out because the parasite creates an autoimmune response, which a vaccine might exacerbate.

On display at the Caxambu meeting, which was largely sponsored by the Brazilian ministry of health, was the latest attempt to break this impasse: molecular genetics. Its centerpiece is an effort by Argentine, Brazilian, Chilean, Mexican, and Venezuelan biologists—along with collaborators in France and Spain—to sequence and map the parasite's entire genome, hoping to identify genes and their protein products that could serve as drug targets. Leaders of the project, including Mariano Levin of the Institute for Research in Genetic Engineering and Molecular Biology (INGEBI) in Buenos Aires and José Franco da Silveira of the Escola Paulista da Medicina in São Paulo, were among those making a report.

The aim, Levin said, is to create a physical map of *T. cruzi* by breaking its genome into well-defined, cloned segments and then sequencing the clones—an effort that he estimated will cost $1 million per year over 3 years. Members have already begun work using existing resources, but they've applied to WHO and other sources for additional funding, which they said will be essential to complete the project.

The project got under way last year, when Daniel Cohen of France's Centre d'Etude du Polymorphisme Humain (CEPH) invited a group of Latin American scientists to visit his lab. There they made clones of a strain of the parasite isolated by Brazilian biologist Zigman Brener. Copies of the clone libraries are now being distributed to interested researchers, while characterization and sequencing of these clones has begun at several labs—including among others Levin's in Buenos Aires, Bianca Zingales's at the University of São Paulo, and Wim DeGrave's at the Instituto Oswaldo Cruz in Rio de Janeiro, a top research center in Brazil formerly directed by Chagas.

Like earlier phases of the war against *T. cruzi*, leading biologists see the genome effort as a means of introducing the latest techniques in biology to Latin America. The Oswaldo Cruz Institute, for example, recently bought a sequencer and a Silicon Graphics workstation for its genome work. "We want the latest technology," says Hooman Momen, vice director and chief of molecular biology at the institute, which is also known as Fiocruz.

But the genome project isn't the only effort to bring up-to-the-minute biology to bear on the disease. Working independently of the project, Samuel Goldenberg, a French-trained investigator at Fiocruz, has cloned and expressed two genes for enzymes vital to the parasite. One plays a role in an RNA editing process that is unique to a type of organism called kinetoplasts; the other is important in energy metabolism. With Gregory Buck of Virginia Commonwealth University in Richmond, Goldenberg hopes to block the enzyme that acts on RNA, disrupting the parasite's replication, and he is also searching for ways to interfere with its metabolism.

Another strategy being pursued by Brazilian researchers in the campaign against *T. cruzi* is so-called rational drug design, in which researchers build on detailed structural knowledge of a pathogen's protein or enzyme to tailor a compound that can block it. One target of these efforts is a unique enzyme known as cruzipain that is essential for *T. cruzi*'s development within a host cell. Julio Scharfstein of the Instituto de Biofísica Carlos Chagas Filho in Rio was one of the first to isolate the enzyme, and James McKerrow of the University of California, Los Angeles, says he and his colleagues have "converged on the same molecule" and obtained images of its structure.

A broader effort in rational drug design is under way at the University of São Paulo at São Carlos, led by a British-educated structural biologist, Glacius Oliva. One of Oliva's graduate students has studied with crystallographer Wim Hol at the University of Washington, Seattle, learning how to crystallize a variety of trypanosome proteins and capture x-ray images of their structures. Oliva and his group intend to use these structures to design and test drugs that would inhibit *T. cruzi* enzymes.

These moves toward cutting-edge science are unnerving some other biologists in Brazil. One fear is that they will divert resources from other basic research—a concern stoked by WHO's recent announcement that it will be redirecting some of its grants for parasite research into genome studies. Others at the Caxambu meeting said they were concerned that WHO has created a two-tier approach. It is urging those who aren't in this elite circle of geneticists or who cannot compete in other special categories, such as drug development, to focus on what biologists in the developing world traditionally used to do—field research. To some, this sounds like "scientific colonialism."

But to Fiocruz's Momen, the effort to build first-rate biology around Chagas disease is a fitting national ambition for Brazil. "We don't agree that there should be second-class research projects for the second world."

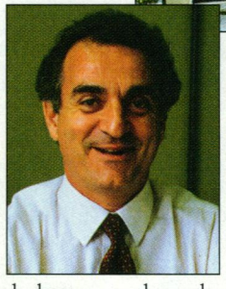
–Eliot Marshall

BRAZIL

Agency is Refuge in Funding Wilderness

SÃO PAULO, BRAZIL—First-World scientists may grumble about problems in getting funding. But their difficulties pale in comparison to those facing their counterparts in Brazil. Take the molecular biologist in Rio de Janeiro who thought he had hit upon the perfect way to beat Brazilian inflation, which in mid-1993 was skyrocketing at 50% per month. When this biologist recently got a grant check from the United States, he decided to cash it and stow tens of thousands of dollars in a safe-deposit box. That way, he thought, he could stabilize the value of his grant. It worked fine—until thieves broke into his bank and emptied all the deposit boxes, abruptly ending his project.

PHOTOS BY E. MARSHALL



Putting science first. São Paulo's funding agency and its scientific director, José Fernando Perez.

The case was exceptional, but many scientists in Brazil say that more conventional sources of funding don't serve them much better than that safe-deposit box did. Brazil's equivalent of the U.S. National Science Foundation—the Conselho Nacional de Desenvolvimento Científico e Tecnológico, known by its obsolete acronym, CNPq—focuses on a variety of targeted programs, stipends, and research institutes, leaving little money for investigator-initiated projects. The other big federal R&D funding agency, Financiadora de Estudos e Projetos (FINEP), favors high-tech ventures. Speaking privately, researchers say they view these two outfits as typical bureaucracies: slow, inward-looking, wasteful, and political. But there is one important funding agency that scientists throughout Brazil know and admire: a revolving fund for science and technology run by the state of São Paulo, called the Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP).

Researchers love FAPESP because it is everything the other agencies are not: efficient, focused on quality, and run with scientists in mind. That tradition got started more than 30 years ago when progressive leaders in the state of São Paulo—Brazil's richest—decided to create a research trust fund that

would operate outside the usual political system. They included in the state constitution a clause stipulating that 1% of all state revenues be set aside each year for research grants. According to FAPESP's present scientific director, José Fernando Perez, the foundation is now receiving about $50 million a year and—using accumulated reserves—plans to spend $70 million to $90 million a year on grants. The money is available only to residents of São Paulo, but often they team up with collaborators in other states.

By law, says Perez, FAPESP cannot spend more than 5% of its budget on administration. The rest goes out to grantees—a striking contrast to the federal agencies, which absorb most of their own budgets administering intramural projects. Unlike some other agencies, FAPESP tries to ban at least the appearance of a conflict of interest, and applications are thoroughly peer-reviewed. Space researcher Umberto Sobral of São José dos Campos, for example, said he was thrilled at how FAPESP handled his application: It read, accepted, and funded new plans to study Earth's magnetosphere, while he had been kept dangling by a federal agency. And a biologist from Rio said he held FAPESP in high regard because even its critical responses show that reviewers read the proposals carefully.

FAPESP is able to put science first because of its independence. At least half of its governing council members, appointed by the governor of São Paulo, have a technical background. As a result, says Perez, "we don't have to align our policies with the government's." However, this could change, because FAPESP's technical orientation has been protected by tradition rather than by law.

But while the going is good, FAPESP wants to expand. According to Perez, the agency hopes to offer a new series of grants aimed at improving scientific infrastructure. Already FAPESP has started the ball rolling by paying to bring the Internet to all Brazilian scientists, including those outside São Paulo. Now, Perez says, FAPESP is planning to invite applications for funding to address equipment needs ranging from air conditioning to lab renovations. In conjunction with the World Bank, which is contributing roughly $100 million, FAPESP is planning to spend $250 million on laboratory equipment over the next 3 years. The word has already gone out, and, based on expressions of interest, Perez says, "the demand appears to be double what we anticipated."

Other Brazilian states are not likely to fill the breach. Their governments have tried to copy FAPESP, writing R&D taxes into their state constitutions. But scientists report that these laws have been ignored: Politicians in other states have not yet been able to stomach anything so weird as an independent, apolitical science agency.

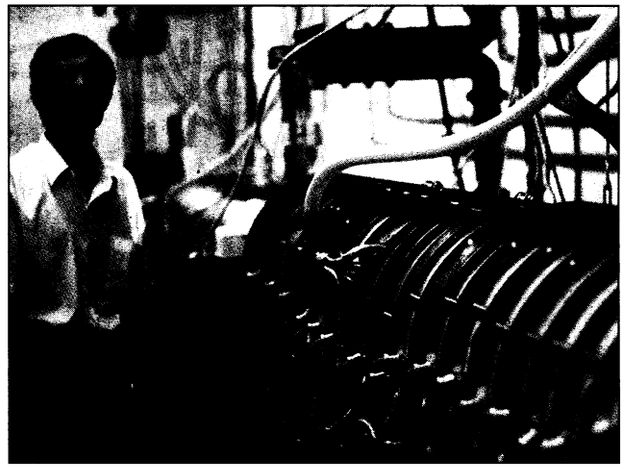
–Eliot Marshall

BRAZIL

Physicists Hand-Build a Synchrotron

CAMPINAS, BRAZIL—On a hilltop on the outskirts of this university town in southeastern Brazil, physicists and artisans have been engaged for the past 10 years in a unique and, many would say, wildly ambitious project. They are building an electron storage ring: a 29-meter-diameter accelerator for electrons. Within a year, if all goes as planned, the ring will spring to life as the heart of the first and only synchrotron light source in the Southern Hemisphere.

The goal is to build a facility comparable to medium-power machines like the one at the Louisiana State University (LSU) in Baton Rouge. The penetrating light thrown off by the billion-electron-volt beam, just shy of hard x-ray power, should enable South Americans to compete with Europeans and North Americans in dissecting new materials and doing exotic biology, such as protein crystallography. And in an extra dose of chutzpah, the Brazilians are building this machine largely by hand. Most of the components are being assembled in special workshops in Campinas because Brazil's economic problems during much of the project ruled out big purchases from overseas.



E. MARSHALL

Ready and waiting. The linear accelerator for the Campinas synchrotron, shown with deputy director Ricardo Rodrigues, awaits the completion of the project, which is scheduled for early 1996.

"Assuming it all works," says Peter Siddons, a physicist at Brookhaven National Laboratory who visited Campinas recently and reviewed parts of the design at the request of the Brazilian team, the machine should be producing "lots of good materials science" in a few years. John Scott, a researcher at the LSU synchrotron, knows the Brazilian effort firsthand because the Campinas center has assembled the experimental equipment for two of the synchrotron's beam lines at LSU for testing. "The craftsmanship is outstanding," Scott says.

Physicist Cylon da Silva, director of the Laboratorio Nacional de Luz Sincrotron (LNLS) argues that besides producing good science, this homegrown effort will generate expertise that should diffuse through the local community, making Brazilian industry more competitive in the world economy. That was the justification for the LNLS when planning began in the early 1980s, da Silva says. And in 1984, this rationale helped win it the status of an official project, backed with funds from the national science council, known as the CNPq. The state of São Paulo also made a donation, kicking in the 90 acres of land adjacent to the university at Campinas where the storage ring is now being built.

But construction has been slower than planned because of budget constraints. In the first years, according to da Silva and his deputy, Ricardo Rodrigues, a few local industrialists were enthusiastic enough to join the board, but no financial support from them materialized. Federal funding has also been less than planned, and the total budget has actually shrunk, dropping from $70 million to $50 million today.

Da Silva thinks the project has now turned a corner. Last year, funds finally came through for construction of the main building. The foundations and roof were in place last fall, and the lovingly crafted magnets and vacuum lines—now housed in a large warehouse on the hilltop—will move into place this year. LNLS is also at work designing research projects, which will use the emitted light for molecular spectroscopy and studies of the fine structure of various solids and liquids, among other things. Sometime in early 1996, da Silva predicts, the whole system will be up and running.

The LNLS staff still faces a challenge in trying to finish the project on this schedule. But if you ask da Silva to name the biggest obstacle he has confronted in getting to this point, he doesn't mention a shortage of money, materials, or personnel. Instead, he says his biggest problem was persuading Brazilian leaders that Brazil could actually build such a complex machine and make it work. In less than a year, his judgment on this point will be put to the test.

–Eliot Marshall