THE AUTHOR FILE

Paola Picotti

Cells brim with activity that a special set of protein assays can help track.

Sometimes the road forks: scientists turn onto either Proteomics Highway or Molecular Biology Lane. Paola Picotti, a biochemist at ETH Zurich, Switzerland, has built a road that connects the molecular biology and proteomics communities. "It makes them finally speak the same language," she says. She uses mass spectrometry—the proteomics workhorse—to analyze 'sentinel' proteins in a sample. These sentinels deliver a snapshot of yeast cell physiology, which is modulated by around 4,000 proteins at any given moment.

Bernd Bodenmiller

Paola Picotti holding a protein model of fatty acid synthase.

Traditionally, molecular biologists might monitor cell physiology by knocking out a gene, altering temperature or changing nutrient levels and then measuring the abundance of specific proteins they know well. But doing this is slow, and it might not cover the spectrum of the cells' physiology, says Picotti.

Proteomics researchers can perturb cells and then use mass spectrometry to measure protein levels on a large scale and all at once. If the scientists are lucky, she says, they see groups of functionally related proteins whose measured values rise or fall together. Although this is a broad approach, many of these proteins might be poorly characterized, making it hard to know their role in a pathway and judge the importance of their changes.

Picotti and her team pored over the literature, scoured databases and surveyed scientists at different universities to curate sentinels, which were selected because of their role in diverse yeast pathways. They selected 570 proteins and whittled down the list by checking which ones they could measure. That led to a group of 157 unmodified proteins and 152 phosphorylated or otherwise modified proteins.

Picotti likens these proteins to leading characters in a movie. The actors are in the spotlight, garnering awards and also under constant scrutiny, "just like our sentinels that are the most experimentally studied and validated proteins."

She and her team developed a one-hour assay to measure all of these sentinels, which provides a simultaneous readout of approximately 200 pathways. "No need for validation," she says. "No need for analyzing long lists." The output of the experiment indicates which of the pathways are active or inactive and their degree of activity.

Picotti completed her PhD in biotechnology at the University of Padua, which was founded in 1222. As she points out, it was the academic home of Galileo Galilei, the father of the scientific method, and Elena Cornaro Piscopia, who in 1678 was one of the first women to graduate with a PhD.

Picotti did her postdoctoral fellowship in the lab of proteomics researcher Ruedi Aebersold, who is a great role model, she says, for his efficiency and his ability to spot a problem's core and sort even complex situations in a "serene and equilibrated manner." She is also a scientific advisor for Biognosys, a company spun out of Aebersold's lab.

Yves Barral, who directs ETH Zurich's biochemistry institute, says he is struck by Picotti's attentiveness and the way she resonates with other researchers. "She grabs very rapidly all what is happening around her and is excellent at translating the interests of the cell biologists, biochemists and geneticists around her into novel systems biology and proteomics approaches, and vice versa to use her approaches to open new questions for the biochemists and cell biologists," he says. She reminds him a little of the Mona Lisa, with a smile and manner that mixes straightforwardness, elaboration, attentiveness and happiness with a slight element of irony, says Barral.

"Eating chocolate always helps."

In her office, Picotti has a walk-in policy to encourage students to discuss their data, ideas and challenges. "I believe it makes the lab a more lively and creative environment," she says.

While on maternity leave, she stayed in constant contact with the lab but was delighted that her team solved problems and finished papers on their own. "So I had to conclude I am not as indispensable to the lab as I thought," she says. "And this is a wonderful sensation."

On the subject of how she finds ideas for her research, she says that "eating chocolate always helps." When she finds the time, she also skis and hikes in the Swiss Alps. And she enjoys inventing creative games for her six-month-old son. "Watching his daily developments is just breathtaking," she says.

She makes it a habit to attend conferences in fields outside of her own as, she says, a "silent spectator," to see how others address problems in their fields. These excursions might lead to collaborations, and she likes the way it exposes her to a mindset that offers valuable perspectives for her own work.

Vivien Marx

Soste, M. *et al.* A sentinel protein assay for simultaneously quantifying cellular processes. *Nat. Methods* **11**, 1045–1048 (2014).