MOUNT GRAHAM TELESCOPE

Red Squirrels 2, Astronomers 0

A federal appeals court last week dealt another setback to the University of Arizona in its plans to build a $60 million Large Binocular Telescope (LBT) on an environmentally sensitive site on Mount Graham in southern Arizona. The 9th U.S. Circuit Court of Appeals in San Francisco, in a 2-to-1 ruling, agreed with a lower court judge that the university cannot build the telescope on its planned site without first conducting environmental and biological studies of the impact on local ecology, including the endangered red squirrel. That process could take more than 2 years, according to some estimates.

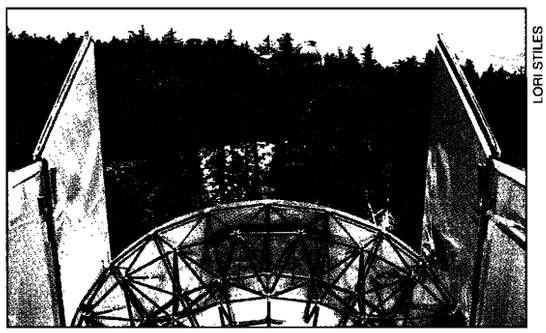
Opponents say the ruling means the university must abide by existing federal environmental laws if it wants to build the LBT, a joint project with the Arcetri Observatory in Italy; the Research Corporation of Tucson, Arizona; and Ohio State University. (Two other telescopes have already been built and are operating at the site.) A 1988 law exempted the university from conducting studies required by the National Environmental Policy Act and the Endangered Species Act for the three telescopes, but the appellate court ruled that the exemption did not apply to a new site, a quarter mile east of the original site, that the government and university chose, ironically, to minimize disruption to the squirrel's habitat.

"What the court is saying is that the special breaks are off and we go back to the basic process that everybody else has to follow," says Washington, D.C., attorney Eric Glitzenstein, who represents a coalition of environmental groups that filed suit in May 1994 after the university cleared 1.5 acres at the new site. The project's backers are naturally disappointed. "We thought we had a strong case," says astronomer George Rieke, deputy director of the university's Stewart Observatory. "We moved there at the request of the government. ... We just want to build one of the world's most advanced telescopes, and now we're facing another big delay."

The ball is now in the university's court, and Sharon Kra, a spokesperson for the president's office, says there are three primary options. One is a request to the entire appellate bench, submitted no later than mid-June, to review the case. However, Glitzenstein says such reviews are usually granted only in cases of "broad legal applicability," which this case doesn't have. In the meantime, the university could begin the necessary studies by asking the U.S. Forest Service to obtain a biological opinion from the U.S. Fish and Wildlife Service about the impact of building the telescope at the new site. Glitzenstein says that could be done in 3 months, although Arizona officials say they have been told it would take at least 2 years. A third option would be to go back to the original site, but Glitzenstein notes that space there might now be at a premium: Under the 1988 law, the telescopes cannot disrupt more than 8.6 acres on the mountain peak, and 1.5 acres have been cleared at the current site.

Astronomer Buddy Powell, associate director of the Stewart Observatory, admits the ruling "leaves us in a quandary." Scientifically, Powell says the project remains on track. The university has $40 million lined up, enough to build one of the two mirrors, and Rieke notes that "we'll go forward with one mirror if we have to, although we're hoping to get the rest of the money for both mirrors." At the same time, Powell admits that older scientists like himself are beginning to worry about whether the telescope will ever be finished. "Somewhere, someway, somehow, we're going to build it," he says. "The question is, where and when? Some of us can't wait much longer."

–Jeffrey Mervis



LORI STILES

Room at the top? Near the LBT's planned site, Germany's submillimeter telescope looks across the mountain at the Vatican Advanced Technology Telescope.

BIOMEDICAL REGULATION

FDA Puts the Brakes on Xenotransplants

The Food and Drug Administration (FDA) has signaled that it intends to regulate the transplant of animal organs into humans—and in so doing has put itself on a collision course with AIDS activists. On 27 April, the FDA suspended plans for a clinical trial to determine whether transplants of baboon bone marrow can repair the devastated immune systems of AIDS patients. FDA's concern: Such xenotransplants might enable animal viruses to infect humans, potentially unleashing a pandemic as devastating as the disease they are trying to cure. Martin Delaney, founding director of San Francisco's influential AIDS activist group Project Inform, immediately objected to FDA's move, characterizing it as "comic-book hysteria."

Despite such criticism, the action indicates that FDA is likely to take a close look at other experiments designed to pave the way for using animal organs to overcome the dire shortage of human organs available for transplant (*Science*, 18 November 1994, p. 1148). Transplant surgeons fear that FDA's involvement could slow down advances in the rapidly evolving field of animal-to-human transplants, or even bring them to a halt. FDA regulation "could stop [transplant] science cold," says transplant surgeon Ira Fox of the University of Nebraska in Omaha, although, he says, "it could be a good thing; ... it could help get the data [on viral transmission] we need."

As it wades into the transplant business, FDA is reaching uncharted regulatory waters. Until now, new surgical procedures have required approval only from local Institutional Review Boards (IRBs) and other institutional panels. But FDA officials decided to act when they learned that AIDS physicians Steven Deeks and Paul Volberding of the University of California, San Francisco (UCSF), and transplant surgeon and immunologist Suzanne Ildstad of the University of Pittsburgh had gotten the go-ahead from UCSF's IRB to transplant baboon bone marrow into AIDS patients. FDA asked the researchers to attend the 27 April meeting, where it became clear, says Deeks, that FDA was requesting that his team formally apply for an Investigational New Drug (IND) approval—just as if the bone marrow were an untested new drug.

Baboons are resistant to HIV infection, so the UCSF-Pittsburgh team, which had intended to start the trial as early as last month, aimed to find out whether transplanted baboon bone marrow—the source of immune cells—could help repair immune systems damaged by the AIDS virus. But FDA fears that the baboon cells may carry viruses that are harmless to their natural baboon host, but which pose an unpredictable and potentially devastating threat to the human population. "It's become clear to the agency ... and to the rest of the Public Health Service that not enough discussion has taken place about the possibility of a pandemic occurring because of the use of baboon tissue," says Philip Noguchi, head of FDA's Division of Cell and Gene Therapy, which seeks to regulate animal organ transplants.

By asking the Volberding-Ildstad group to apply for IND approval, the FDA effectively imposed a long delay on the experiment, because the approval process will entail, among

other things, supplying FDA with details on viral transfer in the few previous transplants of animal livers, hearts, and other organs, including baboon bone marrow. But as there are almost no published data on viral transfer in animal-to-human organ transplants, it could take months to collect the information, if it exists at all, says Deeks. "The protocol will be delayed substantially," he says.

But despite his frustration, Deeks has no quarrel with FDA's scrutiny of the potential risks. "Everything brought up [at the FDA meeting] was very fair," he says, but "some [in the AIDS community] will be very upset." Indeed, when Project Inform's Delaney first learned that the agency was considering asking the Ildstad-Volberding group to apply for IND approval, he shot off a letter to FDA Commissioner David Kessler, urging that FDA avoid "needlessly flex[ing] its regulatory might" when AIDS research is at stake.

Noguchi argues, however, that FDA has a responsibility under the Public Health Service Act to step in if a new therapy carries an infectious disease risk or involves the extensive manipulation of cells outside a patient's body (*Science*, 6 January, p. 19). The agency plans to hold a public meeting sometime in the next few weeks to discuss "the [Volberding-Ildstad] protocol in light of the larger public health issues," says Noguchi.

But experts close to FDA say it won't set safety guidelines until after a committee of the Institute of Medicine (IOM) holds a meeting, scheduled for 25 to 27 June, on the social, ethical, and scientific implications of animal-to-human organ transplants, including the feasibility of screening donor animals for as-yet-unidentified infectious agents. The IOM committee, which is partially sponsored by FDA, plans to release a report on the topic this fall.

Other institutions are keeping close tabs on these deliberations. Early this year a decision that involved senior administrators at Columbia Presbyterian Medical Center in New York City stopped a plan by a team led by that institution's Robert Michler to test baboon heart transplants as a bridge to keep alive babies with heart failure until a human organ could be found. The officials made the decision because of concerns about "protecting public health," says Ralph Dell, chair of Columbia's Institutional Animal Care and Use Committee. Since then, Columbia has created two independent expert committees to ponder the risks of animal organ transplants and is now awaiting the outcome of the FDA's ruminations.

Noguchi believes that delaying the transplants is appropriate. "There's ample evidence that viruses show their worse characteristics when they jump from their [original] host," he says. "It's a very real public health concern."

–Rachel Nowak

DRUG DEVELOPMENT

Rockefeller Strikes Fat Deal With Amgen

Talk about living off the fat of the land. In a deal soon to be completed, Rockefeller University will receive a $20 million payment from biotech giant Amgen for an exclusive license to develop products from a gene that may play a role in determining obesity. The money—the largest upfront payment ever for rights to a university-held patent—will be split three ways: One third will go to molecular geneticist Jeffrey Friedman and two colleagues, and the rest will be divided between Rockefeller and Friedman's employer, the Howard Hughes Medical Institute (HHMI). "It's clearly a powerful statement about what genes are worth," says biotech investment analyst Steven Burrill.

The saga began last November, when Rockefeller began shopping the rights to a potential blockbuster discovery from Friedman's lab: A human gene similar to one that, when mutated, causes a severe hereditary obesity in mice (*Science*, 2 December 1994, p. 1477). Although it's still unclear what role the *ob* gene plays in human obesity, the discovery is seen as an important lead in finding a treatment for a condition that affects one in three Americans. "What makes it so valuable is that there's a clear tie between the gene and gene product to the underlying condition," says Steven Holtzman, chief business officer of Millennium Pharmaceuticals Inc., a Cambridge, Massachusetts–based company that Friedman helped to create in 1993. Millenium is working on drugs against obesity and adult-onset diabetes.

ROBERT REICHERT/ROCKEFELLER UNIVERSITY

Signing bonus. Friedman and colleagues get a third of Amgen's initial $20 million payment.

Friedman's *ob* gene drew a crowd: Some 15 companies expressed interest in obtaining licensing rights to the pending patent. But Millennium's ties to Friedman were no help to the company, which last year inked a $70 million deal with Hoffmann-La Roche. Indeed, Friedman's status as a Hughes investigator prevented the company from securing rights to the obesity gene work before a patent application was submitted. All Hughes investigators agree to assign intellectual property rights to HHMI; the institute retains a research license on any invention and assigns commercialization rights to the scientist's host institution. After a review by an internal panel, Rockefeller invited five companies to submit sealed bids. Amgen was picked because of its track record—two homegrown blockbuster biotech drugs on the market—and its solid in-house research staff, says Rockefeller spokesperson Ingrid Reed. Of course, money also spoke volumes. Amgen's winning offer, in addition to the $20 million signing bonus, includes milestone payments "several times that amount" and unspecified future royalties.

The payment far exceeds those of previous deals: A survey last year of 309 deals by a San Francisco–based company, Recombinant Capital, found that the average upfront fee to universities was only $30,000. "We were rather astounded," says Gregory Hauth, a technology-transfer official at the University of Washington. "We're asking ourselves, 'What did Amgen see that caused it to value the gene at that price?' " Amgen's reply: A potentially vast market for *ob*-derived drugs coupled with the steep cost of developing a drug from scratch. "If obtaining the rights accomplishes a large part of the research process [of drug development]," says spokesperson David Kaye, "then $20 million could be a very strong investment."

Although Millennium is disappointed it didn't win the auction, officials do not see it as a fatal blow. "Jeff was [a company founder] not just because of his efforts to clone the *ob* gene, but because of his expertise in genomics and genetics," says Raju Kucherlapati, chair of the molecular genetics department at Albert Einstein College of Medicine and an adviser to Millennium. "It was explicit right from the beginning that Millennium could compete for the rights to the gene, but there was no understanding that [getting them] was a fait accompli," he says. Friedman declined to discuss the Amgen agreement with *Science*.

The princely sum paid by Amgen troubles small biotech companies, which fear being priced out of the market for hot technologies. "To the extent the [Amgen deal] makes universities greedy for upfront payments, it will make it harder for smaller companies to develop novel products," says Walter Gilbert, a Nobel laureate molecular biologist and cofounder of Myriad Genetics Inc., a small Salt Lake City–based company that Gilbert says did not bid for *ob*. However, Gilbert admits few discoveries are expected to be so lucrative to a university.

In the meantime, Millennium and other players in obesity research are making room for Amgen—their new, sumo-sized competitor.

–Richard Stone