A springboard to success

Can Brazil build on its achievement of completing the first genome sequence of a plant pathogen? That may depend on its willingness to reform its universities, say Colin Macilwain and Ricardo Bonalume Neto.

CRISTIANO MASCARO/FUNDECITRUS

Cover stars: publication of the genome sequence of the citrus pathogen *Xylella fastidiosa*, which is spread by a leafhopper (above), made celebrities of Brazilian geneticists.

When Fernando Perez, scientific director of FAPESP, the Brazilian state of São Paulo's science funding agency, launched an ambitious project to sequence the genome of a bacterium that attacks orange trees, his main objective was to train the state's scientists in the techniques of genomics. But now that the sequence of *Xylella fastidiosa* has been published in *Nature*[1], the project is being hailed as a great deal more than a successful training programme.

The *Xylella* experience proved that Brazil's researchers can hold their own in the big league, turned its leaders into media personalities, and has seen them fêted by the nation's president. "It mobilized public opinion to accept the possibility that we can achieve many things in science," says Carlos Pacheco, deputy minister of science and technology in the Brazilian federal government. The challenge now, for scientists and policy-makers alike, is to maintain the momentum and ensure that other talented Brazilian researchers get a chance to compete at the highest levels.

Encouragingly, the federal government is following São Paulo's lead and stepping up its investment in research. But many scientists warn that, if this spending is to bear fruit, there will have to be major reforms to Brazil's inflexible university system. Indeed, given the rate of progress in genomics, it will be a challenge even to maintain the country's current position in that field. "We have entered a high-speed freeway," says Perez. "We have to adjust to the situation, and make the right choices."

The *Xylella* sequence was undertaken by a consortium called ONSA, the Organization for Nucleotide Sequencing and Analysis, at a cost of US$13 million. The project's leaders carved out their genomics niche by picking an organism that is important to the local economy, and turned to a collaborative model, linking many small labs.

The use of a consortium is not new — the European yeast-genome project took a similar approach[2]. But the subsequent development of the Internet has made such collaborations easier. And the model proved especially appropriate in Brazil, where the fierce competition between individual labs that drives North American and European science is not so evident. "We are not competing with one another necessarily. The push comes from competing with scientists abroad, as a group," says Andrew Simpson, an English-born geneticist at the Ludwig Institute for Cancer Research in São Paulo, who helped lead the project. "We may have hit on a solution for how developing countries might develop their science."

Opportunities and obstacles

Brazilian scientists in other disciplines are already trying to think of ways to replicate the ONSA model, no doubt inspired by the outpouring of national pride that greeted the *Xylella* project's appearance on the cover of *Nature* — recognition befitting ONSA's achievement. Simpson and Fernando Reinach of the University of São Paulo, another leader of the project, were suddenly the centre of public attention. "It has had an enormous impact," says Hernan Chaimovitch, vice-president of research at the University of São Paulo. "The attitude of people in the media to science has changed dramatically."

But as the euphoria dies down, serious questions are being raised about the ability of Brazil's university system to support similar, internationally competitive projects. The rumblings surfaced last month with the publication in *Nature*[3] of a letter from Tomas Prolla, a Brazilian geneticist working at the University of Wisconsin at Madison. Prolla was responding to suggestions that the success of the *Xylella* project might convince young Brazilian researchers to stay in the country rather than leave for greener pastures abroad[4]. "The rigid bureaucracy of Brazilian public universities turns the simplest transaction into a nightmare," he wrote. "For most Brazilian scientists with academic positions in the United States or Europe, returning home remains akin to academic suicide."

Prolla cites poor academic salaries and a lack of support for young faculty members as particular obstacles. And although other scientists are less outspoken, they echo many of

EDUARDO KNAPP/FOLHA IMAGEM

All for one, one for all: Simpson believes that scientists at different Brazilian institutes are competing as a group with researchers in other countries, rather than with each other.

his criticisms. Reinach argues that the universities are too rigid in their allocation of resources to departments — refusing, for example, to employ computer scientists in biochemistry departments. The genome projects "are putting pressure on the system — which is a good thing," he says. The *Xylella* project allowed young researchers to bypass the universities' rigid career structure, Reinach adds, and created a new "culture of accountability" by paying research teams according to their results, rather than seniority. "I hope that doesn't go away."

Room for improvement

"The University of São Paulo is organizing itself to respond faster to this kind of challenge," responds Chaimovitch. Last month, for example, it announced the establishment of a Centre for Bioinformatics, initially with 16 staff, which he expects to serve as the launch pad for a graduate programme in the discipline. Reinach agrees that the strongest universities are making some progress. But overall he laments that the response has been "very, very slow".

For the universities, lack of resources remains a huge problem, in particular when it comes to retaining technicians and the young researchers on whom the future of Brazilian science depends. With universities unable to supply enough permanent support staff, scientists in São Paulo state often hire technicians on two-year FAPESP 'fellowships', which seldom lead to permanent jobs.

"This is not a good situation," says Jesus Ferro of the State University of São Paulo at Jaboticabal, whose lab is a member of ONSA. Talented young scientists, meanwhile, are lured abroad or take faculty positions at Brazilian universities that involve little research — because this is their best chance of getting a permanent job. "We can attract students," says Chaimovitch. "The problem is keeping them from going to Europe and the United States and being paid royally."

The *Xylella* project has also shone a spotlight on the great inequity of Brazilian science: the relative wealth of São Paulo state compared with the rest of the country[5]. Heavily industrialized São Paulo dominates the Brazilian economy, and the state's scientists benefit from statutes that give FAPESP 1% of São Paulo's tax revenues.

But having seen FAPESP's star rise so dramatically as a result of the *Xylella* project, the federal government is eager to get a piece of the action. Even before the *Xylella* sequence was published, it had announced a plan to double its spending on university research next year, boosting funding by US$600 million through 11 goal-orientated programmes. This month saw the announcement of the last three of these — in health, environmental and aeronautics research. The federal government is also launching its own genome effort, establishing five sequencing networks similar to ONSA.

ROSSANA LANA/FOLHA IMAGEM

Hungry for change: Reinach laments that only "very, very slow" progress is being made towards a more dynamic university culture.

ONSA, meanwhile, is moving to build on the *Xylella* project. Twenty-one grants — ranging from US$20,000 to US$600,000 — have been released to laboratories to investigate the function of the pathogen's genes. "Functional genomics is another challenge for us, because it is not something that is so easy to do as a collaboration," says Perez. On the sequencing side, ONSA has decided to concentrate on plant pathogens. Three such sequences are already being worked on, and FAPESP is selecting ten more.

A sequence of sequences

The first of the three ongoing projects is an effort to sequence another strain of *Xylella fastidiosa* that causes disease in vineyards in southern California. The US Department of Agriculture will pay half of the US$500,000 that the project will cost. "We hope that the genes will open up some additional opportunities for disease-management strategies," says Edwin Civerolo, head of the crop pathology and genetics unit at the University of California at Davis.

Meanwhile, a team led by Ferro has almost completed the sequence of *Xanthomonas citri*, which causes citrus canker. This species also attacks many other commercially important crops, including rice, beans, cotton and grapes, raising prospects for future international collaborations. The third project, headed by Luis Aranha of the University of São Paulo at Piracicaba, is focusing on *Leifsonia xyli xyli*, which attacks sugar cane. And FAPESP is planning to use Expressed Sequence Tags (ESTs) — fragments of DNA derived from messenger RNA — to identify genes of scientific and agricultural interest from sugar cane itself. This project will involve researchers outside São Paulo, including the northeastern Brazilian states of Alagoas and Pernambuco.

> The federal government has announced a plan to double its spending on university research.

FAPESP and the Ludwig Institute are also supporting a US$10 million cancer genome project to identify ESTs associated with certain types of tumour, in particular those of the head and neck, which are common in Brazil. The researchers are using a technique called open reading frame EST sequencing, developed by Simpson's team, which homes in on sequences that are translated into proteins[6]. The project already accounts for about 20% of cancer-related ESTs deposited in public databases worldwide, and Simpson aims to have produced a million ESTs by the end of the year. Meanwhile, other researchers want to turn ONSA's sequencing machines loose on parasites that cause disease in Brazil, such as the blood fluke *Schistosoma mansoni*, and *Trypanosoma cruzi*, which causes Chagas' disease.

Whether Brazilian scientists in other disciplines will follow ONSA's example remains to be seen. But the consortium's leaders are confident that the momentum in genomics will not be lost. "A lot of very young guys were on the *Xylella* project, and it turned up some very good people," says Reinach. "They learned the technique and are now using it for their own different things." The experience was "absolutely fantastic", says Sandro de Souza, one of these young scientists, who now runs the bioinformatics programme at the Ludwig Institute in São Paulo. ■

Colin Macilwain is *Nature*'s Senior US Correspondent; Ricardo Bonalume Neto reports for *Nature* from São Paulo.

1. Simpson, A. J. G. *et al. Nature* **406,** 151–157 (2000).
2. Goffeau, A. *et al. Nature* **387** (suppl.), 1–105 (1997).
3. Prollo, T. *Nature* **406,** 826 (2000).
4. *Nature* **406,** 109 (2000).
5. Macilwain, C. *Nature* **398** (suppl.), A16–A18 (1999).
6. Dias Neto, E. *et al. Proc. Natl Acad. Sci. USA* **97,** 3491–3496 (2000).