

IN MEMORIAM

Laura Feltri: Of Schwann cells, matrix, and family

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Laura Feltri (1963–2023) has been a pioneer in the study of extracellular matrix (ECM) in peripheral nervous system (PNS) myelination. Her journey in science began at the University of Milan, where she obtained an MD and did a residency in neurology. Despite being trained as a physician, Laura’s curiosity for understanding the complexity of peripheral nerves drew her toward research. Like several other talented students, she was offered, during her residency, a training fellowship at the University of Pennsylvania. She thus joined the lab of Michael Shy and became fascinated by science and research. The environment at UPenn was vibrant and full of junior physician scientists, combining the passion for science with the desire to better understand the pathological mechanisms that underlie diseases of the PNS. This extraordinary team, composed also of John Kamholz, Steve S. Scherer, and Larry Wrabetz, was instrumental in Laura’s education as a scientist, future career, and life.

In the early ’90s, Laura came back to Milan with Larry to initiate a new chapter in their life. She and Larry eventually married on a beautiful day in September on Lake Como. Until last Christmas, when Laura passed away due to a glioma that she strenuously fought, they had been a unique couple capable of balancing life and career in good and bad, in health and sickness, as they vowed each other on their wedding day.

In addition to creating a new family, they established their first laboratory at the San Raffaele Scientific Institute in Milan. This was a great opportunity for both, as the institute had just been built and was recruiting the best scientists willing to pursue their career in Italy in a multidisciplinary environment.

We were among the first to join the “L&L” lab in Milan, and we remember those years being full of enthusiasm, passion, and fun. We both recall the Monday mornings dedicated to speaking Italian—Larry was taking Italian lessons in the afternoon, and this was “homework time.” However, most of the time, he was making fun of Laura as she could not explain in a crystal-clear way the intricacies of the Italian language.

Those were also difficult days, though, as the funding in Italy was neither substantial nor consistent, and Laura was forced to spend much of her time figuring out how to manage the lab. However, throughout those years, Laura and Larry were able to



Laura Feltri. Photo courtesy of Sandra Kicman, University of Buffalo Office of Communications.

fascinate and guide us in our goal of understanding the beauty of peripheral nerves and of Schwann cells. We got introduced to the power of developing and using transgenic mutants to study the complexity of the interactions occurring in nerves among cells. One of the most important tools developed in those early days, and used throughout the world to question Schwann cells’ function, was the transgenic myelin protein zero-cre mutant that is currently available at Jackson Labs (Feltri et al., 1999).

In addition to that invaluable tool, in the early 2000s, Laura and Larry generated one of the first mouse models for Charcot Marie Tooth 1B disease and demonstrated that gain-of-function mechanisms are the basis of this hereditary neuropathy (Wrabetz et al., 2006). These groundbreaking studies allowed for the identification of cell stress and the unfolded protein response as one of the pathological mechanisms at the basis of this debilitating disease (Pennuto et al., 2008).

However, Laura’s main interest in science was to elucidate the role of Schwann cells and the ECM in nerve development and in myelin formation. She dedicated her scientific life to characterizing the molecular mechanisms underpinning the process of axonal sorting during peripheral nerve development

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and the implications for myelination and Schwann cell-axon communication (Court et al., 2006; Feltri et al., 2015). She made seminal discoveries demonstrating which laminin receptor regulates axonal sorting in time and space. In particular, she described the role of integrin $\beta 1$ (Feltri et al., 2002; Pellegatta et al., 2013) and of downstream signaling activators like Rac1 (Nodari et al., 2007) in the fine regulation of Schwann cell protrusions, which are necessary to interact with and sort axons. She also investigated the role of molecular sensors like YAP/TAZ (Poitelon et al., 2016) in myelination and was among the first to connect the stiffness of ECM components to the changes occurring in Schwann cells during axonal wrapping (Poitelon et al., 2015). Finally, she revealed which molecules reside at the axo-glial surface, as mediators of nerve development and myelination (Della-Flora Nunes et al., 2021).

In 2011, after many successful years in Milan, Laura and Larry were offered the opportunity to direct the Hunter James Kelly Research Institute, currently the Institute for Myelin and Glia Exploration, at the University at Buffalo in New York, where they remained until last year. In this new setting, they continued to contribute new findings aimed at unraveling the mysteries of the PNS, coupled to training and mentoring of young fellows, which represents her most important legacy. Throughout her scientific career, Laura mentored a significant number of students, scientists, and physician scientists. Laura was particularly attentive to the education and support of younger fellows, and she was particularly proud of the numerous scientists she mentored and aided during her career, as many of Laura's fellows are currently group leaders or professors in prestigious universities around the world.

She was able to easily connect with every person that crossed her path in life, whether it be a student, a friend, or the gymnastics teammate she had known since she was a young girl. Indeed, on her funeral day, many of these people were present, coming from many parts of the world, leading us to feel as if we were attending an extended family reunion.

Laura received numerous awards and actively contributed to science by fulfilling several duties. She served as president of the

Peripheral Nerve Society and was recently elected an American Association for the Advancement of Science fellow. She also chaired the Cellular & Molecular Biology of Glia Study Section of the National Institute of Neurological Disorders and Stroke of the National Institutes of Health. While in Milan, she had been responsible for the PhD program in Molecular and Cellular Biology at the San Raffaele Vita-Salute University, and was then distinguished professor of biochemistry and neurology at the University at Buffalo. Since 2023, she held a joint position as professor of histology at the University of Milan, where she was committed to preparing a series of lectures despite her illness.

Laura was not simply an outstanding scientist and an incredible mentor; she was also a true friend that you could talk to anytime. Though we did not follow Laura and Larry to Buffalo, we always remained connected to them and shared ideas, suggestions, new discoveries as well as the sad news of her illness and the course of her disease.

Laura was a wife and life partner to Larry, and most of all an affectionate mother. Larry and Laura had three children who were in her thoughts until the last of her days. They, too, are now citizens of the world, living abroad and sharing her smile, her resilience in the face of adversity, and her passion for life.

We will deeply miss you, Lauretta!

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