THE AUTHOR FILE

Uri Manor

A new way to see actin in action, hearing as others don't, and saved by the guitar.

To Uri Manor, the Salk Institute, where he directs the Waitt Advanced Biophotonics Core and does his own research, feels like the perfect scientific home. "I love interdisciplinary science," he says. "I always knew I wanted to use physics in biology." He studied physics as an undergraduate and did his PhD research in cell, molecular, developmental biology and biophysics in a program run jointly between Johns Hopkins University and the US National Institutes of Health (NIH). He completed his postdoctoral research in the lab of Jennifer Lippincott-Schwartz at NIH.

Manor has been on a difficult road. He was born with impaired hearing, which was not diagnosed until he was 2½. Only then did he get his first hearing aids. "I'm a technophile by nature; I wouldn't be here without my hearing aids," he says. Even to this day, it takes much effort to hear. "The whole concept of tools making life a better place is a deep part of me."

As he hunted for a faculty post, he realized sadly he was going to no longer enjoy access to as many microscopes as he had during his training. When he saw Salk's core facility job ad and then landed the post, it felt like a dream job. He enjoys being at the microscope, training others and collaborating across disciplines from plant biology to neuroscience, from cancer to stem cell research. People come to him with interesting problems. "It inspires me," he says. In addition to work at the core, he and his team pursue their own projects, the latest of which involves probes that shine brightly to illuminate organellar dynamics.

Manor and his team expanded on work involving GFP-labeled actin nanobodies that can be genetically encoded. That research targeted nuclear actin, which is a subset of the actin cytoskeleton. He wanted to find out where and when actin in the cytosol interacts with organelles such as mitochondria and the endoplasmic reticulum. "You've got this enormous background problem," he says. It's like trying to see the stars in broad sunlight.

The team made genetically encoded fluorescent actin nanobodies, small antibody-like structures with membrane-binding sequences to anchor the probes to the membrane of a targeted organelle. When actin moves to within about ten nanometers of the membrane probe, light intensifies and you see "hot spots," he says.

Uri Manor. Credit: C. Manor

Some of the first experiments with the probes wowed him, says Manor, because he could see mitochondrial subdomains. It took considerable validation and control experiments to get to that point.

He hopes many labs find the probes useful. Among his own plans is to use the probes to explore changes in actin–organellar dynamics in some neurodegenerative diseases.

"I first fell in love with microscopy when I saw a hair cell," says Manor. "I was blown away." That was when his PhD advisor and NIH researcher Bechara Kachar showed him confocal and electron micrographs of the neatly stacked rows of the inner ear's hair cell stereocilia.

These stereocilia rows transduce sound by bending, which opens calcium channels. The micrographs made visible the insides of the cochlea spirals Manor had seen so often on the walls of the audiologists' offices he has had to visit.

Manor also has a passion for deep-learning techniques and is working on ways to apply these techniques to infer information missing in micrographs. Inference and connecting the dots of heard, or perhaps misheard, language is a crucial skill for people with impaired hearing. But it can be socially isolating. "I missed a lot of jokes," he says of his high school years. "The thing that saved me was guitar."

Unlike the quick back and forth of conversation with other kids, with music he could relisten to a passage repeatedly or turn up the volume as needed. Manor loved math and music theory and played guitar around four hours a day. He was also in a band and well-liked for his musical talents. The adversity he has faced has made him especially keen on educating and training and being inclusive to all, especially to people who have had less opportunity and faced adversity in their own lives.

Now and then Manor still strums one of his five guitars, a collection that includes a Les Paul electric guitar. But he mainly adores spending time with his wife and children, who empower his work, he says.

"It only takes a few minutes of conversation with Uri to be enthralled by his passion for science, and his unique abilities to fluently connect seemingly discrete concepts to create new experimental strategies or hypotheses," says Kachar.

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How Manor manages a world-class imaging facility, does his own research, does photography, runs, and plays guitar "is a mystery to me," he says. It's "humbling and inspiring" how Manor has overcome his hearing impairment to make his brilliant way in science, and everyone Manor interacts with is bound to feel his radiant generosity and contagiously positive attitude, says Kachar. "Uri embodies our hopes for a new generation of creative leaders in our laboratories and in our communities." ❐

Vivien Marx

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Reference

Schiavon, C. R. et al. Actin chromobody imaging reveals sub-organellar actin dynamics *Nat. Methods* https://doi.org/10.1038/s41592-020-0926-5 (2020).