Melissa M. Rolls

Taking a high school student into her lab that summer was simply out of the question. So when a cell biology colleague at Johns Hopkins stopped her in the hall to fob off a young applicant, Carolyn Machamer was more than a little annoyed. The teenager was Melissa Rolls, then a senior at a Baltimore private high school. "She was standing right there," Machamer remembers. "So of course I had to say that I would talk with her, but I thought this kid was way too young. After five minutes, I realized that Melissa was as sharp as sharp could be."

Machamer quickly decided that, yes, she might have a summer spot after all. Her lab was very small then, Machamer explains—two postdocs, a technician, and a couple of grad students. Rolls settled in at once. Machamer remembers a journal club session at the lab. "I asked the lab to think of a key experiment that would answer a question raised by this study. The postdocs, the grad students, and the tech were all staring at their copies of the paper, trying to come up with something when Melissa pipes up, 'What if you treated the cells with brefeldin A?'" Machamer laughs. "I can't remember the paper we were discussing, but I can remember being blown away by Melissa coming up with this great idea."

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At the bench, Rolls turned out to be both sharp and capable. "I was thrilled to have her," says Machamer. "Everyone in the lab wanted to show her things and get her on their project because Melissa could get things to work." After that first summer, Machamer made sure she got Rolls back for the next three.

Between summers at Hopkins, Rolls was an undergraduate at Yale. Among other distinctions there, she had a first author paper in *Cell* with her Yale mentor Jack Rose on novel infectious particles generated on a viral glycoprotein from self-replicating RNA. After that came a doctoral program at Harvard University with Howard Hughes Medical Institute (HHMI) investigator Tom Rapoport. There Rolls shifted from viruses to *Caenorhabditis elegans* to study targeting of membrane proteins to specific regions in the endoplasmic reticulum. For her postdoc, she went west to the University of Oregon in Eugene to join another HHMI investigator, Chris Doe, and learn about *Drosophila melanogaster*. She was able to apply her cell biology background to study neuronal polarity in live larvae. Those studies led Rolls to intriguing results on dendrite polarity and then a job offer in 2006 from Pennsylvania State University (Penn State) in State College, PA.

Summer Intern Returns

Last spring, almost 20 years after the high school student talked her way into the Machamer lab, Rolls was invited back to Hopkins to give a talk in the cell biology department. Her talk drew a number of neurobiologists from outside the department who wanted to hear about her work on dendrite polarity. The cell biologists were eager to see her *Drosophila* system for imaging neuron regeneration and degeneration in living larvae. For Machamer, the visit was doubly impressive. When Rolls joined her lab in 1991, Machamer had just been named a Pew Scholar in Biomedical Sciences. Twenty years on, Rolls was herself a Pew Scholar. "I wish I could claim credit but I just got lucky," says Machamer.

Shortly after her Hopkins talk, Rolls learned of an additional honor. The ASCB's Women in Cell Biology (WICB) Committee had selected her for its 2011 Junior Career Award, which Rolls will receive this December at the ASCB Annual Meeting in Denver, CO. (See page 11.)

The ASCB Annual Meeting has been good for Rolls. She met one of her regular collaborators, Mark Terasaki from the University of Connecticut Health Center, at a very slow ASCB poster session. Terasaki recalls their first conversation. "It was on the last day of the meeting and practically no one came, at least to my poster. So we started talking. I thought she was a postdoc at least but it turned out that she was just a graduate student."

Meilssa M. Rolls

Rolls, however, was a graduate student with some novel green fluorescent protein (GFP) constructs that Terasaki was able to put to good use on studies of the small G protein Ran in mitosis and meiosis. Terasaki says that Rolls is that rare collaborator, someone with the big picture in mind and the promised materials in hand. "There are many people who have the surface of science down pat. They can talk about how things work but then when you get down to it, their actual content is kind of lacking. When you ask, where's the construct? What do you actually do with it? It's not really there. But Melissa is not like that at all. She doesn't make a big fanfare. She just does it."

Fly Uncorks Polarity

One of the things Rolls has done is pioneer an in vivo model system for studying the cell biology of neurons. Mammals are the name of the game in neuron biology because of their relevance to humans. Yet working in vivo in mammals is expensive and fraught with other issues. As a result, nearly all the fundamental work on the neuronal cytoskeleton has been done with mammalian cells in tissue culture. Rolls believed that by working in live *Drosophila* larvae she could sidestep many of the limitations of cultured cells.

In the Doe lab she started work on a *Drosophila* neuron model of microtubule polarity. An early question in the field was the relative polarity of dendrites and axons. The key studies of cultured mammalian neurons showed that axonal microtubules were always plus-end-out while dendrite populations had mixed polarity—some plus-end-out, others minus-end-out. But no one had ever looked in vivo at dendrite polarity. Rolls thought it would be possible to do this in *Drosophila,* especially after hearing through the grapevine that a Japanese group had a microtubule plus-end binding protein called EB1 tagged with GFP that worked in flies. It would be an easy marker to follow. "I figured that someone else was going to do this experiment. It was so obvious," Rolls explains. "I waited three years after I first heard about it [GFP-tagged EB1], but still no one published. I thought I had better just do this, plus I really wanted to know the answer."

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The actual experiment took less than a day. "I finally sat down at the microscope and it was totally clear," Rolls recalls. Polarity in dendrites was not mixed; it was uniform. All dendrites were minus-end-out. "Now this is completely different from what's in the Alberts textbook (*Molecular Biology of the Cell*). So that meant that the burden of proof went way up."

What's true in one set of *Drosophila* neurons may not be true in all, or it may be true in *Drosophila* but not in fish or mammals. So far, Rolls says, her unorthodox finding has stood up in her own further experiments and in polarity studies on *Drosophila* conducted by other labs. Moreover, the leading figures in neuronal polarity seem to be coming around to her observation, she reports, but data from other organisms are still needed. Meantime, the *Drosophila* model system she took with her from Oregon to Penn State is shedding new light on microtubule reorganization in neuronal degeneration and regeneration. That's a subject with broad implications in human degenerative disease and traumatic injury. Working with graduate student Michelle Stone, Rolls reported evidence in 2009 that after a *Drosophila* axon was severed close to the cell body, one of the dendrites reversed polarity and began growing into a permanent replacement for the missing axon. Her model system has also allowed progress in identifying how microtubule growth is directed and which proteins play what role in microtubule destabilization and regeneration.

Faculty Family

Although Rolls has lived in the U.S. since she was 11, there is still a trace in her crisp consonants of her English origins. Both her parents were Oxford researchers—her father Edmund in computational neuroscience and her mother Barbara in nutritional physiology. In 1984, Barbara Rolls took an appointment at Johns Hopkins and moved Melissa and her younger sister to Baltimore. "It was major culture shock," Rolls reports. To soften the blow, her mother put her into the all-girls Bryn Mawr School where Melissa eventually found her

cultural balance and her life focus in the high school biology class of Mrs. Betty Thompson.

In Rolls's sophomore year at Yale, her mother accepted an endowed chair in obesity research at Penn State and moved to State College. Rolls caught up with her mother 14 years later when she accepted her own faculty position in Biochemistry and Molecular Biology at Penn State. She arrived in 2007 with her husband Greg Kothe and their toddler son. Her Penn State offer, her lab, and her colleagues were all great, but Rolls also confesses, "I had a two-year-old. So being near grandma was huge." Two months after she arrived, Melissa had a baby girl. (Grandma had also become a publishing celebrity. Barbara Rolls's *The Volumetrics Eating Plan* climbed *The New York Times Book Review* diet book best-seller list while garnering enthusiastic reviews from leading weight control experts.)

At Penn State, Rolls pulled together researchers with interests in cellular processes from half a dozen departments across campus into a Center for Cellular Dynamics. They hold monthly brainstorming, poster, and collaboration sessions. Rolls has also been active in increasing diversity in faculty hiring and departmental programming. Her own mother's struggle to build a career in science was fierce, says Rolls, but her generation of young female scientists is still coming up against subtle and not-so-subtle barriers. "I didn't really notice it at the graduate and postdoc level where it's easily 50–50 male–female now. But as soon as you step out into the faculty world that is not the case." Rolls notes that the building where she works has 20-plus laboratories but only two female PIs, herself included.

Rolls and Kothe, who teaches in the same department, have two children but two sets of surnames. Rolls explains that she always considered last names arbitrary and long ago decided that any boy should be named for his father and any girl for her mother. William Kothe is now six. Cecilia Rolls is now four. They all live in Bellefonte, the sleepy county seat, a few miles north of booming State College. Bellefonte is noted for its Gilded Age architecture and its hardy Appalachian plateau climate. Rolls loves Bellefonte for the quiet and the space for her extravagant English cottage–style flower garden. "My husband thought I would not be able to have a garden as good as the one I had in Eugene, but I think I have risen to the challenge," Rolls says with real pride. ■

—John Fleischman

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