FACES OF MASS SPECTROMETRY / Stefani Thomas

Anne Brenner and Hayes Simpson are sciences writers at Technica Editorial

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Committed to making mass spectrometry "for the masses"

Although Stefani Thomas sits still for the duration of our interview, we soon learn that she was born to move. She has crisscrossed the country many times in pursuit of research opportunities that would allow her to gain experience in the analytical approaches associated with mass spectrometry.

Since early childhood, Stefani has known that science sparked her interest. She developed a passion for science even before she was in college, traveling from the West to the Southeast to immerse herself in a high school biological sciences program. Later, a strong foundation in mass spectrometry, built in the labs of the University of Southern California and the University of Maryland, led Stefani in the direction of clinical and translational biomedical research. As a research associate in the Center for Biomarker Discovery and Translation in the Johns Hopkins Department of Pathology, Stefani integrated her experience with analyzing proteins to trace the molecular mechanisms implicated in ovarian cancer using clinical proteomics approaches. Her research achievements and interest in clinical translation led her to pursue clinical chemistry fellowship training at Johns Hopkins toward becoming a board-certified clinical chemist.

Now planted firmly between the East and West Coasts at the University of Minnesota, as an Assistant Professor in the Department of Laboratory Medicine and Pathology, Stefani brings a distinct perspective to her research lab, while implementing mass spectrometry in the clinical lab. Her résumé in the field is impressive—applying liquid chromatography mass spectrometry to virtually everything she does, she has been instrumental in using mass spectrometry to make major contributions to some of the most important issues in medicine today, such as Alzheimer's disease and ovarian cancer.

Stefani is especially committed to making mass spectrometry "for the masses"—that is, reducing any reluctance to incorporate mass spectrometry in the lab. In particular, she is passionate about making mass spectrometry more widely utilized so that a more generalized group, outside of those who are highly specialized in the field, can clearly comprehend its significance and potential.

Aside from a decorated career as a scientist, Stefani also has created an established presence in the performing arts realm, particularly in music and dance. In each city that Stefani calls home, she finds a way to connect her current of creativity to an outlet that draws her into a larger community network. The cultural and performing arts have helped her create a well of creativity and abundance to draw from. Her set of talents, both inside and outside the lab, brings her unique spirit to whatever community she is engaged with.

After obtaining your degree in biological sciences from Dartmouth, how did you first get your start in mass spectrometry?

It was kind of by chance. After I completed my undergraduate education, I knew that I wanted to pursue a career in science, but I wasn't exactly sure how that would look. I started working as a lab technician at the University of Southern California. It just so happened that this lab was focused on mass spectrometry–based proteomics at the time. When I was looking for experience as a lab technician, I wasn't necessarily looking for a specific type of research that was being conducted. I was just looking to make sure that the overall research environment would be stimulating. Austin Yang was the one who hired me, and the first mass spectrometer that I worked on was a Thermo Finnigan LCQ Classic (quadrupole 3D ion trap).

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The Thomas lab team (from left to right): Stefani Thomas, Jolene Duda, Jesenia Perez, Carly Twigg, and Joohyun Ryu (second row, center). (Courtesy of Joohyun Ryu.)

How did you choose to focus on the biological sciences and specifically on the pharmaceutical sciences?

Going back to elementary school, during the summers, I participated in a summer enrichment program at the California Museum of Science and Industry in Los Angeles, CA. That was my first introduction to science outside of a classroom or school environment. That route is what really sparked my interest in science and biological science. In high school, my interest in biological science was furthered by my participation in a summer program at the University of Georgia (UGA) that was targeted towards women. The participants came from high schools from all over the country, and we each had the opportunity to do research in a lab at UGA. That was my first "official" introduction to research within a university environment and it inspired me to pursue a major in biological sciences at Dartmouth. In terms of majoring in pharmaceutical sciences at the University of Southern California, I was basically looking for graduate programs where I would have the opportunity to participate in drug target identification and characterization. There are two sides to pharmaceutical sciences: drug target identification and drug development. I was on the drug target identification side and my graduate studies were focused on the functional proteomic analysis of altered protein signaling modules in Alzheimer's disease.

How has mass spectrometry helped with research into Alzheimer's disease?

Back in graduate school, when I was researching Alzheimer's disease, I was focused on identifying and characterizing post-translational modifications (PTMs) of two of the main proteins that are implicated in the disease: amyloid beta and tau. I had a couple of publications related to the identification of specific phosphorylation, methylation, and ubiquitylation sites on the tau protein that correlate with different stages of disease progression. It's exciting that now some of these markers have been developed into biomarker candidates with validated immunological assays. Those assays are commercialized and are being used as specific markers of not only Alzheimer's disease, but also of different forms of neurodegeneration.

How has your work contributed to our understanding of ovarian cancer?

Following graduate school, I worked for a few years as manager of a proteomics shared service facility, but I wanted to get back into research, instead of a service. That's when I joined the lab of Dr. Bob Cotter at Johns Hopkins as a postdoctoral fellow. In his lab, the project I was fortunate to work on was related to ovarian cancer, and mass spectrometry–based proteomics was really the focus of what I was doing. After Dr. Cotter's passing, I joined the Center for Biomarker Discovery and Translation (CBDT), also at Johns Hopkins. The CBDT is led by a phenomenal group of Principal Investigators: Drs. Daniel Chan, Hui Zhang, and Zhen Zhang. At that time, that group was involved, and continues to be involved, in an initiative that is coordinated by the National Cancer Institute of the National Institutes of Health called the Clinical Proteomic Tumor Analysis Consortium. The real thrust of that program is to apply large-scale proteogenomics methods to understand the molecular mechanisms of cancer, including ovarian cancer. One of the main outcomes of the ovarian cancer project that I worked on was the demonstration that proteomics can complement genomics in providing additional insights into pathways and processes that drive ovarian cancer biology in association with established clinical phenotypes.

How have you applied liquid chromatography mass spectrometry (LC-MS) to your research?

LC-MS is at the fundamental core of almost everything that I do in my research lab. Several of my research studies begin in the biomarker candidate discovery phase. The main goal of my research program is to deploy proteomic methodologies to understand determinants of treatment response in the context of ovarian cancer. The historical precedent has been, "Do you rely upon a patient's genome to stratify them for treatment?" But what has been found is that even when we stratify patients for treatment based on their genome, the patients who theoretically should respond well to these treatments really don't respond well. But again, we're relying on their genome to determine that information. My goal is to rely on the patient's proteome, or the information that's contained within their protein profile, to determine whether

Stefani Thomas performing with Coyaba Dance Theater in Washington, D.C. (Courtesy of Efan Graddy.)

that data can provide a better predictor of treatment response. Initially, we conducted several discovery-based studies, but now we're developing targeted mass spectrometry assays to validate some of these candidates that we identified as being associated with ovarian cancer treatment response.

Why did you decide to pursue clinical chemistry fellowship training after having spent several years engaged in basic and translational research?

I became aware of the field of clinical chemistry during after I joined the Center for Biomarker Discovery and Translation (CBDT) as a research associate following my postdoctoral fellowship in Dr. Cotter's lab. It just so happened that the CBDT was associated with the Division of Clinical Chemistry within the Department of Pathology at Johns Hopkins. Seeking to link my interest in conducting translational research with fundamental clinical laboratory principles toward a goal of improving patient care, I decided to pursue postdoctoral training in clinical chemistry. I applied to a few different programs and decided to accept an offer from Johns Hopkins. I was really fortunate to be selected as their fellow for 2017–2019. The program's faculty included Drs. Daniel Chan, Bill Clarke, Mark Marzinke, Lori Sokoll, and Claire Knezevic. I would also like to gratefully acknowledge the staff of the Johns Hopkins Hospital Core Laboratory who were an integral part of my clinical chemistry training. Now, as a board-certified clinical chemist, I can see that I bring a unique perspective to the projects that are conducted in my research lab.

What are some ways mass spectrometry is now being used in the clinical lab?

In general, there has been a historical precedent of clinical labs being reluctant to implement mass spectrometry assays. Now, we're entering into a phase where the unique value that mass spectrometry can bring to the clinical lab is being more widely understood and appreciated. For example, several clinical labs deploy mass spectrometry therapeutic drug monitoring, toxicology, and endocrinology assays, which is really exciting. Once you make the initial investment for the instrumentation, there is a great deal of flexibility regarding the assays that can be brought up on a particular mass spectrometry platform. On the cutting edge, you have targeted mass spectrometry assays that are being used to quantify proteins. I'm excited about seeing these targeted mass spectrometry–based assays make their way into a clinical environment for the purpose of matching patients with optimal treatments based on their proteomic profiles.

Aside from science, what led you to first start pursuing dance as an interest outside the lab?

I began my formal dance training during my elementary school days. I started with ballet, then jazz, hip-hop, house, and West African dance. I was a member of a house dance company called Bmore Houseful for 10 years in Baltimore, MD and I was a member of a Washington, DC-based West African dance company called Coyaba Dance Theater for 8 years. Now, I'm a member of a West African dance company called Duniya Drum and Dance in Minnesota, where I currently live. In addition, in elementary school through undergrad I played the flute, and I was a member of various chamber music ensembles and symphony orchestras. The performing arts have always been, and will continue to be, a part of my life.

What are your predictions for the future of mass spectrometry?

I am observing a trend toward more standardization for mass spectrometry. To draw an analogy: a PC was, originally, a gargantuan-sized machine, and you needed specialized knowledge to use one. Over the years, they've become smaller, and we've become accustomed to using them in various facets of our lives. With mass spectrometry, some similar concepts apply—when those instruments were initially developed, they would take up an entire room. But over the years, they too have gotten smaller and more user-friendly. By consequence, the barrier to entry into learning how to become an operator of a mass spectrometry system has lessened. If we want to see the use of mass spectrometry in a more widespread fashion in the research and clinical laboratory sectors, we will still need to continue on that trajectory of making these instruments more standardized. Right now, there's still a certain level of background knowledge and a highly specialized skill set that's required to operate them. So, I do foresee even more standardization and, again, a decreased barrier for the adoption of that highly versatile technology. It's fascinating to have witnessed the evolution of mass spectrometry throughout the past two decades, and I look forward with great anticipation to the many novel ways in which mass spectrometry can be applied to support advances in basic and translational research and patient care.

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