telling students: ‘Here's some money, now you're on your own.’” NSF has begun reviewing proposals to select 100 winners from the 280 colleges and universities bidding for up to 40 slots each.

The number of scholarships could grow further under a bill, S. 1804, introduced by Senator John McCain (R-AZ). It would lift the cap—now 115,000—on the annual number of visas issued, which should pump more money into scholarships, and award grants aimed at beefing up math and science education at all levels. “We want a bigger bang for our buck,” an aide explains.

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