THE AUTHOR FILE

Anna Moroni

An optogenetic tool for inhibiting neurons and how to sail across the Tree of Life.

Anna Moroni, a researcher in plant physiology and biophysics at the University of Milan, turns to reach for a sizable glass trophy. She received it from Columbia University Irving Medical Center in 2016 for research in human physiology, along with a grant and a fellowship. Moroni shows the plaque to colleagues to indicate that she is not only a "plant person." Her interest in and training about ion channels in plants, viruses and neurons takes her across the Tree of Life. She likes to embrace new fields and ask a newcomer's naive and simple questions. "I'm attracted by what I don't know," she says.

The latest development from Moroni's lab is BLINK2, an inhibitory optogenetic tool. She and her team expressed this blue-light-sensitive synthetic potassium channel in the neurons of zebrafish, mice and rats. Using BLINK2, the team reduced pain in an experimental animal for more than half an hour. Blue light inhibits neuronal firing for tens of minutes after illumination. That's desirable, she says, because continued illumination to achieve inhibition risks overheating cells.

Many inhibitory tools are based on chloride channels, but these tools do not work in all neuron types. BLINK involves potassium channels, which play a role in action potentials. BLINK2's older sibling is BLINK1, which worked in many systems but was not expressed well in neurons, says Moroni. With BLINK2, an experimenter inhibits a neuronal signal well just by manipulating a few channels. BLINK2 works better than BLINK1, she says, and she hopes others will like using it, not just neurobiologists. She has heard from a UK plant physiology lab about early successes with BLINK2.

Activation-oriented optogenetic tools matter as much as inhibitory ones, but the toolbox for inhibition is rather limited, says Moroni. Labs have mainly used light-gated pumps, which turn over fast and tend to not inhibit beyond a time frame of seconds.

The next sibling, BLINK3, is more than a gleam in Moroni's eye—it's in the works in her lab. BLINK2 uses blue light, which does not penetrate deep into tissue and requires implanted fiber optic cables for illumination. The use of red and infrared light would help to avoid that, she says. Such an approach would enable broader use of this inhibitory tool and noninvasive optogenetics more generally.

Anna Moroni. Credit: Photo: G. Thiel

Perhaps more than any other investigator, Moroni has shown the modularity of ion channel function and how to engineer sensors for opening and closing ion channel pores of chimeric proteins, says University of Wisconsin–Madison researcher Gail Robertson, who co-taught a Cold Spring Harbor Laboratory course that Moroni took. "Anna had a passion for science but expressed doubts that, as a woman, she had a clear path to success," she says. The late Rita Levi-Montalcini is among Italian science's remarkable female icons, but role models in daily professional life were few and far between. "I encouraged her to follow her passion, but she was full of life, irrepressible, really, and she would have done it anyway," says Robinson.

Moroni and her husband Gerhard Thiel, a researcher at Technische Universität Darmstadt and co-developer of BLINK2, hold a European Research Council grant on noninvasive optogenetics. She is proud of their successful long-distance marriage and collaboration. Low airfares in Europe enable such relationships, of which she knows quite a few. She pursued her career in Italy and he in Germany without either needing to sacrifice for the other.

Among their pastimes are weekends in the Italian countryside or on ski slopes. "Being in Milano, I love to go to the opera, to La Scala," says Moroni. She is also a competitive open-water swimmer. "During swimming I have a lot of ideas," she says. Although the Italian research budgets are tight and scientists have a high teaching load, she says, they also have considerable freedom to pursue scientific questions of their choosing.

> "I'm attracted by what I don't know."

Originally, Moroni's parents pressured her to become a lawyer. It was a rebellious time in Italy and she chose plant physiology instead. Quantitative approaches in physiology and biophysics intrigued her and she developed a passion for ion channels. She completed her PhD research in plant physiology in Milan and at the University of Toronto with Eduardo Blumwald.

She realized the similarities between what she studied in plants and what Dario DiFrancesco, a researcher two floors above hers in Milan, was studying in heart physiology. For her postdoctoral fellowship, she moved to his lab to learn the patch-clamp technique along with molecular cloning and ion channel characterization. When she started her own lab, she pursued work with ion channels in plants, animals and viruses. "That was," she says, "really the bursting point of my career." ❐

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Reference

Alberio, L. et al. A light-gated potassium channel for sustained neuronal inhibition. *Nat. Methods* https://doi.org/10.1038/s41592-018-0186-9 (2018).