THE AUTHOR FILE

Judit Villén

Measuring phosphoproteins reproducibly and taking time to bike.

Cells eat, react to change, grow, take the garbage out, and the cell's proteins help with getting these tasks done. Proteins can be set into action or turned off, much like a light by its switch, says Judit Villén, a researcher in the University of Washington's (UW) Department of Genome Sciences. The switch can be a chemical change, such as phosphorylation, which is the addition of a phosphate group to an amino acid.

Noemí Villén

Judit Villén

Phosphorylation can transmit messages: protein A phosphorylates protein B, and protein B phosphorylates C, and so on, until the message arrives. Using phosphoproteomics techniques, researchers measure this type of cellular information flow. The techniques have led to celebrated achievements, yet a boatload of experimental challenges remain. Villén and her UW team have developed a resource to make these experiments easier, not just for proteomics experts.

Scientists use targeted mass spectrometry to survey a cell's phosphosites, which are sites on a protein where phosphorylation occurs. The approach is a little like scanning the dance floor of a crowded club for dancers with certain moves. First, proteins are chopped into peptides for mass spectrometry analysis, and researchers need to provide the mass-to-charge ratio for each phosphorylated peptide they want to measure. Phosphorylation can, however, make peptide generation unpredictable and tedious. "Overall, setting up an assay with tens to hundreds of peptides would take several weeks," says Villén.

The team developed Phosphopedia, an assay portal and database, to make targeted phosphoproteomics experiments easier to design, to speed up the search for the assay most likely to succeed and to allow phosphosites to be consistently measured. The project grew out of an idea by graduate student Robert Lawrence and presents to users the most observable phosphopeptide and mass-to-charge data from more than 100,000 phosphosites on more than 11,000 proteins, says Villén, and it is helping the lab to flexibly and quickly select and measure hundreds of phosphosites. She wants to grow the resource, for example, with quantitative data and with data collected across many biological conditions.

As a chemistry PhD student at Universitat de Barcelona, Villén became captivated by the prospect of being able to study all the proteins in a biological system in one experiment and in a quantitative way. She says she "couldn't stop thinking about the endless possibilities," such as the many biological questions and the potential experimental scale.

This excitement helped turn her into a proteomics researcher fascinated by systems biology, cellular signaling and control mechanisms. Before landing her UW faculty position, she completed a postdoctoral fellowship at Harvard Medical School in the lab of Steven Gygi, where she had spent three months as a graduate student. While she was in his lab, the phosphorylation field changed plenty, says Gygi. Many of these changes "can be directly ascribed to her research," he says, and involved steps that have made global phosphorylation analysis more routine.

As a high school and college student, Villén was a sprinter and long jumper, which requires delivering an energy explosion in a few seconds. "As I have grown as a scientist, my style has turned into that of trail runner: endurance and hard work are important, and we get to enjoy running up and down the hills," she says.

Villén likes collaborative projects; she has been involved in more than 40 of them since her early postdoc days. They involve getting familiar with a range of biological questions and combining expertise from different disciplines.

She can now develop more such projects in Seattle, home to a growing, diverse proteomics community with groups focusing on instrumentation, technology development and software. Researchers differ in their training and practices, "so there is a lot we can learn from each other," she says. Seminars and a journal club bring everyone together regularly, and these informal chats with others deliver her many ideas for the lab. She and her husband are both scientists who spend long hours in the lab, and they now also make time for their three-year-old daughter. As Villén says, "I enjoy my time with her and love to see her grow as a little person."

> "My style has turned into that of trail runner…"

Originally from a sunny part of the globe, Villén admits it has been hard to get used to Seattle's gray skies and dark winters. Yet the summers are perfect for the outdoor pastimes she enjoys such as hiking, running and biking. "The rain is not so bad after all," she says. "Unlike in Boston, here I can commute by bike year long."

Vivien Marx

Lawrence, R.T. *et al.* Plug-and-play analysis of the human phosphoproteome by targeted high-resolution mass spectrometry. *Nat. Methods* **13**, 431–434 (2016).