

system messenger called interleukin-2 (IL-2) can help prevent disease and death. The study, which went through a stringent but unusual review process because NIAID director Anthony Fauci holds a patent on the treatment, will involve 210 sites in 18 countries, creating an enormous new clinical trials network that will include some of the world's leading AIDS clinicians. "It's tremendously ambitious," acknowledges Jack Killen, head of NIAID's Division of AIDS. "But this is about as good a shot as we're going to get at answering a very important question."

Whether the so-called Esprit trial is likely to yield meaningful results is, however, being fiercely debated within the AIDS research community. Some researchers believe its flexible design and relatively healthy subjects may blur any results. And numerous other logistical, procedural, and ethical questions have also dogged this trial since it was first conceived 3 years ago, including whether the costly study is needed when smaller IL-2 trials are already planned in sicker subjects.

Small-scale studies have shown that genetically engineered IL-2 significantly boosts levels of CD4 cells in HIV-infected people. (CD4s are the main white blood cells that HIV selectively destroys.) "We have seen changes in CD4 counts, but we don't know what they mean clinically," explains NIAID's clinical director Clifford Lane, who pioneered this treatment strategy and shares the patent with Fauci and NIAID's Joseph Kovacs. (The patent is assigned to the government, and Chiron, the maker of engineered IL-2, has a license; the researchers are entitled to a maximum of \$150,000 of any payments each year, which Fauci donates to charity.) Specifically, none of the trials have yet shown that the CD4 increases result in longer, healthier lives, and the treatment does not seem to decrease the amount of HIV in a person's bloodstream.

The trial aims to mimic the diverse ways IL-2 would be used in the real world. In the first 6 months, 2000 people already taking any combination of anti-HIV drugs will give themselves injections of IL-2 for 5 days every 8 weeks. After those three cycles, physicians will use their discretion to determine the frequency of subsequent cycles of IL-2 treatment, which can cause flulike symptoms. Another 2000 people who are taking only anti-HIV drugs will serve as the control group. "This will give some pretty clear information," asserts Lane.

Others aren't so sure—including the peer-review group that ultimately gave the trial a thumbs-up. "A lot of people are skeptical about whether it will be possible at the end of a large trial like this to sort out the cause and effect when people cycle through different treatments," acknowledges Killen. And the link may be further blurred because Esprit

will recruit people who have suffered relatively modest immune damage from HIV and thus are more likely to respond to the immune booster; to be eligible, HIV-infected people must have at least 300 CD4 cells per millimeter of blood at the trial's start. (The normal range is 600 to 1200.) As a result, it may take longer than 5 years to see enough AIDS-related disease and death to determine conclusively whether IL-2 helps. "You could be holding your breath a long time," says Robert Schooley of the University of Colorado Health Sciences Center in Denver, who heads the AIDS Clinical Trials Group (ACTG), an NIAID-supported network that conducts most trials of AIDS drugs.

The fact that ACTG will not be running this trial is another point of contention. James Neaton of the University of Minnesota, Minneapolis, a biostatistician who is Esprit's principal investigator, says he couldn't interest ACTG. "People I worked with [in the ACTG] wanted to participate, but they couldn't get approval from the executive committee," says Neaton. Schooley explains that not only would the expense overwhelm the ACTG's budget, but ACTG is already conducting a smaller scale trial of IL-2 in sicker patients. "Our feeling is it really offers more to people with advanced disease," he says. (Indeed, Chiron last month launched a large efficacy trial of the treatment in people with 50 to 300 CD4s.) Schooley also questions whether patients with relatively high CD4 counts will choose this toxic and expensive drug. "If you have 700 CD4s, you're going to do well for a long time," says Schooley.

Neaton also considered another NIAID-sponsored clinical trials network, the Community Programs for Clinical Research on AIDS (CPCRA), but it did not have enough sites to recruit the needed number of patients. So, on advice from NIAID, he turned to a mechanism that is rarely used to fund large clinical trials: He submitted an investigator-initiated, "R01" grant.

To help avoid the perceived conflict-of-interest issues raised by Fauci's patent, the ad hoc "study section" of peers set up to evaluate the proposal was convened by the National Cancer Institute, not NIAID. "I can tell you for a fact that Tony had no influence whatsoever on the process of review or the decision about the funding of this," says Killen. Lane, who did help design the trial, says National Institutes of Health lawyers gave him a waiver for that purpose.

Unlike ACTG and CPCRA, study sections evaluate proposals behind closed doors. But interviews with members of the study section and documents provided by Neaton suggest that it received a rigorous review. When the study section first evaluated the proposal in June 1998, it gave it a score of 322, which put it in the unfundable 59.3 percentile. Among

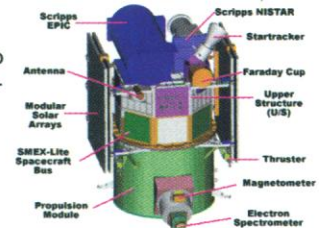
ScienceScope

Triana Troubles A blistering internal critique of NASA's Triana satellite project, which would beam back video and data on the whole Earth, has infuriated NASA officials. NASA Inspector-General (IG) Roberta Gross last week concluded that Triana's changing mission, from inspirational to scientific, and increasing costs—from \$50 million to more than \$75 million—demand a reassessment.

NASA officials fear that the report's timing—it was released just

days before this week's expected Senate vote on Triana funding—sounds the project's death knell. "I question the urgency to issue the report in such a hurry," says Ghassem Asrar, NASA's earth science chief. Other officials complain that Gross overstepped the IG office's traditional focus on fraud.

But Triana's Republican opponents on Capitol Hill (who view the mission, inspired by Vice President Al Gore, as a waste) embraced the findings. They have already convinced the House to kill the spacecraft's funding; NASA officials fear the Senate will follow suit.



Czechmate? Many Czech scientists will face a day of reckoning next year, after their government launches an evaluation of its universities and ministry-run institutes (*Science*, 27 March 1998, p. 2033). But the Ministry of Health is shaking up scientists already: It intends to fold its research institutes into university-based hospitals, to the chagrin of affected scientists. The move "will ultimately harm biomedical research," says Jiri Zavadil of the Institute of Hematology and Blood Transfusion (UHKT) in Prague.

Health Minister Ivan David recently announced plans to dissolve up to 12 institutes and shift staff to hospitals by the end of this year, arguing the move would improve clinical research. But scientists at UHKT and three other institutes fear the debt-laden hospitals will deprive them of scarce research money. "We are concerned about what will happen once we become part of the huge money-losing hospitals," says UHKT director Petr Jarolim.

Eyeing the drama is the Czech government's R&D council, which will begin its review early next year with help from foreign scientists. But the council can't make the ministry hold off, says Vice Chair Josef Syka: "We can only pressure them to do the reform in a proper way."

ing science budgets. "We're making a paradigm shift in leadership; it's clear the regents place a high value on corporate management skills," says Chris Wemmer, who directs the Smithsonian's Conservation and Research Center in Front Royal, Virginia.

The Smithsonian is best known as one of the United States' foremost tourist attractions, having lured 30 million visitors last year to its zoo and 16 museums, many of which line

knowledge—and that there was a point to putting 'increase' first," he told *Science*. There is "no great educational institution where research is not also considered enormously important," he says, adding that although "being a scientist is a wonderful way to spend your life, it doesn't necessarily prepare you for leading a large organization."

His own résumé includes 27 years at Citicorp, eight at Fannie Mae, and dozens of ap-

pointments to nonprofit boards. That background, observers say, should equip him well for the job of streamlining the Smithsonian's bureaucracy, a task Heyman began that earned him high marks from some researchers. Small will also have useful connections when it comes time to raise money, whether lobbying Congress for the 70% of the Smithsonian's budget that comes from taxpayers or seeking corporate gifts for a major upcoming capital campaign. Indeed, one of the new secretary's most valuable assets "may be his Rolodex," jokes

one researcher. But Small says he also has a lighter side, pointing to his year in Spain studying flamenco guitar and a number of other "scholarly passions."

Small will get plenty of suggestions on how to spend any new funds. Many researchers, for instance, would like to see more money for graduate stipends and postdoctoral fellowships, noting that those budgets have eroded dramatically since the 1980s. The number of fellowships available at the Natural History Museum has

slumped from more than 20 a decade ago to about five, researchers note, while the astrophysics center now has just two junior slots available annually on a staff of 300 Ph.D.s. "We are also falling behind in our computing capability," notes Irwin Shapiro, director of the astrophysics center.

For the moment, however, Small is keeping quiet about any plans he has for the organization. Indeed, he notes that he will have his hands full in the short run just finishing off two new projects—an annex at Virginia's Dulles Airport for aerospace exhibits too large for the existing facility on the mall, and a new Native American museum—that were begun by his predecessor.

—DAVID MALAKOFF

THE SECRETARIES OF THE SMITHSONIAN INSTITUTION

Name	Background	Tenure
Joseph Henry	Applied physics	1846–1878
Spencer Fullerton Baird	Natural sciences	1878–1887
Samuel Pierpont Langley	Aeronautics/astronomy	1887–1906
Charles Doolittle Walcott	Geology	1907–1927
Charles Greeley Abbot	Earth science/astronomy	1928–1944
Alexander Wetmore	Ornithology	1945–1952
Leonard Carmichael	Psychology/college president	1953–1964
S. Dillon Ripley	Ornithology	1964–1984
Robert McCormick Adams	Anthropology	1984–1994
I. Michael Heyman	Law/academic administration	1994–1999
Lawrence Small	Banking	2000–?

Washington, D.C.'s grassy mall. Less visible are the institution's more than 600 scientists, who toil amid world-class collections of everything from spiders to gems and conduct studies at seven far-flung research institutes, including the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts, and a tropical research institute in Panama.

Over the last decade, some Smithsonian scientists say their influence—and funding—has waned as the institution expanded and spent aggressively on new art galleries and flashier exhibits. "There has been a slow but inexorable shift away from scholarship and toward public entertainment," believes spider expert Jonathan Coddington of the National Museum of Natural History. He and others worry that the perceived trend—which some have termed "Disneyfication" and others say is "dumbing down"—could undermine the institution's scientific prowess. Small says he has no desire to see research or educational outreach suffer under his tenure, which could last a decade or more. "I am more than aware that [Smithsonian founder] James Smithson's estate was bequeathed for the 'increase and diffusion' of



Break with tradition. Small will be the first nonacademic, and only the second nonscientist, to lead the Smithsonian.

ScienceScope

Distance Learning Agency directors are supposed to go to any length for their boss. But most aren't called on to travel as far as National Science Foundation (NSF) chief Rita Colwell (right), who last week flew to Christchurch, New Zealand, to accompany President Clinton as he visited the agency's staging facilities for Antarctic trips. Clinton attended the Asian Pacific Economic Cooperation summit in Auckland and got a 2-hour tour from Colwell of the International



Antarctic Research Center before giving a speech on Antarctica's environmental value. "I was pleased with his keen interest in the science there," says Colwell.

After a state dinner, Colwell climbed aboard Air Force One for the long flight home. Did she use the time to push NSF's 2001 budget request now being prepared? Well, White House Chief of Staff John Podesta had already signaled the president's strong support for research, she diplomatically said (*Science*, 17 September, p. 1827). And the end of a 5-day tour may not be the best time to lobby, she added: "To be honest, most people slept on the plane."

Thumbs Down In an embarrassing retreat, the Department of Energy (DOE) has withdrawn a controversial \$100,000 grant that critics charged would support discredited "cold fusion" studies.

In June, after physicist Edwin Lyman of the nonprofit Nuclear Control Institute in Washington, D.C., and some DOE researchers challenged the science behind a concept for transforming radioactive waste into harmless byproducts, DOE officials said they were reconsidering the peer-reviewed award to nuclear engineer George Miley of the University of Illinois, Urbana-Champaign (*Science*, 23 July, p. 505). Miley said his experiment was not cold fusion—which seeks to spark nuclear fusion at room temperatures—but this month six new reviewers recommended that DOE spend its money elsewhere.

Miley couldn't be reached for comment. But DOE officials say the episode will prompt changes in its Nuclear Energy Research Initiative (NERI), touted for using top-notch reviews. Promises NERI manager John Herczeg: "We'll be taking a closer look from now on."

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