FACES OF MASS SPECTROMETRY / Lisa Jenkins

Kristin Elise Phillips, Health and Science writer at the University of Texas at Austin

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The Catalyst in Bethesda

*The most illuminating number linked to **Lisa Jenkins** is 200 - she has co-authored articles with over 200 fellow scientists for journals that include Nature, Biochemistry, and PNAS.*

Jenkins, currently the manager of the Mass Spectrometry Resource at the National Cancer Institute (NCI), is a catalyst among her colleagues. After joining NCI in 2005, where she cultivated a web of collaborative relationships and incorporated mass spectrometry into her research, she essentially wrote her own job description and has managed the mass spectrometry unit for the last six years.

After growing up in Northern Virginia—just about an hour from the property where she harvests her favorite Cherokee Purple tomatoes in the evenings—Jenkins completed a double major in chemistry and biology at Winthrop University before moving on to a doctorate in Biochemistry and Molecular Biology at the University of Georgia.

As she wrote in an author biography for the Journal of Cell Biology in 2015, "I first discovered the fun in studying proteins in the labs of Pascale Legault and Jim Omichinski. I found that I most enjoyed being able to operate the spectrometer: setting up experiments to get at particular questions and processing and analyzing the data to get a glimpse of the protein. The amount of information at my fingertips could be staggering, and I was able to obtain unique insights into the protein function."

Reading her words, it is easy to hear her deeply warm voice full of upbeat energy. She is a dynamo.

What is most exciting about your research?

I enjoy operating large instruments. As a graduate student, I used an NMR spectrometer that required specific expertise for operating, and I had a similar challenge using the mass spectrometer at NCI. It is very powerful: no one can walk up, push a few buttons, and get beautiful data.

I am the head of a collaborative resource for 25 researchers and PI's in the Center for Cancer Research. What's really cool is that I help integrate mass spectrometry into their research on critical biological problems like HIV and cancer, and so my work spans the gamut of dominantly protein-based mass spec. It helps if you are slightly ADD! *[deep laugh]* What is fascinating is that we have multiple projects that converge—like with RNA/protein pull downs to identify protein interactors of RNA—and that can be combined to provide a much larger picture of what is going on. For example, we had a project working on RNA interactors and another with a separate investigator focused on protein interactors of a tumor suppressor that converged on a three-way complex [Chaudhary, R., *et al., eLife.* **6**, e23244 (2017)]. In another area, a lot of people come to me with interest in exosomes, and I've been able to help create a little exosome community and make better samples for publication.

I have also done quantitative mass spec looking at changes in protein levels [Paul, C.D, *et al., bioRXiv.* 233361, (2017), doi: 10.1101/233361]. One of the PI's, Kandice Tanner, is very interested in how malignant cells traffic and where they go - specifically why some breast cancer cells go to the brain or the bone. With a large scale, global proteomic experiment, we found a subset of proteins that direct bone-targeting cancer cells to the bone. But the brain-targeting cancer seems to be less protein-specific.

Could this cancer research occur without mass spec?

No, I don't think so. If you really want to get to the mechanism of why something is happening, you need to know proteins. Mass spec gives a very large, unbiased picture.

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What is your favorite research project?

As a grad student, I looked at small molecule inhibitors of the nucleocapsid protein of HIV [Jenkins, L.M., *et al., J. Med Chem.* **48**, 2847–2858 (2005)]. I first used NMR and then different biochemical techniques with the idea of targeting the virus by targeting the protein. Recently, we've used mass spec to map an inhibitor that is covalently modifying its target by adding a group onto the residues that bind zinc. This causes the protein to unfold so that it cannot function or bind RNA [Jenkins, L.M., *et al., Nature Chem. Biol.* **6**, 887–889 (2010); Jenkins, L.M., *et al., J. Am. Chem. Soc.* **129**, 11067–11078 (2007)]. So what we are doing is a permanent modification of the target, and we are using mass spec methods that allow us to better understand how this molecule is working.

We are now moving forward with nonhuman primate studies to ultimately get FDA approval. To me, these are not diseases that affect abstract people. Both cancer and HIV have affected people that I know and have loved. This helps pull the research, but at the end of the day, it is really fun. If it's not fun, then there is a problem. *[deep laugh]*

What was your career path to NCI?

As I was finishing my grad research on HIV, I was invited to be a post doc in the lab of a collaborator, Ettore Appella. I grew up in Northern Virginia, so I was very aware of the research being done at NIH, and I knew that I didn't want to go into academia. Somehow grant writing is not what I really wanted to do.

I was really excited to work at NIH and work with Appella studying how p53 is modulated by modifications that are added onto proteins after they are made. I learned the mass spec as part of this research, and, by the time my post doc was finishing, I had a lot of collaborators who liked having instant access to someone with the biology and technical expertise to make the best experiment. Mass spec is really powerful and unbiased: if you put garbage into it, you are going to get garbage out. The leaders at the Center for Cancer Research within NCI recognized that it is sometimes important to sit down with a mass spec expert, so I became a resource within a large lab.

What do you enjoy outside of the lab?

My husband is a chef. He worked in commercial food service for a long time, most recently for assisted living facilities. It was hard to have a day off; he would literally have a bed in his office on snow days because people need to be fed. After we talked about the work-life balance, he changed jobs so that he has his own schedule. We really enjoy vacations without the phone ringing constantly.

We are now working on making a good-sized garden on our two acres. Last year, we had so many tomatoes that we were just giving them away at church—I teach Sunday school and lead a Bible study—each week. It is amazing how excited people get about eating a tomato that doesn't taste like a Nerf ball. We tried rows of corn, one decorative and the other for eating, and learned that they cross-pollinate very readily. Our crop was pretty to look at but too starchy to eat! We also grow lettuce, herbs, watermelon, beans, peas, and potatoes. It is some good summer eating; there is something magical about a dinner with vegetables from your garden.