FACES OF MASS SPECTROMETRY

Fabio P. Gomes

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Defying the Odds

When Dr. Fabio Gomes started his life's journey in one of the world's largest cities, São Paulo, Brazil, he learned to focus on the big picture even when surrounded with the commotion of that huge metropolis. Dr. Gomes, who is Afro-Brazilian, a minority ethnic group in São Paulo, kept his eyes and ears open, taking in words of wisdom and gaining powerful life lessons while growing up in a disadvantaged neighborhood.

Poised to figure out how he would make a mark in the wide world, Dr. Gomes was motivated by his mother's sage advice to be strong when he needed to be and to study. With the help of involved teachers Dr. Gomes excelled in math and other academic subjects, went to college, and earned a master's degree in Brazil.

Mass spectrometry became of interest to Dr. Gomes while he was pursuing his master's degree. Before long he was working directly with mass spectrometers in the United States, and then he was off to Australia to earn his PhD and conduct studies on vitamin D and its metabolites in biological fluids, which he found fascinating. However, over the course of his Ph.D., Dr. Gomes became very interested in protein structure mass spectrometry, and he moved to the lab of Prof. Catherine Fenselau at the University of Maryland where he was trained in biochemical techniques and proteomics with emphasis on top-down proteomics.

After Prof. Fenselau's retirement, Dr. Gomes became a Postdoctoral Research Associate at The Scripps Research Institute with Prof. John Yates, who describes him as "an outstanding up-and-coming mass spectrometrist." Dr. Gomes is currently leading efforts to structurally elucidate protein-protein/ligand interactions using native mass spectrometry and proteoforms using top-down proteomics. Dr. Gomes is applying these mass spectrometry-based methods to many different research projects.

Recognizing the importance of role models while he was himself a student in Brazil, Dr. Gomes once organized a tutoring program for the youth in his community. Now he has become a mentor himself, guiding graduate students on top-down strategies. Currently at Scripps, he is excited to be co-mentoring a visiting PhD student from his native Brazil. Dr. Gomes' top-notch work in the field and strong leadership will soon earn him an independent academic career. Having a broad view in life and in his scientific work has led Dr. Gomes to defy all odds.

How did you get your start in the mass spectrometry field?

Over the course of my master's degree, I became very interested in mass spectrometry, but unfortunately, I did not have the opportunity to work with this powerful technique. After finishing my master's degree, I had an opportunity to work as a professional collaborator at Torion Technologies/Brigham Young University (Department of Chemistry and Biochemistry) where I worked with a portable GC-MS. It was very exciting because at that time this miniaturized technology was under development. But I really gained hands-on experience with mass spectrometry in my Ph.D. research where I developed several LC-MS methods for analysis of small molecules in biological fluids. Although my Ph.D. research was based on the use of a triple-quadrupole mass spectrometer, I also worked with other MS analyzers such as QTOF and ion trap.

What was your specific focus with Prof. Catherine Fenselau's group?

Dr. Fenselau is a pioneer in the field of biological mass spectrometry, and I was fortunate enough to begin my postdoctoral training in her lab. Under her guidance I received in-depth training in biochemical and proteomics techniques that allowed me to interrogate intact proteins in complex samples. My primary work focused on the use of top-down mass spectrometry to elucidate the structures of synthetic conjugated proteins (e.g.,

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Dr. Gomes enjoying dinner with his mother in Brazil.

ubiquitin-Rub 1) and intact truncated proteins in extracellular vesicles. My work in the Fenselau group led to the publication of three research papers, and a travel award from the American Society for Mass Spectrometry to attend the 2017 ASMS Fall Workshop on Top-Down Mass Spectrometry.

What was some of the research you conducted in Australia that was associated with Royal Brisbane and Women's Hospital?

Premature infants are the main recipients of pasteurized donor human milk, when their mothers are unable to provide their own. Breastmilk is an important source of vitamin D for these neonates who are often vitamin D deficient. As a Ph.D. student, I developed mass spectrometry-based methods for quantification of vitamin D and its metabolites in breastmilk (historically a significant analytical challenge) and applied these methods to evaluate the effect of pasteurization on breastmilk. The findings demonstrated that the total content of vitamin D in breastmilk is low and is negatively affected by the pasteurization process. This work was performed in collaboration with the Royal Brisbane and Women's Hospital, and it was published in the International Journal of Food Sciences and Nutrition.

How long have you been working for the Scripps Research Institute? What is your research focused on right now?

When Dr. Fenselau retired in 08/2018, I moved to the lab of Dr. Yates at The Scripps Research Institute to continue my training. Dr. Yates is globally recognized as an innovator and leader in protein mass spectrometry. In his lab, I received in-depth training in grant/manuscript writing. My primary work focuses on the use of innovative mass spectrometry-based methods to define biomolecular structure, link structure to function, and translate to biological relevance. We are currently characterizing protein complexes in breast cancer cells. We are also developing top-down strategies for the analysis of single cells and bovine sperm. I recently submitted a Mentored Research Scientist Development Award (K01) to the National Cancer Institute (NCI) on the relationship between ERα proteoforms/complexes and malignant breast tumors. I am also putting together an R21 application. This proposal is based on a protein assembly that we recently identified in breast cancer cells that seems to be a potential target for drugs and biomarkers for breast cancer.

What is top-down mass spectrometry?

Top-down mass spectrometry is a powerful technique for the analysis of intact proteins. Top-down analysis can provide unique insights into a protein's structure by in-depth proteoform characterization and the identification of multiple posttranslational modifications (PTMs) in a single proteoform. "Proteoform" is a term used to define all different protein products from a single gene that are produced from a variety of biochemical processes including proteolytic processing, hydrolysis, site mutations, and PTMs.

What are some of the problems that you hope to help solve using mass spectrometry?

One of my goals is to better understand the molecular pathways that govern metastatic breast tumors and resistance to endocrine therapy based on a deeper knowledge of the estrogen receptor alpha's structure. There is a wealth of data on estrogen receptor alpha ligands, PTMs, and interacting proteins in different cellular locations and genetic backgrounds., But how these factors are integrated by the ensemble of estrogen receptor alpha's proteoforms is unknown. I hope my research findings will aid in the design of more effective drug candidates that target key estrogen receptor alpha's proteoforms and suppress breast cancer growth. It will define the molecular mechanisms of resistance to endocrine therapy which will help overcome this critical obstacle for achieving long-term therapeutic benefits.

How has tutoring and mentoring helped you grow and develop as a scientist?

Fortunately, I have had the opportunity to teach different levels of students at different types of institutions in different countries, from lecturing graduate students to acting as a teaching assistant for economically underprivileged young school children. During my master's degree, I co-supervised two undergraduate students, and I have co-mentored graduate students, visiting professors, and colleagues in the laboratory, offering guidance ranging from teaching fundamentals in chemistry and proteins to establishing protocols in proteomics, mass spectrometry, and separation sciences. I am currently co-mentoring a visiting Brazilian graduate student at Scripps who is seeking to gain research experience with top-down proteomics. These experiences have significantly enriched my life on both professional and personal levels by


Dr. Gomes in the laboratory

helping me to develop strong leadership and communication skills. I have also enhanced my capability of motivating and encouraging students, colleagues and friends. Importantly, it has significantly helped me to become a better scientist and team member.

Tell us about your work with label-free mass spectrometry and branched proteins.

The label-free mass spectrometry work was a collaborative study between the Yates lab and a research group from Brazil. This collaboration resulted in a publication in Scientific Reports. In this study, we used label-free mass spectrometry to quantify seminal plasma proteins from Holstein bulls with low and high sperm freezability. This work was an important contribution to the field of male fertility.

Regarding the work with branched proteins, PTMs by the covalent attachment of small signaling proteins (e.g., ubiquitin) define the functions and fates of cellular proteins. However, studies of the relationship between these bioactive structures and their functions represent a significant analytical challenge. At the Fenselau lab, we developed an LC-top down-mass spectrometry strategy for the characterization of branched proteins, a strategy that allowed us to elucidate unknown structures of two-component branched proteins.

What kind of work have you done with capillary electrophoresis?

Capillary electrophoresis is a powerful analytical tool with high separation efficiency, speed, and sensitivity. At the Yates lab, we have recently shown the value of this technique for the separation of intact seminal plasma proteoforms, and this work was published in Analytical Chemistry. Our current efforts have focused on the use of capillary electrophoresis as a direct infusion platform for analysis of non-covalent protein assemblies. We also published a review article "Recent Trends of Capillary Electrophoresis-Mass Spectrometry in Proteomics Research" in Mass Spectrometry Reviews. These recent efforts have received attention from the capillary electrophoresis community, and I was invited to give a talk at the CE-MS symposium (ACS Fall National Meeting 2021).

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What are your interests outside of the lab?

When I'm not working, I enjoy many different things, such as listening to music, watching movies, swimming, going out with my wife, spending time with my friends, playing soccer, and having a good beer. I also enjoy calling my mother and niece in Brazil. Getting together for barbecues is also fun. My wife and I used to have barbecues on the beach before the pandemic, but since the pandemic, we haven't barbecued, although whenever it is possible, we go to the beach.

How did your childhood and upbringing in Brazil influence your path as a scientist and mass spectrometrist?

The underrepresentation of black scientists in Brazil is a problem. This issue is certainly attributed to the lack of social networks and resources necessary to promote the development of academic/scientific careers. There are tremendous obstacles to many talented black children. In my childhood, I impressed my teachers with my self-learning skills and strong ability to solve mathematical problems/equations. But with no role models, it was initially impossible for me to aim for a career in science, especially with mass spectrometry that is a highly complex and expensive technique.

When I was a child, my dream was to be a soccer player, but it did not work because I broke my knee. Fortunately, my mother's powerful voice convinced me to forget it and to pursue education because it would certainly give me a comfortable life. I am very grateful and thankful to my mother who guided me throughout my youth and sacrificed herself to make sure that my priority was to pursue education. Despite enjoying my college courses in chemistry and pharmaceutical sciences, my internship experience confirmed my interest in chemistry. When I was working as a volunteer student at the University of São Paulo, I was initially trained in organic chemistry and learned how to perform complex chemical reactions and to apply nuclear magnetic resonance spectroscopy for structural elucidation of small molecules. From this wonderful scientific experience, I decided to translate knowledge from the bench to the bedside and then pursued master's and doctor's degrees. In my master's degree, I developed several chromatographic methods for analysis of small molecule drugs and their degradation products in pharmaceutical formulations. Although I did not work with mass spectrometry at that time, I realized its critical role in drug discovery leading me to learn and become an expert in this technique.