Christine Jacobs-Wagner

Photo by Paul Fetters

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Jacobs-Wagner's discovery in *Caulobacter* of the IF-like protein crescentin is yet another chapter in the increasingly complex story of bacterial cell organization.

Consult an ancient cell biology textbook—ancient being anything more than 10 years old—and there it is in black and white: Prokaryotes do not have a cytoskeleton. The dynamic cellular infrastructure of tubulin, actin, and intermediate filaments (IF) belongs solely to eukaryotes, or so say the old texts. Today the prokaryotes are striking back.

The rewriting began early in the decade when researchers working with bacteria identified prokaryotic homologs for both eukaryotic tubulin and actin. In 2003, the Yale laboratory of Christine Jacobs-Wagner filled out the cast of principal actors in the cytoskeleton with the discovery in the bacterium *Caulobacter crescentus* of a prokaryotic IF-like protein. Jacobs-Wagner and her postdoc, Nora Ausmees, called the protein crescentin.

It was a startling find, according to William Margolin of the University of Texas Health Science Center at Houston. "Her discovery that *Caulobacter* contains an intermediate filament-like protein [crescentin] required for its curved shape was stunning, showing the world that bacteria now have homologs in all three of the major cytoskeletal proteins of eukaryotes." Moreover, Jacobs-Wagner's discovery of crescentin is only one of a string of major papers from her lab, which has been at Yale only since 2001. In Margolin's opinion, her scientific record and her early career stage made Jacobs-Wagner a prime candidate for the ASCB's Women in Cell Biology (WICB) Career Recognition Junior Award.

Yet in this strange prokaryote's life cycle are all the big, fundamental issues of cell biology—polarization, localization, differentiation—but in one well-defined, if small, model organism, says Jacobs-Wagner.

Bags of Enzymes No More

It was an opinion—and a nomination—seconded by Lucy Shapiro of Stanford University. The winner of the 2007 WICB Junior Award, Jacobs-Wagner, notes that she had the good fortune to arrive in the brave new world of prokaryotic cell biology at the right time. New technologies and new curiosity were in play.

Shapiro described her former postdoc as "an absolutely first-rate scientist" and listed a string of "significant discoveries" in Jacobs-Wagner's short career. These discoveries address how bacteria signal internally, move proteins, set landmarks, manage asymmetry, and control cell division. Jacobs-Wagner's productivity also shows how radically prokaryotic biology has changed, according to Shapiro. No longer were bacteria considered little more than "bags of enzymes with DNA and 'schmutz' [debris] swimming around inside."

Shapiro believes that Jacobs-Wagner's discovery of the IF-like protein crescentin is yet another chapter in the increasingly complex story of bacterial cell organization. "The major point is not that these [IF] molecules have been found in bacteria but that the [prokaryotic] cell is highly organized," Shapiro declares. "It really does exist as a complex, three-dimensional organization, and it behooves us to understand how it is regulated and what its functions are."

Not the Smart One

Jacobs-Wagner was born in Liège, Belgium, in 1968, the middle child between an older sister and younger brother. "My mother was extremely supportive of education in general, but after that, it was up to us," Jacobs-Wagner recalls. "For me and my sister, it was science. For my brother, it was art. You know how every family has a label for each child? Well, my sister was the smart one. I was the athlete. And my brother—I guess he was the troublemaker."

The family athlete, however, was good enough in science to follow her sister into biology at the University of Liège but branched off into biochemistry, whereas her "smart" sister took the other curriculum track into immunology. In 1990, she went to fulfill her research requirement with a subsidized internship in the lab of microbiologist Staffan

Normark at Washington University in St. Louis. There she discovered her passion for bacteria and the problem of beta-lactamase induction.

Under attack by common antibiotics such as penicillin or cephalosporin, resistant bacteria secrete the enzyme beta-lactamase to cleave a four-atom beta-lactam ring common to these drugs. Jacobs-Wagner returned to Belgium to enroll in a doctoral program in protein chemistry. However, she quietly determined to follow the problem wherever it led. Over the next five years, her quest led her to labs in Liège, St. Louis, Paris, Boston, and finally Stockholm.

Jacobs-Wagner discovered that beta-lactamase induction was part of a pathway regulating the bacterial cell's recycling of breakdown products shed internally by the cell wall. By monitoring the ratio of breakdown products to cell wall precursor, the beta-lactamase pathway could "see" an antibiotic attack as degradation products increased inside the cell. Jacobs-Wagner's discovery of this "unexpected mechanism has opened the door to new antibiotic targets that bypass some routes of drug resistance," according to Shapiro. It also earned Jacobs-Wagner's thesis the Grand Prize in the 1997 Pharmacia/*Science* Magazine Young Scientist Award.

Asymmetrical Swarmers

For her postdoc, Jacobs-Wagner went to one of the powerhouses of the new prokaryotic cell biology, the Shapiro lab at Stanford. There careful genetics and new imaging technologies had made *Caulobacter* the hot new model organism. Yet in this strange prokaryote's life cycle are all the big, fundamental issues of cell biology—polarization, localization, differentiation—but in one well-defined, if small, model organism, says Jacobs-Wagner.

It was in *Caulobacter* that Jacobs-Wagner and Ausmees discovered crescentin, the IF-like protein that so startled the eukaryotic community. Jacobs-Wagner says that they stumbled upon it. She gives full credit to Ausmees for realizing that a peculiar "straight" *C. crescentus* mutant in a mass visual screen might be worth closer study. In turn, Ausmees credits Jacobs-Wagner with fostering a lab atmosphere where an unexpected phenotype was not brushed aside as a distraction. "You know, later on when we talked with other *Caulobacter* people about this," Ausmees remembers, "many of them said, 'Oh yeah, we've seen straight *Caulobacter* before.' But nobody thought it was anything worth pursuing. They didn't want to get sidetracked." Jacobs-Wagner was not afraid of chasing a weird phenotype, says Ausmees. Ausemees is now on the faculty at Uppsala University in her native Sweden.

"Christine is terrific to work with because she's so enthusiastic and so open," Ausmees continues. "She knows how to inspire people, to give credit, and to encourage you. There are places where everyone is secretive, but Christine wants everything to be very democratic and out in the open. She's a wonderful scientific leader."

Bio Hazards Take Cup

Jacobs-Wagner admits that, outside the lab, her old family identity as the athlete lives on, at least on the soccer fields of Yale's intramural league. This year, Jacobs-Wagner played for the Bio Hazards, the biology graduate coed soccer team that defeated both the medical and law school teams for the championship. The team includes "graduate students plus a few old people like me," she explains. "We're not very good but we have a lot of fun. And I'm very proud that we're the champions." Playing soccer was also how she met her husband, Matt Wagner, a web developer. They married in 2000, and they later joined last names and both became Jacobs-Wagner. Today they live just outside New Haven in Hamden.

Jacobs-Wagner loves her job nearly as much as she loves bacteria but admits that her original decision to pursue a career in the United States was a "no-brainer." "I miss Belgium in many ways," Jacobs-Wagner allows, "but what I really like here is that even though starting a lab can be brutal, at least you get a nice jump start. Here's your set-up money. You're on your own. If you crash, you crash, but it's your own thing."

If scientists crash and burn, so do model organisms. "People used to study bacteria," she points out. "Before that it was viruses. Then they moved on to study 'higher organisms'—eukaryotes. But they left all this fascinating biology behind." Now some of the most exciting cell biology today is being done on lower organisms that a decade ago were barely considered organized. "I think there is a boom but that we're just at the beginning." She likens the buzz surrounding the prokaryotic cytoskeleton to the excitement 40 years ago following the breakthrough discoveries in eukaryotes of tubulin and actin. "And you know where that led. It was huge. Two-thirds of the ASCB meeting is still about the eukaryotic cytoskeleton," she laughs. "But even that's changing now." ■

—John Fleischman

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