ASCIB PROFILE

Claire Walczak

Claire Walczak, winner of the 2003 Women in Cell Biology Junior Career Award, considers herself a member of the second generation of women cell biologists and the beneficiary of the hard-won victories of the first. Walczak is an Assistant Professor of Biochemistry and Molecular Biology at the Indiana University in Bloomington. In her five years at Indiana, Walczak has built a national reputation while clearing the expected assistant professor’s hurdles of establishing a lab, securing research funding, and attracting a following of graduate students and research fellows. Married to developmental geneticist Wayne Forrester, she is also the mother of two small children. Walczak has stayed at the cutting edge of her field, microtubule dynamics, with her work on a novel subtype of the molecular motor kinesin called Kin I.

Walczak came upon Kin I (pronounced Kin “i” for “intermediate”) early in her post-doctoral fellowship with Tim Mitchison at UC San Francisco. Working with Arshad Desai who was then a graduate student, Walczak discovered that Kin I was not an ordinary molecular motor, powering cargo along the microtubule highways. Instead, Kin I was a destabilizing factor for the cytoskeleton, triggering the catastrophic disassembly of the microtubule grid and its reassembly into the bipolar mitotic spindle during cell division. Puzzling out the role of Kin I and related molecules in the assembly of the mitotic machinery remains the focus of her lab in Indiana.

Walczak is proud of her research, her family, and, of course, winning the WICB Award, but she claims that her life in science is no longer remarkable for women of her generation. She says that women in the first generation of modern cell biologists faced starker choices between family and career. Some emphasized one at the expense of the other. A few seemed to manage both effortlessly. "There were also those who did have kids and a science career but realized just how hard it was. They worked to make things better. Today an academic research career and a family life are no longer that unusual," says Walczak.

"At a place like Indiana, most of my women colleagues have kids. This is a very supportive place but I think people and institutions in other places are becoming more supportive, too."

Born in 1965, Walczak came of age at a time when girls with her evident math and science talents were finally being taken seriously in school. Walczak grew up in a single-parent, blue-collar household in suburban New Jersey and chose Renesselaer Polytechnic Institute (RPI) in Troy, New York, for her undergraduate studies. In the mid-1980s, RPI was known for its world-class math, chemistry and engineering programs as well as for being largely male and "nerd friendly." The women in the Class of '87 were distinctly in the minority, Walczak recalls, but they didn’t see themselves as pioneers or outsiders. Walczak majored in chemistry and went straight on for her doctorate in biochemistry at the University of Wisconsin-Madison.

Walczak was already fascinated by dynein molecular motors—her 1993 thesis focused on dynein motors in ciliary motility—but she was also following an-
other motor protein rapidly emerging in the literature, the amazing kinesin "superfamily." In her last year in Madison, Walczak sat in on an advanced seminar course about cell cycle regulation to hear the visiting speakers, Tim Hunt and Lee Hartwell, lay out the latest data on the regulation of mitotic progression. Fired up, Walczak was determined to find a postdoctoral fellowship in which she could work on linking the cell cycle machinery to the regulation of mitotic motors.

When she arrived at UC San Francisco in late 1993, the Mitchison lab was working out the details of spindle assembly using Xenopus egg extracts as a model system. She set out to identify the mitotic kinesins from a Xenopus library and then probe their function in vitro using the extract system. Desai showed her the assay procedure. "This was the very first day that I made spindles," Walczak recalls, "and immediately we saw that something was really wrong with the spindle. We checked my procedure and then we looked at each other and it was like, 'We have the catastrophe factor!' It turned out we were right but it took a couple of years to prove it. Certainly when we first told Tim, he didn't believe us. So we went back to the experiment and then we started to get skeptical. The phenotype was just so dramatic, it rang with artifact. But by then, Tim was telling everybody, 'We've identified the catastrophe factor!' Eventually, we worked out a proof." Kin I was no artifact.

"It's one of the catastrophe factors," says Yixian Zheng of the Carnegie Institution of Washington in Baltimore. "This kinesin of Claire's is the major microtubule-destabilizing factor in mitosis, so more exactly it's a microtubule depolymerase. It's been known for many years that when the cell transits from interphase to mitosis, microtubules become much more dynamic. There were some genetic studies suggesting that the motor proteins might be playing a role in destabilization, but there were no biochemical indications until Claire's work uncovered the major player in spindle assembly. If you don't have this kinesin, you cannot make a good bipolar spindle."

Walczak's discovery of Kin I was more than the isolation of yet another novel protein, says Rebecca Heald, a longtime friend and collaborator now at UC Berkeley. "It was a new class of motor proteins that had a new kind of function. Ten years later, we're just now dissecting how it works and how it's regulated. This protein provides a rich source of things to study, but it's broader than it sounds. Rather than just studying a molecule, Claire is really studying a complex process, how the spindle forms, how the kinetochores function and how they are regulated. Claire has used Kin I to get at a whole complex process in the cell."

Indiana turned out to be the ideal place to set up her own lab and pursue her Kin I breakthrough, says Walczak. For one, Bloomington offered the holy grail for scientific couples: double appointments.

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Forrester is in the Biology Department of Indiana University's main campus in Bloomington.

A big university's big enrollment gives new PIs like herself a big talent pool to
fish for lab staff, says Wałczak. “We’re typically midwestern so we get a typical bell curve of graduate students. I’ve been very fortunate to get people for my lab from the top of the curve. And it becomes self-selecting. Good people have a good work ethic and students who don’t feel comfortable in this kind of focused environment don’t stay.”

Taking up their first faculty posts in 1998, Walczak and Forrester felt it was the ideal time to start a family. Christopher is now four and Katie is 18 months. “Christopher loves trains and dinosaurs. Katie loves trains, although basically Katie loves everything Christopher loves,” says Wałczak. “Early on, Christopher expressed the train and truck genes. So we were curious: would Katie express the doll gene? So far, she’s upregulating the train and truck genes, so they are definitely not y-linked.”

Starting two careers and a family at the same time has worked out for them, says Wałczak, but she remembers the endless discussions back in grad school and post-doc days with other women about the “best” time to have children. Yixian Zheng, who herself won the 1999 WICB Junior Award, vividly remembers those conversations at UCSF. “Claire always said, ‘I’m going to have two,’” Zheng recalls. “So when I heard about Katie, I wasn’t at all surprised. How many women do you know in cell biology who started their own lab and had two kids at the same time and succeed? That’s Claire.”

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