

FACES OF  
MASS SPECTROMETRYLjiljana  
Paša-Tolić

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## Promoting the Team Effort

**L**jiljana Paša-Tolić was born in Croatia and earned her master's and PhD from the University of Zagreb. Although she specialized in physical organic chemistry, Ljiljana notes that her true passion has always been in the field of molecular biology.

More specifically, she enjoys developing novel analytical methods, refining research strategies, and designing innovative instrumentation for studying biomolecules and molecular processes. Throughout her career, Ljiljana has made significant contributions to numerous areas of mass spectrometry related science, including the realm of high-performance mass spectrometry. Moreover, the study of proteins has formed a major chapter in Ljiljana's body of work thanks to her pioneering research in the field of top-down proteomics. Some of her recent research projects involve advancing mass spec performance to characterize molecules in the context of small, limited samples, such as biopsies or single cells.

Ljiljana has spent most of her career working at the Pacific Northwest National Laboratory (PNNL), where she is a PNNL Lab Fellow and lead scientist for visual proteomics with the Functional and Systems Biology group in the organization's Environmental Molecular Sciences Division and Environmental

Molecular Sciences Laboratory user program. While working at PNNL, she has led the development of a series of high-performance mass spectrometers, the most recent of which is the 21 Tesla Fourier Transform Ion Cyclotron Resonance spectrometer. (Figures 1 and 2.) One of the many things she enjoys about the PNNL work environment is the emphasis on collaboration, multidisciplinary research, and team science, which Ljiljana describes as her preferred way of operating. In fact, she believes that an important improvement for the sciences in general would be to update the system of rewards to better support teamwork. Along these same lines, Ljiljana is grateful for the way her job allows her to develop transformational tools and apply them while working with researchers from around the world.

Over the course of her career, Ljiljana has authored more than 300 peer-reviewed publications. Her membership and service to ASMS spans over two decades. During this time, she has organized and chaired sessions on instrumentation and top-down mass spectrometry at several ASMS conferences and has served on numerous committees. She also served on the ASMS board during the COVID-19 years, 2020–2022. She notes that she particularly enjoys attending smaller conferences because they allow her to easily connect with colleagues and discover new opportunities for collaboration. Ljiljana was recently honored in the 2024 Analytical Sciences Power List as an instrumental innovator and as the 2024 recipient of the International Mass Spectrometry Foundation's Jochen Franzen Award.

## Did your interest in mass spec begin in Croatia or when you came to the United States?

My interest in mass spec started in Croatia, but it's a bit of a convoluted story. I did my master's and PhD in Croatia during the war in the 1990's. It was a challenging time to do much of anything, let alone scientific work. My intent was to study and work in molecular biology, but there weren't any resources to do that at the time. I ended up pursuing some of my other loves: quantum chemistry, theoretical chemistry, and physical organic chemistry. While I was a student, my advisor got a brand-new mass spectrometer, a 3 Tesla FTICR, and asked me if I'd be interested in overseeing care of this amazing new device. Of course, I said yes! That is how my mass spec journey started. It can be good to throw yourself into a new adventure from time to time and enjoy the journey. You never know what saying yes can lead to, but you can be sure that saying no will close off new opportunities. Alan Marshall then selected me to be his first postdoc at Magnet Lab. Subsequently, I joined Dick Smith and his team at PNNL, continuing high-field FTICR mass spec developments, yet always looking for potential biological applications.



“ I often think about how we, as a society, could change the system of rewards to better support teamwork in science. ”

*Lili celebrating Jasna's and Cathy's birthdays and legacy at the 15th international Mass Spectrometry in Biology and Medicine (MSBM) Summer School (<http://msbm.org/>) in Dubrovnik, Croatia along with fellow organizing committee (OC) members (from left to right): Ron Heeren (Maastricht University, OC), Laura Bindila (University Medical Center Mainz, OC), Garry Corthals (University of Amsterdam, OC), Cathy Costello (frequent lecturer at the MSBM Summer School; Boston University School of Medicine), Jasna Peter Katalinić (founder of the MSBM Summer School; Universities of Rijeka and Muenster, retired), and Lili. (Photo courtesy of Ljiljana Paša-Tolić.)*

**Why did you decide to focus specifically on protein abundance?**

Proteins were not my focus at first, because I was more focused on analytical science and studied many different types of molecules. But my passion has always been molecular biology and biology-related research; therefore, proteins have been a significant part of my career. Specifically, my focus has been on what we call top-down proteomics. I've always had a passion for developing approaches to studying intact proteins (i.e., proteoforms) and more recently, protein complexes. Today, I aim to develop technologies that will provide information at a systems level, looking at DNA, RNA, proteins, lipids and metabolites. We recently established some very cool methods to map proteoforms across tissues, and to look at transcripts and proteins from the same single cell. We keep moving in the direction of multiomics and systems biology aiming to understand basic principles of biology.

**What brought you to your current position at the PNNL Environmental Molecular Sciences Laboratory?**

I have spent most of my career at PNNL—more than 25 years, to be exact. It's been a long and interesting journey! One of my main motivations for both getting here and staying here over such a long period of time is the emphasis on teamwork and collaboration. Being at a national lab is different from being in an academic lab, or in industry. At a national lab, the emphasis is on team science—people working together. It's all about multidisciplinary research when you're trying to answer some of the significant big questions in the medical or environmental field. This is challenging, sometimes almost impossible to do in an academic context. At PNNL, I can be a part of a team effort by developing transformational tools and applying them while working with many kinds of people—not only across the United

States, but all over the world. This is something that has kept me at PNNL for all these years. I genuinely like team science; it has always been my preferred way of working. I believe that building relationships is the most skill in life and in work, because strong, genuine relationships can provide not only new opportunities, but a sense of belonging, support and joy!

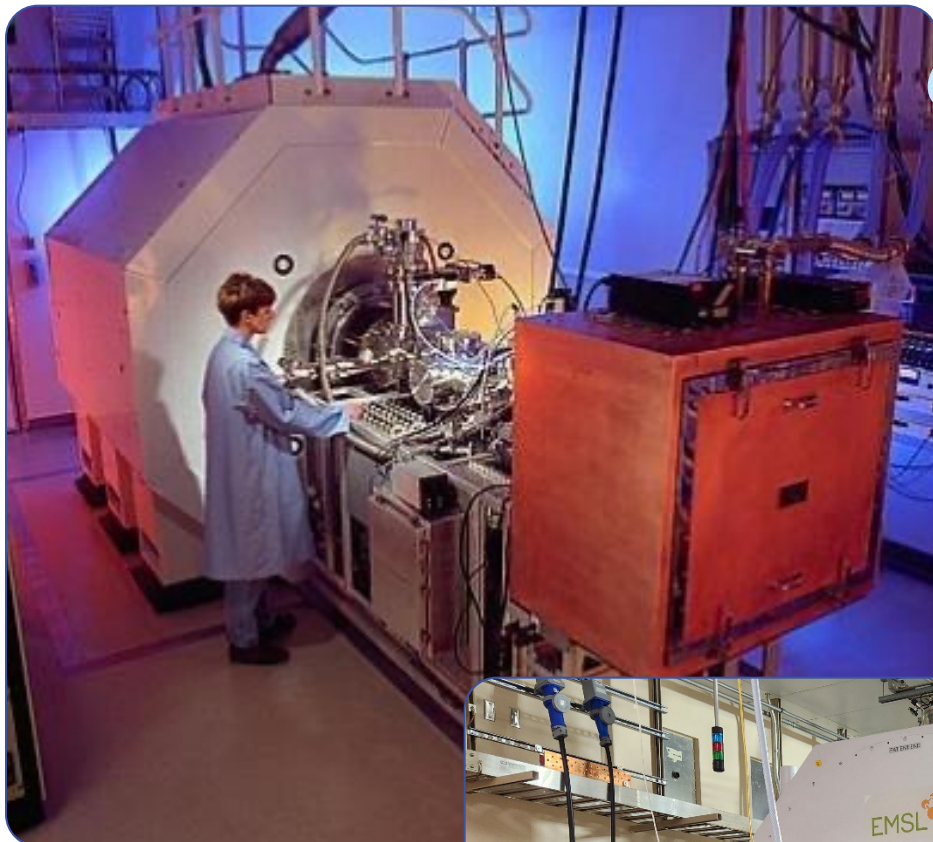
**We understand you served on the ASMS board from 2020 to 2022. How has working with ASMS helped you grow as a scientist?**

Being a part of the ASMS community has been invaluable to me. If you asked me to do anything for ASMS, I would always say yes! I am truly thankful to ASMS for giving me many opportunities to engage and contribute. I have been to almost every single ASMS conference, although I know I missed one when I was giving birth to my daughter! Personally, in addition to the annual conference, I've always enjoyed the smaller conferences. They are a very easy and effective way to connect with colleagues across the field, which has resulted in many new opportunities in terms of collaboration and friendships.

**We understand you have been included in the Analytical Sciences Power Lists. What does this honor entail?**

The Analytical Scientist Power List, released annually, features emerging and established leaders and influencers in the field of analytical science. I am honored and grateful to have been included for several years, most recently in the 2024 Power List. It is extremely humbling, and really an out-of-this-world experience to see my name among all these famous names! Being recognized is a great honor, one that reminds me that there are so many other people who deserve recognition for all the amazing things they

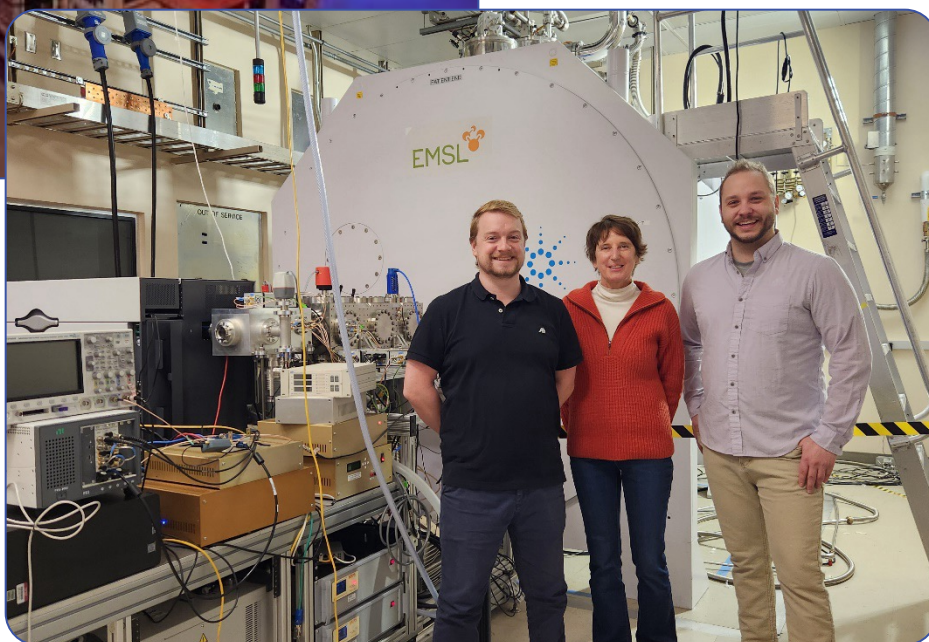




“ It’s all about multidisciplinary research when you’re trying to answer some of the significant big questions in the medical or environmental field. ”

Lili acquiring first data from the EMSL’s 11.4 Tesla FTICR, the highest magnetic field strength instrument at the turn of the century. (Photo courtesy of Ljiljana Paša-Tolić)

Lili with colleagues Will Kew (left) and Kevin Zemaitis who led a recent upgrade to the EMSL’s 21 Tesla FTICR mass spectrometer. (Photo courtesy of Ljiljana Paša-Tolić)



have done. Most importantly, I want to acknowledge my mentors, colleagues, students, and friends I have had the honor to work with throughout my career.

**Are there any emerging applications of mass spec technology that you’re excited about?**

I am excited about the ability to do things on a very small scale, such as characterizing all the molecules within a specific cell in the context of a tissue or environmental ecosystem. We want to understand how each of these different members of the ecosystem, or each of the cells within the tissue function and interact with each other to generate a specific phenotype. Answering this question includes not only advancing mass spec performance in terms of sensitivity, dynamic range, and throughput, but also looking at the various ways we can

manipulate a small amount of material. Most recently, my work has involved different microfluidic approaches to deal with limited samples, such as biopsies, or even single cells. To accomplish this, we have developed novel methods to isolate small tissue pixels, down to single cells. There are so many challenges and so much space for growth in this arena. Defining the proteoform landscapes across cells, tissues and ecosystems to better connect to function and phenotype is another major challenge, and a long-standing interest of mine. Another thing I’d mention in terms of advancements is the power of AI in guiding us through some of these experiments. It’s something that I see as up and coming. AI has clearly become part of our lives, especially lately, and has the potential to make a big impact within mass spec capabilities and applications.

***How does your current work environment promote interdisciplinary research and collaboration?***

Collaboration in science is not as well recognized or rewarded as it should be. Across the board, most people tend to look at whether you are the first author or the last author, and if you're somewhere in the middle, it doesn't really count for much. In my mind, there needs to be some restructuring to make team science more appealing to people and advance interdisciplinary work. I believe we need to find better ways to celebrate team contributions in addition to individual achievement in science. As I touched on earlier, our multidisciplinary teamwork at PNNL is quite different in a positive way from the more structured work that you might find in academia. I often think about how we, as a society, could change the system of rewards to better support teamwork in science. We need to stop rewarding individuals and PIs, and instead shift the emphasis toward promoting group effort with the idea that the whole is greater than the sum of its parts.

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***When you are outside of the lab, what are some of the activities you and your family enjoy?***

I love being out in nature, hiking and walking, along with reading and cooking. I also love traveling and getting to see new places—this is something I enjoy as part of my work as well, because my job often takes me to amazing locations! I do a little bit of yoga, which helps a lot with the physical exhaustion that working can sometimes entail, and it allows me to calm my mind and think more clearly. I am trying hard—but not very successfully—to dedicate more time and effort to health and wellbeing, both for myself and my coworkers. I hope to do better next year! And because my husband and I are both from Croatia—specifically the beautiful Dalmatian coast—we often go back and just lay on the beach with friends and family for the entire day. It's a wonderful thing to do!