

maintain the germ plasm collection by annual planting—has now been turned over to a new CIP facility in Quito, Ecuador. And his Huancayo staff has been pulled back to Lima, where they merely have to keep pace with the 2000% annual inflation and stay clear of the burgeoning crime being created by economic hardship.

Sawyer says, "It's not terrorism per se, but we're living in a country where there are food shortages, shortages of a number of the basics." Lima now has an estimated 7 million inhabitants, one fifth to one quarter of the country's population—a large number of them poor people who have migrated from rural areas because of security problems. "Under such conditions you get the kind of crime that's very different from terrorism," says Sawyer.

For CIP, says Sawyer, keeping a low profile is the "principal security factor" in Peru. "If you're working in a developing country and want to drive the flashiest car and live in the best house on the street you're asking for trouble." That is why "we maintain a very low image," Sawyer explains. "Our buses have no names on them. We try to present a very modest face. Our facilities are not country-club style."

Inflation is a serious fact of life for CIP employees. Pay and privileges for the internationally recruited staff, about 100 of the 500 CIP total, are set according to international organization standards. Local hires—Peruvians—are not so well insulated from inflation.

But Sawyer says, "We have not had any trouble getting good staff. Whenever we advertise, we get large numbers of qualified applicants, including excellent candidates for my replacement."

If things continue to deteriorate, can CIP continue to operate in Peru, which Sawyer calls the home of the potato? "Periodically, there is a rumor that CIP is moving out of the country," he says. "But we have no intention of leaving." There is too much at stake.

Sawyer says that CIP has received "tremendous support" from the Peruvian government over the years, and he believes that CIP has made substantial contributions in return. Most important, he says, is that several hundred Peruvians at CIP have become "professionals in their own right because of on-the-job training and experience for the last 10 to 18 years. This would be something that would be very difficult to replace in a developing or a developed country." Sawyer hopes that civil strife can be brought to an end so that CIP and the people of Peru may resume their collaboration on potatoes of the 21st century.

■ JOHN WALSH

Gene Therapy Clears First Hurdle

"We want to do for our patients what they can't do for themselves," R. Michael Blaese said last week at a meeting of the National Institutes of Health's biosafety committee. Blaese is an authority on ADA (adenosine deaminase) deficiency, a rare but severe immune disorder that often leads to death in children who are born without a fully functioning gene for ADA.

Blaese appeared before the biosafety committee to ask permission to give his patients the ADA gene in the expectation that they will then be able to develop a healthy immune system. It is the first time anyone has submitted a proposal for real human gene therapy. After a review that lasted more than 2 hours, Blaese got a green light—the first of at least four more he and his colleagues will need before all the regulatory hurdles are cleared and the first patient can be readied for therapy.

Blaese, a National Cancer Institute scientist, is principal investigator on a protocol that includes Kenneth Culver of Blaese's lab, W. French Anderson of the National Heart, Lung, and Blood Institute, and Martin Eglitis of Genetic Therapy Inc.

For years, ADA deficiency has been high on the list of disorders that might yield to gene therapy. Researchers have assumed that the best strategy would be to insert the gene into the bone marrow stem cells, which give rise to all blood cells, including the white cells of the immune system. Armed with the ADA gene which they lack, the stem cells would go on to produce immune cells with plenty of ADA. However, stem cells have turned out to be incredibly difficult to harvest in therapeutic quantities, and that plan is now on hold.

What Blaese and Anderson are proposing is one step removed from that ultimate bone marrow approach. Their proposal is to insert the ADA gene in lymphocytes, which can be grown using interleukin-2 (IL-2) as a growth stimulant (*Science*, 10 November 1989, p. 746). The ADA-bearing lymphocytes would then be infused into the patient.

During the past several months, Blaese, Anderson, and Steven A. Rosenberg of the cancer institute have gained considerable experience with this procedure, which is already the basis of ongoing gene transfer studies in patients with terminal melanoma. Using a marker gene rather than a potentially therapeutic one like ADA, the Rosenberg team has shown that a gene can be added to IL-2-stimulated tumor infiltrating lymphocytes (TIL) and safely administered to patients (*Science*, 23 June 1989, p. 1430.)

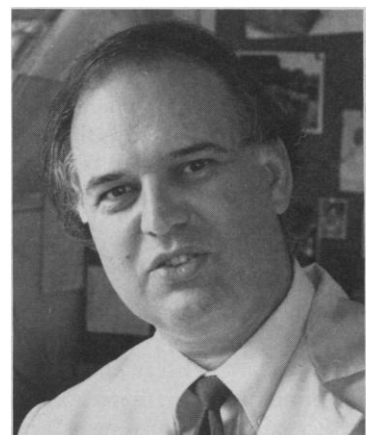
Says Blaese, "Our protocol for the ADA study is virtually identical to the protocol we have been following in the melanoma patients. We will use the same procedures and follow the patients in the same way."

None of the six melanoma patients treated so far has shown any evidence of toxicity from the transferred gene (in this case, the gene for neomycin resistance) and that study will be expanded to include as many as 40 additional patients.

A deficiency of the ADA gene accounts for about one quarter of the 70 children worldwide who are known to suffer from severe combined immunodeficiency disease (SCID). Blaese knows of only 15 who have no ADA at all, so the patient pool for this first test of human gene therapy is small. Although bone marrow transplantation from a matched donor sometimes succeeds as SCID therapy, Blaese reports that in the ADA-deficient group the failure rate is close to 60%, and for these children, he believes, there is no really effective alternative treatment. "As a physician, I feel very comfortable about going ahead," he told *Science*.

Blaese and his colleagues face their next review on 30 March at a joint meeting of the NIH's Recombinant DNA Advisory Committee (RAC) and the RAC's human gene therapy subcommittee. If those groups OK the test, approval must then come from the director of NIH and from the Food and Drug Administration. Anderson says he is optimistic.

■ BARBARA J. CULLITON



R. Michael Blaese

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