Cuban biotechnology

Progress despite isolation

Havana

CUBA's energetic attempts to develop its own biotechnology research base and apply it to human and animal health-care were proudly paraded before 900 delegates from 41 countries last month at the Second Cuban Seminar on Interferon. Some of Cuba's technical achievements — such as the cloning and expression of α_2-interferon in yeast at high yield — are undeniably impressive, given the total economic blockade by the United States. Visiting US scientists found their Cuban counterparts dedicated and well trained, but some came away with reservations (shared by some Cubans) that a new emphasis on central research planning and pressure to find practical applications might still leave the country short of basic research expertise in a few years' time.

Cuba's decision five years ago to devote a new research centre almost exclusively to the production and purification of interferon — the Centre for Biological Research (CIB) — still seems surprising, given the economic problems the country faces and the relative lack of research in, say, physics. The explanation offered by vice president and minister of education and science José Ramón Fernández, who occupies his spare time compiling books of reprinted articles on biotechnology, is that he and Fidel Castro decided that biosciences could be Cuba's economic salvation next century. He cites Cuba's restricted agriculture (sugar cane is overwhelmingly the largest crop) and poor mineral resources. Fernández says the science budget, as far as it can be distinguished from education, has almost doubled in 5 years to 140 million pesos (1 peso = US$1.18). The claim that great importance is attached to health care is backed up by impressive statistics: infant mortality and life expectancy are close to the US figures (respectively, 14.3 per thousand, and 74 and 75 for men and women).

One explanation heard for the interferon effort is that it was selected as a "model" to develop the infrastructure for cloning and protein harvesting; other products will follow. Interleukin-2 has been cloned within the past year. But although outside Cuba most now recognize that interferon will probably not be the wonder drug the popular press was proclaiming a few years ago, Fernández seems undaunted.

To emphasize further its seriousness about biotechnology, Cuba is spending 50 million pesos on a new Centre for Genetic Engineering and Biotechnology (now under construction) that will house 150 scientists by this summer and include sterile animal rooms and a P4 containment laboratory. Cuba was a candidate location for one of the two biotechnology research laboratories to be built by the United Nations Industrial Development Organization (UNIDO), but withdrew its offer to avoid competing with India; it then decided to build one on its own, which is likely to be in operation before the two UNIDO laboratories, now being built in New Delhi and Trieste.

Although it concentrated initially on interferon, CIB has diversified. Under the control of a government agency known as the "Biological Front", CIB is now developing a vaccine for the cattle disease caused by *Clostridium haemoliticum* (antigens have been expressed in *Escherichia coli*), and it plans a new animal research centre.

Many of CIB's scientific staff were trained at the older and much larger National Centre for Scientific Research (CENIC), founded in 1965 on Castro's instructions. More than 8,000 scientists have been trained there before moving on to other institutions; the scientific staff, numbering 1,000, is down from the peak of 1,400 a few years ago. About 50 papers are published each year in international journals, with more in in-house publications. Research at CENIC focuses on public health and the synthesis of drugs and biologicals, as well as some environmental science and corrosion research; the new biotechnology is used wherever possible. But unlike the early days (which were "anarchy", according to director Manuel Limonta) research has recently been placed under much tighter control by the National Academy of Sciences, a division of central government. The process by which research areas are selected is characterized vaguely as a mixture of priority areas handed down from the academy and suggestions funelled up from the laboratory bench. The deputy prime minister, Fernández, described CENIC as a haven for the basic researcher, but it is clear that a researcher has to obtain the support of a superior before a suggestion will go anywhere. Independent peer review seems to be considered a luxury that Cuba can do without, and researchers and laboratory chiefs make no bones about their preference for research with forseeable applications.

Many of the health-related research projects are using new techniques of molecular biology. Cuba is perversely proud of the fact that atherosclerosis, normally thought of as a disease of developed countries, is now the major cause of death among males, and efforts are under way to isolate a monoclonal antibody against the apolipoprotein-B receptor to study genetic predisposition to the disease.

Plant biotechnology has recently been recognized as a national priority and is now a major CENIC activity, much of it focusing on sugar cane. Somaclonal variation is being exploited to produce new varieties which have been introduced on farms and are now found in seven of Cuba's fourteen provinces. Five different varieties have been identified that are resistant to eye spot disease, *Helminthosporium sacchari*, and a protein has been identified in the plant whose quaternary structure seems to correlate with resistance. Other major research efforts concentrate on improving the amino acid composition of yeast for animal feed, extraction and characterization of active substances in plants and ways of using waste from sugar refining, such as producing biogas. Dr Jorge Benitez of the genetics department has constructed stable hybrids of *Saccharomyces cerevisiae* and *Candida utilis* that can be fused (as protoplasts) with the parent strains to give segregants that grow on D-xylose but also show β-glucosidase activity (the enzyme responsible for cellulose breakdown).

None of Cuba's science would be possible without a good educational system, and 220,000 students are in some form of higher education (out of a population of about 10.6 million). Especially talented high-school students are picked out in their teens for fast-track treatment, and Fernández wants to see more fast-track education. Students' exchanges at both undergraduate and postgraduate levels are considered vital, and many researchers were trained in Moscow and other Eastern bloc countries (including Angola) as well as Mexico, Britain and France; about 10,000 Cuban students are now studying abroad. And despite the current US administration's crackdown on relations with Cuba (US citizens are not allowed to visit as tourists) there are even some studying in the United States. At the University of Havana most professors are expected to spend a quarter of their time doing research (there are a few full-time researchers); research decisions are made at faculty council level but priority goes to areas that are being recommended by the Academy of Sciences. Again, applied biotechnology is very much to the fore.

There are informal collaborations with US scientists, particularly through the organization NACSEX (North American Cuban Scientific Exchange) run by Harlyn Halvorson of Brandeis University. But not as many as the Cubans would like. Dr Rudolfo Maribona of CENIC, who works on the molecular biology of eye spot disease in sugar cane, said plaintively "we invite the US scientists but they don't come". Be that as it may, Cuban biotechnology is making progress. **Tim Beardsley**

The Second Cuban Seminar on Interferons and First Cuban Seminar on Biotechnology, Havana, 20 – 22 February. Tim Beardsley's visit to Cuba was paid for by the Cuban National Academy of Sciences.