

FACES OF
MASS SPECTROMETRYAdriana Franco
Paes Leme

Anne Brenner and Susannah C. Moore are science writers at Technica Editorial Services

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When Dedication Runs Deep

Adriana Franco Paes Leme's career as a scientist spans continents and disciplines. Her work exemplifies the diverse range of research focuses found in the field of mass spectrometry. She initially developed an interest in mass spec as a graduate student in the School of Dentistry at the University of Campinas. The techniques and instrumentation of mass spec were invaluable in her Ph.D. research on oral biofilms.

Subsequent postdoc opportunities at the Butantan Institute and the University of Virginia School of Medicine continued her effort in mass spec. Her work during this time further explored the uses of mass spec to advance the knowledge on snake venom proteases and envenomation.

Following her postdoctoral years, Adriana returned to her home country of Brazil to serve as a Principal Investigator and the Head of the Mass Spectrometry Facility at the Brazilian Biosciences National Laboratory (LNBio), a National Laboratory from the Brazilian Center for Research in Energy and Materials (CNPEM). She remains engaged with the broader mass spec community through her work with the editorial advisory board of the *Journal of Proteome Research*. Additionally, Adriana has organized an annual proteomics workshop at her lab for the past 11 years, which involves speakers from all parts of the international and national mass spec community.

Adriana attributes her dedication toward her work to the prospect of improved quality of life, especially when thinking of future generations, such as her own children. The potential of her work in proteomics and oral cancer makes up just one vital example of how the research done in the field of mass spec benefits the world.

How did you get your start in mass spec? Was it while you were living in the Brazilian countryside? Or was it after high school when you moved to the big city of Brazil?

My interest in science started after I moved to the big city. During my childhood, I was curious about everything. But it was when I was a grad student at the School of Dentistry at the University of Campinas that I really became interested in mass spec.

When did you make the transition from studying dentistry to studying mass spec?

It is funny that only a few people have a similar background. My curiosity about basic science through the biochemistry discipline started in the first week of my undergraduate courses. The first studies in the Biochemistry lab at the School of Dentistry, supervised by Dr. Jaime Cury, strengthened my wish to be a scientist and guided me to more complex studies to understand oral biofilm formation in the presence of carbohydrates. Under the supervision of Dr. Cury—together with Dr. Claudia Bellato at the Center for Nuclear Energy in Agriculture and Dr. Hyun (Michel) Koo and Dr. Gurrinder Bedi at the University of Rochester Medical Center—the need to discover the role of proteins in oral biofilms led me to explore the proteins deeply, and then the use of mass spec was a certainty. In my Ph.D. thesis, we hypothesized that proteins could modulate the mineral reservoirs in oral biofilms, and mass spec was the best technique for answering this hypothesis. That's when I discovered mass spectrometry and proteomics—while working on my Ph.D. thesis. Therefore, the journey through the School of Dentistry was fundamental to meeting mass spec.

How did having a background in dentistry, and in medical science in general, impact your work in mass spec? How has it shaped your research interest in the field?

As I mentioned, the studies of proteins from oral biofilms and saliva using mass spectrometry started in my Ph.D. in the Biochemistry lab, and this path shaped my career. When I finished my Ph.D., I recognized that I needed to dive into mass spectrometry. I had singular opportunities as a postdoc at



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Adriana with MS specialists, Bianca Alves Pauletti (front) and Romênia Ramos Domingues (back), working on their latest instrument at LNBio, CNPEM (Photo courtesy of Cristiane Delfina Santos Duarte.)

the Butantan Institute and the University of Virginia School of Medicine (UVA), exploring another fascinating fluid: snake venom. The next step was to define my journey as a principal investigator (PI), and I was committed to apply this incredible technique to benefit society by embracing oral health. Therefore, I decided to apply the mass spec knowledge to study oral cancer through mining biomarkers and therapeutic targets to future assist in the clinical decision-making and improve patients’ quality of life.

How did your time as a postdoctoral fellow at the Butantan Institute and the Biomolecular Research Facility at the University of Virginia—impact your career?

After finishing my Ph.D., I decided that I needed to go deeper in the mass spec field, because I have already envisaged using mass spec in my future own lab as a PI. I had the opportunity to perform my postdoc at the Butantan Institute and UVA to study snake venom proteins using mainly mass spectrometry-based proteomics. The experiences with incredible supervisors and institutions—specially Dr. Solange Serrano at Butantan Institute and Dr. Jay Fox and Dr. Nicholas Sherman at the UVA School of Medicine—were unique due to infinite opportunities to learn mass spectrometry guided by biological experiments. This knowledge empowered me to face new challenges as a PI and supported my future path in mass spectrometry.

What first brought you to your current position at Brazilian Biosciences National Laboratory (LNBio), Center for Research in Energy and Materials?

I had several opportunities in the United States that I loved, but I decided to continue my career in Brazil and employ what I had learned here. I applied to a position at Brazilian Biosciences National Laboratory (LNBio), one of the National Laboratories of the Brazilian Center for Research in Energy and Materials (CNPEM), which is a private nonprofit organization under the supervision of the Ministry of Science, Technology, and Innovation (MCTI). I chose to perform my career at CNPEM because it is a center of excellence in science. It also has unique infrastructures that support competitive and collaborative research and mentoring, and it provides access to the scientific community, with the training of Brazilian and foreign researchers and students.

What kinds of discoveries have come from your work with snake venom?

I performed several projects during my postdoc, and two were particularly challenging. In one developed at Butantan Institute, we assessed the in vivo effects on skin and plasma proteins of a high hemorrhagic metalloprotease using diverse proteomic and peptidomic strategies. We used animal models to investigate which proteins can be affected in vivo. This study revealed direct and indirect effects promoted by the proteolytic activity of this



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Adriana with her children, Alice Franco Paes Leme Squina (left) and Luísa Franco Paes Leme Squina (right) (Photo courtesy of Adriana Franco Paes Leme.)

protease, resulting in tissue injury and disruption of hemostasis. In another study, developed at UVA, we took a different approach—we were using plasma proteome-derived peptide libraries and mass spectrometry to explore the peptide bond specificity of snake venom metalloproteinases (SVMPs). Through this, we improved the understanding of the specificity of these SVMPs. Altogether, these projects opened new avenues to elucidate the mechanism of action of snake venom metalloproteinases in the complex pathophysiology of snakebite envenomation.

How has your work helped advance the treatment of oral cancer?

I started my research line focusing on head and neck cancer (HNSCC), including oral cancer, in 2009. Over the years, I was very committed to finding candidates as biomarkers and therapeutic targets for HNSCC using discovery-based and targeted-based proteomics. In this scenario, we have been organizing the experimental designs into two connected paths. In the first, we have been trying to discover potential markers or signatures for HNSCC diagnosis and prognosis using patient samples. Once the protein is associated with the relevant clinical characteristics, this protein is selected to be tested in the second path, including the use of several methods to study the protein–protein interaction and functional assays. Moreover, I should mention that we are

focusing on HNSCC initiation and progression, such as lymph node metastasis—it is known that the lymph node metastasis is the worst prognostic factor. Our hope is that spin-off proteins can be potential therapeutic target and/or predict whether a patient has metastasis or not, guiding the clinical decision-making.

During my time studying this, I have placed much effort on bringing together people with diverse areas of expertise—including mass spectrometry scientists, pathologists, dentists, oncologists, biologists, pharmacists and bioinformaticians—to provide guidance for relevant clinical questions that proteomics can elucidate and how to accomplish them. With this team, we have been able to study, through proteomics, patient samples with premalignant and malignant lesions in several microenvironments, such as saliva, plasma, tears, extracellular vesicles, and fresh and formalin-fixed, paraffin-embedded tissues. Besides developing and optimizing both mass spectrometry-based discovery and targeted proteomics, data analysis, and omics integration, we have been improving our knowledge on tumoral biology and have identified potential HNSCC initiation- and metastasis-associated signatures. Currently, the selected candidates are in different phases of development for clinical translation, and they will be able to accelerate and provide more accurate decision-making in clinical routines.

How did your work on the editorial advisory board of the Journal of Proteome Research help your work in the mass spec field?

It was a great opportunity to join this team. It has been very interesting to get to see how proteomics have been developing over the world and somehow help those researchers who have been submitting their manuscripts. Through that work, I've been able to increase my connections in the field, and I think I will be able to do so even more once the pandemic is totally behind us and we can have more in-person meetings, although the virtual meetings have still been very helpful.

What accomplishment are you proudest of?

I am very proud to have the opportunity to train, supervise, and teach students and researchers in the Mass Spectrometry Laboratory at LNBio, CNPEM. Moreover, every year, we have a proteomics workshop, which I have prepared and organized for 11 years now. We have speakers from all around the world, and it's something I'm quite proud to be leading! I am also proud of my science family, built over the years in the several labs I could work in, and my current and former teams at CNPEM, who have been conquering distinguished positions worldwide. Finally, I am very proud of the science we have been delivering over the years, supported by CNPEM, The São Paulo Research Foundation (FAPESP), and National Council for Scientific and Technological Development (CNPq). With this support, I can also open novel opportunities for young scientists. Finally, I am very proud of having the opportunity to follow my chosen career, overcoming the diversity of being a woman and mother in a country with many needs, reflecting the effort behind mass spectrometry research.

What are some of your interests outside of the lab? Has being the mom of two children influenced those interests?

The last eight years were the best time of my life because, together with establishing my research line as PI, I had also to learn how to be a mother. Many challenges arose, and dealing with them daily, I noticed that they unpredictably strengthened me—whenever I faced the limit of exhaustion, I realized that I still have energy as a scientist and mother because so much love is involved in both. We always want to be a good example for our lab team and kids. Through mentoring and doing research, I feel I'm helping to build a better world in the future for young researchers and my kids. My interests outside the lab very much center around my family, such as traveling to visit my parents' home, which my whole family loves to do every year. It's always the best way to recharge myself.

What advice would you give to scientists working in or entering the field of mass spec?

In whatever you choose to do, you need to be as dedicated and motivated as possible. If everyone had a deep dedication to their field, the world would be so much better than it is now. It's important to learn the mass spec principles as deeply as possible to be able to translate this knowledge to improve people's lives; the rest flourishes naturally.