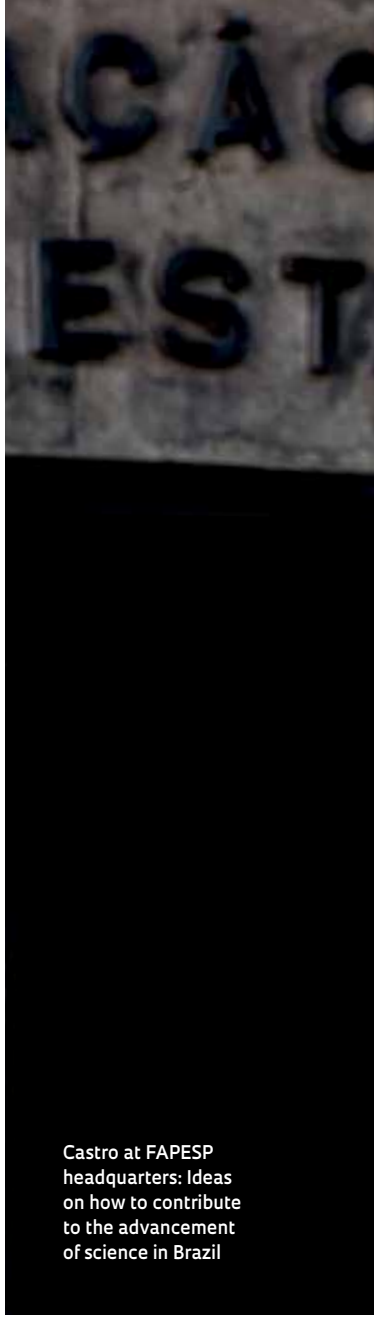
A BOOST FOR BOLD RESEARCH

New scientific director shares his vision for science and the future of FAPESP and reflects on his career as a plant geneticist

Alexandra Ozorio de Almeida, Fabrício Marques and Neldson Marcolin

PORTRAIT **Léo Ramos Chaves**

PUBLISHED IN JUNE 2023



Castro at FAPESP headquarters: Ideas on how to contribute to the advancement of science in Brazil

Marcio de Castro Silva Filho, a geneticist from the state of Minas Gerais, has been familiar with FAPESP since the beginning of his scientific career, when he was invited to join the Young Talents program at the University of São Paulo (USP) in 1994. The aim of the initiative was to attract researchers who had recently graduated and had studied abroad to work at the institution. With Castro, this goal was achieved. Within just a few years, he built a strong scientific career at the Luiz de Queiroz College of Agriculture (ESALQ-USP), including his own laboratory and research projects funded by the foundation.

Almost 30 years later, Castro went from a FAPESP beneficiary to the agency's director. On April 27, he was appointed scientific director, replacing neuroscientist Luiz Eugênio Mello. The move will provide an opportunity to improve processes that, as a user, he felt could be more effective.

Marcio de Castro was born in Belo Horizonte and studied agronomic engineering at the Lavras College of Agriculture, now known as the Federal University of Lavras (UFLA). During an internship at EMBRAPA Maize and Sorghum, he began to specialize in plant genetics, which he studied further during his PhD work in Belgium and later in research carried out at ESALQ. One of the topics he studies is interactions between sugarcane plants and insects. As part of a collaboration with a group from the University of Campinas (UNICAMP), he showed that biological information and digital information have the same mathematical structure.

At the turn of the century, Castro began helping the Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES) in the evaluation of graduate programs and went on to become director of the agency between 2011 and 2016. When he was named scientific director at FAPESP, he was working as dean of graduate studies at USP. In the interview below, conducted in person at the foundation's headquarters in São Paulo, the new director talks about his most important scientific work and lays out some ideas about how he intends to contribute to the advancement of science in Brazil.

AGE 62

FIELD OF EXPERTISE
Plant genetics, science and technology management

INSTITUTION
University of São Paulo (USP)

EDUCATION
Undergraduate and master's degrees from UFLA, PhD from the Catholic University of Louvain, Belgium

SCIENTIFIC OUTPUT
80 articles and 4 patents

You graduated as an agronomist and became a geneticist. Why the change?
First, we need to go back a step. I am the son of Marcio de Castro Silva [1931–2015], a respected angiologist and vascular surgeon from Belo Horizonte. My intention, ever since I was a child, was to study medicine. But when the time came to apply, I asked myself, "Will I even have the chance to work in the same field as my father?" I loved nature and the farms where I spent my childhood vacations. When it was time to sign up for the enrollment exam, I decided on agronomy instead. Soon after, I went to talk to my grandmother on my father's side, who often used to say that he was the pride of the family. She greeted me by saying, "So we're going to have another doctor in the family." When I told her that no, I was going to study agronomy, she responded, "No, don't do that! Everyone knows how to work in the garden." The funny thing is that if I had studied medicine, I think I still would have ended up in genetics research.

Agronomy is a broad field, isn't it?
Yes. I often joke with people that if you don't know what to do, study agronomy. It covers human sciences, health, biology, agriculture, agricultural economics, rural economics, sociology... You will find something that suits you. You will find your path. That's how it was for me. I did the degree but not the undergraduate research project. As a fresh new graduate, still very young and not really knowing where to go, I received a fellowship from EMBRAPA. I went to Brasília to see where I could work, because they have units all over Brazil. Someone there asked me, "What field do you want to work in?" I didn't know what to choose. The person I was talking to looked at me and said, "You look like a geneticist."

Is that true?
It is. I didn't even like genetics when I studied it as an undergraduate, but I started working in the area and realized that it was my thing. I went to EMBRAPA Maize and Sorghum in Sete Lagoas,

Minas Gerais, where I met a fantastic researcher called Ricardo Magnavacca. I always listened to him closely, and when he told me about his experience of doing a PhD in the USA, I realized that I wanted to study abroad. Ricardo advised me to do a master's degree in Brazil and a doctorate abroad. He said it would be good to do a master's degree here while I matured and saw if this was really the path I wanted to take.

Did you follow his advice?
I did. I studied my master's degree at Lavras College of Agriculture, which is now the Federal University of Lavras. I was one of the last to do a full doctorate abroad with a scholarship from the CNPq [Brazilian National Council for Scientific and Technological Development]. In the 1990s, they started doing sandwich courses, through which doctorates are studied in Brazil but with part of the research done abroad. That makes things a lot cheaper. Instead of sending one person overseas, they can send four or five. When I went, almost everyone who applied for an agronomy fellowship from the CNPq was given one and did their PhD at an institution in another country.

Why did you choose Belgium?
I wanted to work with the Belgian scientist Marc Van Montagu. He and Jozef Schell [1935–2003] won an important prize in Japan for their contributions to science, including the discovery of the mechanism behind horizontal gene transfer between *Agrobacterium tumefaciens* and plants. But his group was full, since geneticists from all over the world wanted to work with him. I ended up in another laboratory at the Catholic University of Louvain. My advisor, Marc Boutry, was also a brilliant scientist.

And how did you end up at ESALQ?
During the last year of my PhD, I saw an ad for USP in Nature. It was an announcement by Erney Plessmann de Camargo [1935–2023], who was dean of research at the time, saying something along the lines of "Brazilians abroad: Don't you want to work at USP?" He had created an initiative called the Young Talent program. I had always studied in Minas Gerais and never in São Paulo. At that time, USP seemed like it was out of my reach. I submitted my résumé, and

> "I didn't even like genetics as an undergraduate, but I started working in the area and realized that it was my thing

one day, I received a fax from the director of ESALQ at the time, João Lúcio de Azevedo. It said, "This is a formal invitation to work at the Luiz de Queiroz College of Agriculture of the University of São Paulo." I was practically jumping for joy. I defended my thesis as soon as I could and then started working at the Genetics Department in Piracicaba. And that's where I built my career.

After arriving in São Paulo, how long was it before you became a recipient of funding from FAPESP?
The foundation was essential to me. Even before I arrived, I already had a research project in mind. My advisor said, "When you return to Brazil, avoid administrative positions. Work on developing your scientific career. That will make you invulnerable. Focus on your career." So I came back to Brazil and submitted my research proposal, and it was rejected. I got in touch with Rogério Meneghini, who was on the scientific board's advisory panel, to defend my project and appeal the decision. In the end, it was approved. Three years later, I submitted a thematic project, and this time, it was approved without any problems. Once I started working at ESALQ and managing my projects, I needed more physical space and more people to work with me. My workbench was attached to my desk, with little room to move. It was difficult. I used FAPESP's infrastructure program to improve and expand my lab. The new space was incredible and allowed me to progress with many collaborations. I made a great career of it and started receiving requests from CAPES to help with graduate course evaluations in the early 2000s.

Let's go back a little bit to the 1990s. What were your early studies like at ESALQ?
I wanted to understand how proteins inside a cell are directed to their respective addresses. Plant cells, like any other eukaryotic cell, are divided into organelles: the nucleus, mitochondria, chloroplast, endoplasmic reticulum, etc. There is intense protein traffic inside the cell, with every protein traveling in a certain direction. A protein that goes to the mitochondria does not go to the nucleus, for example. Nucleus proteins do not stay in the cytosol [the liquid that fills the cytoplasm] because they need to perform their function in the right place inside the cell. When I arrived at ESALQ, I tried to find a more practical application for this knowledge. My first project was to introduce a protein called leghemoglobin into a cellular organelle (the chloroplast in tobacco and potato plants in this case) to promote carboxylation of the RuBisCO enzyme, increasing photosynthesis. During my PhD, I had studied an unusual targeting sequence, and I invested in a collaboration with USP professor Carlos Menck. It was the first study showing that a protein could be simultaneously directed to two distinct locations within a cell, to the mitochondria and chloroplasts.

When did your research on plant-insect interactions begin?
At the end of my PhD, a Canadian postdoc friend of mine suggested that I could work with plant-insect interactions, which is a more applied field. When I arrived at ESALQ, I met Professor [José Roberto Postali] Parra, who is really knowledgeable in this area. And there was also Walter Terra, a biochemistry professor at USP's Chemistry Institute. I thought it seemed like a really good path, so I started studying plant-insect

interactions in sugarcane. That's how I later got involved in Bioen [FAPESP's Bioenergy Research Program]. I dedicated myself to understanding how plants produce defense mechanisms to prevent insects from using them as food or hosts. I studied several mechanisms, including how insects break down barriers to start using a plant as a host.

Soon after that, you made other discoveries related to this complex plant-insect interaction. Can you tell us more about them?

In a study that started more than 10 years ago, we investigated the complex interaction between sugarcane, its biggest pest, the sugarcane borer (*Diatraea saccharalis*), and fungi that were considered opportunistic—but we showed that they are not. We published papers emphasizing that the fungi control the plant and the insect as a means of propagating through the production of molecules that we call volatile compounds. When the plant is infected by the fungus, it produces volatile compounds that attract uninfected insect females. The females lay eggs on the plant, and when the caterpillars hatch, they bore into the plant and become infected. When the insects become adults, they are attracted to healthy plants. Thus, the fungus controls both the plant and the insect.

In the late 1990s, you were part of the Organization for Nucleotide Sequencing and Analysis (ONSA), a consortium of laboratories that sequenced the genome of the bacterium* Xylella fastidiosa *and then several other organisms. What was your role?

José Fernando Perez, then scientific director of FAPESP, and Fernando Reinach, one of the ONSA coordinators, called me right at the beginning because they knew I had been working with André Goffeau [1935–2018] of the Catholic University of Louvain, leader of the group that first sequenced an entire eukaryotic organism, a yeast species called *Saccharomyces cerevisiae*. They also called on Marcos Machado of the Agronomic Institute, João Carlos Setúbal from USP, and UNICAMP's João Meidanis, as well as Paulo Arruda, also from UNICAMP, for the bioinformatics parts. I participated in several meetings. People ask me why I didn't coordinate one of the *Xylella* groups. I considered doing so because the role included a public call for proposals with the prospect of major funding. But at around the same time, my first thematic project was approved. I sought advice from Walter Terra, who said, "Marcio, take care of your own area of expertise. It's more important that you develop your line of research. You'll become a point of reference in the field." I chose to go with the thematic project, but it pained me greatly that I couldn't do both.

Do you still think you made the right decision?

It would have been easier if I had joined the Genome Program. It received funding that allowed it to set up larger labs than ever before, but I think I made the right choice. The formation of the ONSA network was a daring and risky initiative that ended up turning out really well and generating great results. Developing a methodology capable of delivering a genome sequence was extremely important, and many people were trained in this area. Nowadays, it is possible to sequence dozens of bacteria in one day, and the new challenge is to ask scientific questions based on this information, build hypotheses, design experiments that explain natural phenomena, and transform it into knowledge that can be applied. There were lots of important scientific questions to be asked, but not every group was able to do so. The researchers who really stood out and established a guiding thread for their careers were those who had a good scientific question to follow, such as Parra, Menck, or Terra, to name a few.

> "The ONSA researchers who developed a guiding thread for their careers were able to do so because they had a good scientific question to follow

During your managerial career, you chose not to leave the lab. Do you plan to continue like this?

In the interview for the scientific director position, they asked me, "This role is going to take up a lot of your time; how are you going to deal with that? And your research?" I didn't want to say too much, but I don't plan on giving it up. I started at CAPES in 2011, then I was an associate dean at USP, and I supervise five doctoral students, a postdoc, and an undergraduate. I go to the laboratory pretty frequently to speak to them. "How are you? How are things going? Tell me about everything." I've changed a little bit in terms of the need to be by the students' side every day. We know what needs to be done; we have regular meetings. Almost all of them are also doing exchanges abroad, so they come and go. I'm a CNPq 1A researcher, and I still have my fellowship, with high-quality work now appearing in important journals. Curiously, I don't have any students from ESALQ, just one undergraduate student. All the rest are from other institutions, who see our work at conferences or in publications and seek me out. It's a fantastic group, and I can keep my eye on them from afar. They see the opportunities and have a strong interest in everything moving forward—they want to do more; they want to discover more things.

What is your opinion on the importance of encouraging researchers with different backgrounds to work together?

Interdisciplinary research is crucial to the advancement of knowledge, for science to move beyond an incremental level. The big leaps arise from interdisciplinary work. All over the world, the organizational structure in closed, monothematic departments is being left behind. When I was researching protein transportation, I was approached by two PhD students who worked with Reginaldo Palazzo Jr.

in the UNICAMP electrical engineering department. They had already been in touch with several researchers, but none were interested in collaborating with them. I went to talk to Palazzo, who is a brilliant researcher, and we decided to work together on mathematical explanations for biological phenomena. To put it simply, we showed that every DNA sequence has a mathematical structure behind it based on error-correcting codes, which are similar to the codes used in digital communication. Biological information and digital information have the same mathematical structure. We thought the work would have a great impact, but there was a lot of mathematics in the paper and it was published in an electrical engineering journal. However, it was only possible for us to achieve what we did by stimulating dialogue between different fields, with a group of electrical engineers talking to a geneticist.

How can we encourage interdisciplinarity?

Before I answer, let me point out that the two places most resistant to change are cemeteries and universities, by free choice of the people who reside there, okay? It is very difficult to encourage interdisciplinarity in an environment where people are so comfortably settled within their areas of expertise. One approach is to robustly fund transversal topics that require different expertise to generate answers. If you look at funding from the National Science Foundation, you'll see that it is directed toward transversal subjects. Two years ago, I was in London at a Research Councils UK event, and two colleagues invited me to dinner at the organization's restaurant. Dinner cost £80–100, but if you sat at a table near the entrance, which could seat about 12 people, you only had to pay £10. The goal was to encourage academics from different fields to sit next to each other and talk. Researchers from the humanities and applied social sciences also need to be involved. Isolation leads nowhere. Many of the answers to scientific questions will come from this type of collaboration.

Interest in graduate courses is on the decline. How can we deal with this problem?

The value of fellowships is one of the important variables, but not the only one. There is less interest because our graduate courses date back to the second half of last century. Students don't feel encouraged to continue in research. There are hardly any physicians doing graduate studies anymore. At USP and many other universities, students are starting their PhDs at the age of 33. They finish at 37 or 38 and start working aged almost 40. In Europe, the USA, and Canada, people finish their PhDs at 27 or 28 years old. Instead of wasting time talking about subjects, they have to interact, develop skills, gain international experience—at USP, 15% of doctoral students do fellowships abroad. That's fantastic. But there are other factors involved in the problem, and they do not only occur in Brazil. A recent editorial in *Nature* described the graduate education crisis as a global phenomenon. I spoke at an event in Egypt last year with the associate dean of the Technical University of Munich, and he said that 90% of the PhD graduates from the institution leave academia to work for private companies, government agencies, or NGOs or to set up their own business. At USP, we created a graduate course called Entrepreneur Scientist. It teaches basic concepts, and at the end, there is a workshop in which students have to solve a problem faced by society through an interdisciplinary approach.

> “The two places most resistant to change are cemeteries and universities, by free choice of the people who reside there

How can an agency like FAPESP help induce or promote this type of change?

One example would be for graduate fellowships to include social security contributions. I came back from doing my doctorate at the age of 33, and my father gave me good news. He told me he had paid my social security contributions during my studies. That will help me out in my retirement. If these students start contributing only when they graduate at age 38, they will have a very different professional life than they would have had in other careers. We could also establish new graduate study models. The master's degree has become a professional program. Only a third of master's graduates go on to do PhDs, but we continue to insist on demanding a master's degree as part of a researcher's training. Wouldn't it be better to reinforce doctoral and postdoctoral studies? While fewer people are looking for research-focused graduate courses, enrollment in MBA programs is exploding, reflecting the current demands of society. We need to create an environment of interaction with society through which researchers are taught to solve problems, participate in interdisciplinary projects, and work as part of a team in contact with diversity. If we don't stimulate these changes, there will be no jobs for PhD graduates.

Compared to developed countries, Brazil has proportionally fewer researchers in general and far fewer working for private companies. What is your perception of this?

The academic environment is not favorable to interactions with the private sector. There are certain initiatives that have been successful—EMBRAPII, for example, which unites support from universities, federal funding, and business resources, with companies defining what they want. There are many interesting projects bringing new knowledge into the company. At FAPESP, we have Engineering Research Centers/Applied Research Centers [CPEs/CPAs], but they involve partnerships between universities and what is still a restricted group of companies. It is not part of a development policy, which is what Brazil needs. There were people who said that this doesn't matter and that it's easier to just import from China. Then, the pan-

demic came, and we ran out of microchips, syringes, and drugs, almost all of which came from India.

Does your experience as a researcher funded by FAPESP give you any ideas on what to do as scientific director?
Of course. I have benefited greatly from FAPESP over the years. I'm receiving an ongoing grant at the moment, and I submitted two other proposals before taking on my new position. One example is that I think we can simplify our processes because we still get lost in the rules sometimes. Not just at FAPESP but in graduate studies as well, we have this habit of maintaining structures that were established a long time ago and never stopping to wonder whether they still make sense. We want to give researchers more autonomy and reduce bureaucracy.

Could you give an example?
Sure; I'll talk about my own case. My thematic project was for five advisors. Nowhere in the world does that. Three approved it the way it was, one asked for further details on the methodology, and the other wanted to reduce the budget by 10%. What response did I receive? Denied. To appeal the decision, I had to ask the whole group to come in and reconfirm their interest and then fill out a huge number of forms all over again. They were allowed to ask for more information about the materials and methods or to reduce the budget. Then, FAPESP would see if it was acceptable or not and would forward it for a comparative analysis. There is a huge firewall blocking the entrance to FAPESP and only a small one at the exit. Is your work incremental or disruptive? Was it used to formulate public policy, a new law, a change in understanding, or to open a new branch of knowledge? That's what we want to know.

So the idea is to avoid micromanagement and the need to monitor day-to-day activities, instead giving the community more space and trust—within certain limits—to do what it considers best for the development of the research. And the other side of the coin is demanding more from the results.
That's right. In the end, I can say that the result was disruptive, but whoever is evaluating it might say, "No, your findings didn't change anything. You described something that had already been discovered by A, B, and C. When your next application is submitted, we will compare it to this." Of course, my approach comes with risk. Those who dare cannot always achieve their aims, but we need to encourage people to become more daring anyway. Boldness can yield results in the future, at the end of the project or when submitting the next proposal. I have always been in favor of giving autonomy with responsibility because in the end, everyone's work is evaluated. If you give people autonomy but without evaluation, then there is a risk. But autonomy with the right oversight, particularly in terms of results, then yes. We need to slightly deconstruct the system that has developed in Brazil, where the means is gaining more relevance than the end. This should never be the case. The end result is what we must be focused on. The means must serve as the way of achieving the end, not the other way around.

> "I have always been in favor of giving autonomy with responsibility because in the end, everyone's work is evaluated

FAPESP has some special programs, such as Biota and Climate Change. Is there a chance of any new programs?
This is a role that FAPESP must continue to fulfill. Our understanding of the knowledge we have in certain fields should show us which challenges are most important. But this cannot be done alone. The foundation needs to increase its interactions with other agencies. FAPESP serves a lot of individuals—very few of its beneficiaries are companies. The foundation could also cooperate more with scientists from other states and other countries. It has already been doing this very well abroad. We need to reach out across the entire country because there is room to advance in partnerships with other research-funding agencies.

How do you see the future of the RIDC program?
The RIDC [Research, Innovation, and Dissemination Center] is a FAPESP trademark used to fund long-term projects. The approach, within the current structure, is interesting because it stimulates actions that are a little more interdisciplinary than thematic projects, which are more focused on a specific area. In the best RIDCs, there is a little more complexity and greater opportunity for more comprehensive research. I'm only just starting in my role here, but I think this is an aspect that should be thought about, to assess what things were like before this long-term investment and what changes it has caused in the knowledge of a given field. This kind of assessment is really important and needs to be done. The structure of an RIDC should encourage interdisciplinarity and more transversal research because there is a kind of permanence that allows people to be bolder.

In your inaugural speech, you mentioned scientific integrity and good research practices, among other things. Are there going to be any new guidelines?
FAPESP was the first agency in Brazil to create rules, guidelines, and regulations for the system. Universities followed suit—some more than others. It is an area that is well structured here. But now there is the challenge of artificial intelligence, which did not exist two years ago. We're going to have to adapt to that. That's the way the world is now. If you want to write a proposal about any research field today, just ask ChatGPT, and it writes it for you. We're going to have to think a little bit about the dynamics of AI and how to deal with it. ■