From Bench to Boardroom: Promoting Brazilian Biotech

The dynamo behind Brazil's sequencing of a crop killer is now calling the shots for the country's biggest biotech venture capital fund

SÃO PAULO—Brazilian biologist Fernando de Castro Reinach remembers exactly when his nation decided to become a global player in genomics. It was during a 1 May 1997 phone call with Jose Fernando Perez, scientific director of the State of São Paulo Research Foundation (Fapesp), the country's third-largest science and technology funding agency. "Let's sequence a genome," Reinach told Perez, who had recently visited several prominent U.S. labs and come away depressed about the state of molecular biology in Brazil. Perez didn't hesitate. "Good. Send me a proposal," he told Reinach.

Three-plus years later, the work that Reinach and his colleagues performed landed on the cover of *Nature* (13 July 2000). The scientists had completed the full sequence of *Xylella fastidiosa*, a bacterium that destroys $100 million worth of Brazilian citrus every year. In addition to putting Brazilian genomics on the world scientific map, the achievement highlighted Reinach's pivotal role in efforts to apply modern molecular techniques to one of the country's most important economic sectors.

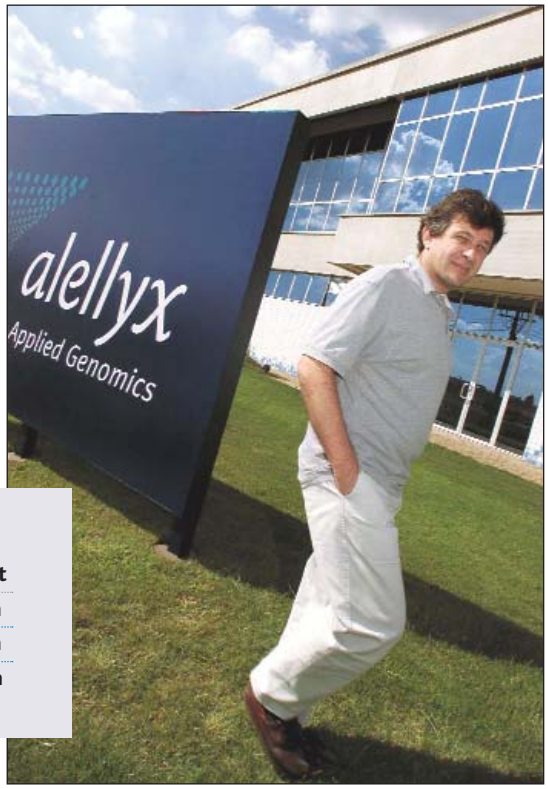
Building a Biotech Industry

Company	Starting date	Investment
Canavialis	March 2003	$7 million
Scylla	June 2002	$1 million
Alellyx	March 2002	$11 million

A 47-year-old professor at the University of São Paulo (USP), Reinach has for more than a decade led a double life as a scientist and entrepreneur—a rarity in Brazil. Last year, he picked up the pace, becoming general partner for life sciences at one of the country's largest venture capital funds, Votorantim Ventures. Reinach hopes his scientific acumen, political savvy, and disarming smile will help nurture his nation's nascent biotechnology industry. "Brazilian agriculture is already very competitive," he says. "We want to make it even better."

Challenging the king

Clad in jeans and a casual shirt, Reinach doesn't look like the typical captain of industry. And don't ask for his business card: He's probably left it at home and will scribble down his phone number and e-mail on the back of a card belonging to his second wife, Lucia Hauptman. "He doesn't like to think about everyday things," says Hauptman, a banker formerly with Credit Suisse First Boston and JP Morgan. "He sees his mind like RAM on a computer: It is limited, so you don't want to fill it with trivial stuff."



Capital ideas. Alellyx is one of three biotech companies that Fernando Reinach has started with money from Votorantim Ventures.

Reinach has been eager to link the public and private sectors of Brazilian science ever since he completed a Ph.D. with Donald Fischman at Cornell University Medical School and a postdoc with Alexander McLeod at the Medical Research Council's (MRC's) Laboratory of Molecular Biology in Cambridge, U.K. "In the early 1990s, the most successful funds in the U.S. were from the biotech area," his brother Marcos recalls. "So Manoel [de Sa Benevides, a colleague] and I talked to my brother about what kind of business we could start."

Pooling their savings, the three men joined one of Reinach's former graduate students, Martin Whittle, to form Genomic. Founded in 1990, it was one of the first Brazilian companies to perform DNA tests, and one of the first to reach the market with a product. The company immediately became involved in a paternity scandal surrounding Brazil's soccer king, Pelé. At the request of a Brazilian court, Genomic was tapped to test the DNA of a woman who claimed to be Pelé's daughter. Seven years later, a sheepish Pelé acknowledged the woman as his offspring. The very public legal battle was good business for Genomic, now one of the largest DNA testing companies in Brazil.

Founding and running the company didn't keep Reinach from his research on proteins that control muscle contraction. A year after the company was founded, he became a full professor at the University of São Paulo. At 35, he was one of the youngest ever to attain that rank. In 1997, he was among the first group of seven Brazilian scientists to receive a grant from the Howard Hughes Medical Institute. "He is not only good, he is one of the best," says biologist Paul Matsudaira, a biologist at the Massachusetts Institute of Technology in Cambridge who worked with Reinach as an MRC postdoc.

But even a Hughes grant wasn't enough to occupy Reinach. After getting a green light from Perez, Reinach put together a proposal to sequence *X. fastidiosa* by divvying up the work among many labs. At $15 million, the project was not only the biggest ever funded by Fapesp, but it also broke the mold of awarding small grants to individuals. Not surprisingly, many senior scientists saw the project as a threat to the status quo and an unwise use of scarce resources. "I was being criticized for taking all this money to do what they saw as Fernando's project," Reinach recalls. Fortunately, he had strong backing from Perez, who jokes that "I usually don't have good ideas, but I can recognize them."

Worried that his visibility could undermine the project, Reinach declined to even apply for the job of overall project coordinator. Instead, the post was filled by Andrew Simpson, who was a senior cancer geneticist at the Ludwig Institute for Cancer Research in São Paulo. Reinach quietly agreed to head

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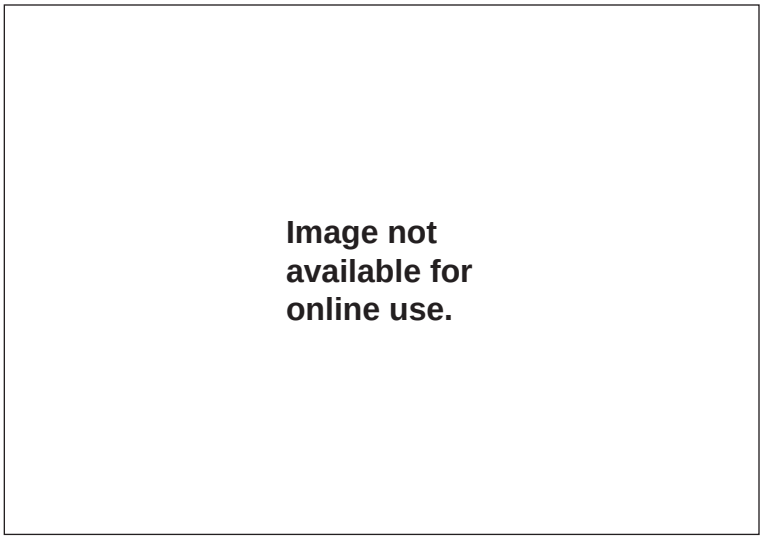
up one of two main labs that oversaw the sequencing going on at the 30 other labs, keeping the scientists on track and training researchers. Against all odds, the project was a smashing success. "Everything was new for us," says Simpson. "We weren't experts in sequencing or in pathogens, but we did it."

Through it all, Reinach remained active in his own lab. *The Science Citation Index* from 1981 to 1999 (a year before the *X. fastidiosa* paper was published) places him in the top 0.1% of biomedical researchers in Latin America, and in the top 2.5% worldwide.

Despite a full plate, Reinach decided in 1999 to launch another private venture, .comDominio, an Internet hosting service that aimed to bring major sectors of the country online. Reinach worked closely with Persio Arida, former head of Brazil's Central Bank and a major backer of the new venture, which soon became the country's second-largest hosting service provider. "I learned to be a businessman by looking at the way Lucia and Persio worked," says Reinach, who served as the company's chief technology officer.



Bearing fruit. Brazilian scientists hope that sequencing the bacterium *Xylella fastidiosa* will be the first step toward reducing its toll on citrus crops.

A personal touch

Reinach's winning personality is as important to his success as are his scientific skills, say his friends. "There is always something interesting to experience with Fernando," says Matsudaira. "If you see him sitting at the lunch table, you want to sit down next to him and talk."

That combination of talent and charisma also captivated venture capitalist Paulo Henrique Oliveira Santos, president of Votorantim Ventures. Santos met Reinach after his company, a $300 million, multisector venture capital fund affiliated with Brazil's largest industrial conglomerate, invested in .comDominio. Many researchers "know a lot about science but little about business," Santos says. "Fernando has both skills."

On the job for a little more than a year, Reinach has moved quickly to promote private sector liaisons in the life sciences. The fund put up $1 million to start Scylla, a bioinformatics start-up headed by a *X. fastidiosa* project veteran, João Meidanis. It also ponied up $11 million for Alellyx (another company had already claimed its intended name, which is *Xylella* spelled backward), which hopes to apply genomic information to improve crop quality and productivity. Besides retaining Reinach as temporary CEO, Alellyx includes four veterans from the sequencing project: Jesus Ferro, Paulo Arruda, Ana Claudia Rasera da Silva, and João Paulo Kitajima.

Reinach is also temporary boss of a company formed this spring with $7 million in seed money from Votorantim Ventures. The company, Canavialis, intends to develop disease-resistant varieties of sugar cane and to improve productivity using genetic engineering techniques. Again, its five partners are academic scientists who, in the last 30 years, have developed 22 varieties of sugar cane. These varieties represent 60% of the sugar cane grown in south-central Brazil.

A fast start doesn't guarantee success, of course. "In the short term, I don't think it will be possible to use any sequencing information for practical applications," says Ernesto Paterniani, an agronomic engineer at Esalq-USP who has spent 40 years working on crop enhancement. Even 20 years may not be long enough, he speculates.

At the same time, the *X. fastidiosa* project has greatly increased Brazil's capacity to do additional sequencing. It trained at least 50 young molecular biologists, some of whom have gone on to complete the genome sequences of two other pathogens, *Xanthomonas citri* and *Xanthomonas campestris*, which are responsible for citrus canker and black rot in crucifers. At least 10 genomes are now being sequenced in Brazil.

Some scientists also wonder if Brazil, where most research is carried out in public universities, is even ready for private-sector research. "We don't have the tradition of protecting intellectual property produced in our universities," says USP biologist Sergio Verjovski de Almeida. Almeida says that most cash-strapped universities are reluctant to encourage their scientists to apply for patents, much less to operate an aggressive technology-transfer office. "It is not clear to me how we will deal with this transfer of technology," he says.

Outside Brazil, Reinach's hands-on role in the companies that Votorantim Ventures is funding might represent a huge conflict of interest. Not so in Brazil, says Luiz Orenstein, a partner at Dynamo asset management, an investment company based in Rio de Janeiro. A conflict of interest exists only "if you are the CEO of the company and the fund you manage has in its portfolio companies that compete with it," he says.

Indeed, many scientists see the companies that Reinach is creating as a welcome opportunity for researchers to work in the private sector. "The Brazilian universities have not been able to absorb all the Ph.D.s that graduate each year," says Walter Colli, former director of USP's chemistry institute.

Reinach agrees that his biotech bets are risky. "This is the first time a large Brazilian private-sector group has put money on an academic spinoff," he says. And there are cultural barriers to overcome. "The universities can't see why it is worthwhile to spin off companies," Reinach says. "They generally think they are losing researchers to the private sector."

This spring, Alellyx scientists announced that a very aggressive mutant of the citrus tristeza virus is the culprit in a newly described "sudden death" disease that caused $20 million in damage to orange crops in Brazil last year. The company hopes to market a laboratory test for detecting the disease within the next 6 months. It's already landed an $8 million contract with Citrovita, a Brazilian company in the Votorantim group that is the third-largest exporter of orange juice in Brazil. Alellyx and Citrovita will work together to improve citrus productivity and resistance to the new virus.

Last year Reinach sold his shares of the privately held Genomic and .comDominio to his partners. Although he declined to mention a figure, he says "it was a good deal." Now he's thinking about new investment targets for Votorantim Ventures. "I am looking in the biodiversity area," he says with his usual disarming smile. Given the country's vast range of ecosystems, it seems an appropriate setting for Reinach to demonstrate his skills as a scientist, entrepreneur, and visionary. **–ALESSANDRO GRECO**

Alessandro Greco has just completed a Knight science journalism fellowship at the Massachusetts Institute of Technology.