Lynne Quarmby

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Lab lineage is terribly important in cell biology. Fly people come from fly labs. Worm runners train in the *C. elegans* world. People who work with the single-celled green alga, *Chlamydomonas*, can usually trace their descent from a lab hooked into the worldwide "Chlamy Clan." Not so Lynne Quarmby. Now an associate professor at Simon Fraser University in British Columbia, Quarmby is a pillar of the worldwide "Chlamy" community. Yet she cheerfully admits that she never trained in a *Chlamydomonas* lab and didn't belong to a "real" Chlamy lab until she started her own. "I like to say that I had wonderful 'telephone mentorship' from the *Chlamydomonas* community, but for many years I was at institutions where no one else used *Chlamydomonas*," Quarmby explains.

Quarmby recruited herself soon after she entered the biochemistry graduate program at the University of Connecticut (UConn), Storrs, in 1985. Her advisor was Richard Crain, a lipid biochemist. Crain had an interest in whether inositol phospholates were involved in the IP3-mediated calcium-signaling pathway in large tropical plants. Quarmby suggested that the work might be easier in one-celled algae. Quarmby, who grew up exploring the lakes and tide pools of Vancouver Island, came to Storrs with a master's in Oceanography from the University of British Columbia. She knew something about algae, at least in the wild. Crain left her to the algal lab literature and then the telephone, where Quarmby stumbled into the helpful arms of the *Chlamydomonas* community.

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Making the Cilial Connection

The *Chlamydomonas* community exists largely because there is no better model on earth for studying cilia and flagella. Secondary cilia and flagella are the tiny hair-like motile structures that drive so many of life's basic processes, from sweeping the respiratory tract to powering sperm. Within the last five years, Chlamy labs working on defects in primary cilia—nonmotile structures found on virtually every eukaryotic cell— have turned up startling links to polycystic kidney disease (PKD) and other human disorders. These new "ciliopathies" affect everything from the human eye to the human embryo. All this has made cilia a hot field and *Chlamydomonas* a hot organism.

Back in the late 1980s when Quarmby began teaching herself *Chlamydomonas*, it was a "niche" lab organism with a small if dedicated following. Yet Quarmby made a small discovery in her first Chlamy experiments. Calcium signaling was involved in one distinctive behavior, deflagellation. This shedding of waving arms, either under stress or shortly before cell division, was well-known behavior. The *mechanism* was a black box. Over a dozen years, and in several non-Chlamy labs, Quarmby struggled to develop deflagellation as a genetic assay. That work is now paying off handsomely, says Yale's Joel Rosenbaum, a senior figure in the *Chlamydomonas* community.

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Quarmby's contribution to the recent excitement has been her use of mutants defective in deflagellation to uncover yet another novel role for ciliary proteins—as regulators of the cell cycle. Rosenbaum explains, "It's long been known that every time the cell divides, the cilia resorb prior to division. It's never been known whether that's a cause or an effect." The mechanism is still not understood, he adds. However, new evidence from Quarmby and others points to the ciliary-based basal body, which emanates from the centriole and duplicates during mitosis to become part of the spindle apparatus. If Quarmby's defective deflagellation proteins affect such a fundamental organelle, they could well have an impact on cell cycle timing, notes Rosenbaum.

Inside the Chlamy Clan

Ursula Goodenough is another senior member of the *Chlamydomonas* community and one of Quarmby's "telephone mentors." Now at Washington University in St. Louis, Goodenough remembers hearing the young, un-

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known researcher speak for the first time at a *Chlamydomonas* meeting. "It was instantly obvious to me that Lynne was extremely smart and extremely imaginative. I went out of my way to get to know her," says Goodenough. They became friends and Goodenough has seen Quarmby in her lab, at meetings of the ASCB's Women in Cell Biology Committee, and at the lecture podium, many times since. "It's been a joy to watch Lynne develop," says Goodenough.

Goodenough says that when Quarmby first made the decision to screen for Chlamy mutants that couldn't deflagellate, there was nothing obvious about a possible connection to cell cycle control. "Maybe other people suspected it, but it was news from my perspective," Goodenough says with a laugh. Cells do lose their flagella when they go into mitosis but that happens in part by an independent process where the flagella shorten, rather than pop off. "This idea of calcium-induced popping of cilia and their resorption (in the mitotic spindle) was, at best, a speculation. It was Lynne who pulled this together and took it beyond speculation. Like any good scientist, Lynne followed her nose."

Lynne Quarmby has always followed her own star. Neither of her parents finished high school. Growing up in the Canadian pulp mill town of Duncan, 50 miles north of Victoria on Vancouver Island, Quarmby sensed her family's high expectations regarding hard work and integrity. But career expectations for a girl were low. When her high school math teacher told her mother that Lynne was quite bright and should consider medicine, her mom responded, "Oh, I don't think Lynne would like to be a nurse." Yet Quarmby says that her family's lack of expectations liberated her to find her own way. When she left Duncan for the University of British Columbia (UBC), Quarmby fished around for professional programs that involved chemistry and biology. "In pharmacy school, I lasted a week in the starched lab coat. It just wasn't me."

Hostile Waters

Her love of the Vancouver coast and her talent for science led her to Oceanography. It was also the first time that Quarmby had her "nose rubbed" in academic misogyny. When Quarmby was appointed the "scientific captain" of a UBC research cruise, the vessel's captain treated Quarmby with derision, pumping the bilgewater overboard in the middle of a critical sampling run as a "practical joke." Her prospects in the early 1980s were equally discouraging, Quarmby recalls. A senior faculty member liked to tell departmental gatherings that he never worried about flooding the job market with graduates: "Why do you think I have so many women students? They get their graduate degrees, have babies, and drop out." Quarmby decided to change course and pursue a biochemistry doctorate at UConn in 1990.

In Connecticut, Quarmby found her own way to *Chlamydomonas* and to its curious deflagellation behavior. For her first postdoc, Quarmby went to the biochemistry lab of Nobel laureate Alfred Gilman, at the University of Texas Southwestern Medical Center, to study calcium ion channels. There wasn't an alga in sight. In Texas, Quarmby learned the craft of rigorous research but never stopped thinking about the possibilities of *Chlamydomonas*.

Two years later, Quarmby steered her career back to *Chlamydomonas* by convincing a cardiac physiologist who knew nothing about algae to take her on as a postdoc. The physiologist was Criss Hartzell of the Emory University School of Medicine. Quarmby heard Hartzell speak at an ion channel meeting and came up afterwards. The two hit it off immediately. Over coffee, Quarmby sketched out her idea of using an alga to get at calcium ion channel pathologies in mammalian hearts. They emailed back and forth until Hartzell came up with a year's worth of very soft money at Emory and the offer of bench space.

"I really didn't know anything about *Chlamydomonas* at the time," Hartzell recalls, "but Lynne had this passion and intellectual excitement about her. She was clearly very smart. But I've had a lot of smart postdocs in my lab who in the end didn't succeed. Lynne stuck with it. She was convinced that this weird deflagellation response was important. In addition, Lynne was a huge intellectual stimulus for me and for my lab."

Follow the Phenotype

"It was brave of Criss to make room for me," says Quarmby, "and it was foolhardy of me to leave Gilman's lab, uproot my family, and do a lot of scrambling, but it seems to have worked out." Quarmby stayed at Emory for eight years, first as a research associate and then as junior faculty in the Cell Biology department. There she finally set up her very own Chlamy lab. Equally novel was the presence of another Chlamy lab just down the hall run by Win Sale. Quarmby says that Sale was an important mentor and resource as she launched her grueling, two-year-long saturation screen for deflagellation mutants. It yielded three oddball

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genes, one of them encoding a Nek-family kinase. The mutant led not to a calcium channel defect phenotype, but to a temporary arrest in the cell cycle at G2.

Rip Finst was Quarmby's first graduate student and collaborator on the saturation screening. Finst says he entered Emory and Quarmby's lab with the understanding that his ambitions extended beyond academic science, toward an eventual career in business or law. "Lynne embraced that, letting me pursue my interest in science while knowing full well that I had these other goals," says Finst, who later added a J.D. to his Ph.D. Finst, who is now an intellectual property litigator with a Bay Area law firm, says Quarmby was the ideal mentor for him—intensely focused on the science but undeterred by conventional expectations.

Finst recalls, "Here we were in a medical school setting working on *Chlamydomonas*, which really didn't fit the conventional approach to problems like ion channels or cancer genetics. But Lynne had a vision of how you could answer medical-type questions using this basic system. That has paid off massively for Lynne in the work she's now doing in kidney cells. It's remarkable how she's persevered."

Back in 1999 though, an algae-based lab in a medical school remained a hard sell to prospective graduate students and to funders. One afternoon, Quarmby was leafing through the back pages of *Nature*. "And there was Simon Fraser looking for me," she remembers.

Today Quarmby feels very much at home again in British Columbia, at Simon Fraser University (SFU), and in the Canadian research funding system. "The size of our grants is small by U.S. standards," Quarmby says, "but the funding rates are higher." SFU has a spectacular setting atop Burnaby Mountain on the east side of Vancouver. It has been known until recently for its undergraduate program, but Quarmby says that is changing. Both the number and quality of graduate students at SFU are steadily increasing, she says. "In graduate programs, you need a critical mass, and we're just about there now."

The Alga that Came in from the Cold

The cilia–PKD connection has finally ended the old prejudice that *Chlamydomonas* is too far removed from human biology to be medically relevant. For the first time last year, Quarmby received a grant from the Kidney Foundation of Canada. Also for the first time, she brought another organism model into her lab and is working with cultured mouse kidney cells. She spent part of last year on sabbatical to learn the etiology of cysts in mouse tissue at the Hospital for Sick Kids in Toronto. "But I'm not switching my lab!" Quarmby declares. "I want to be able to go back and forth with mammalian cells, but Chlamy is always going to be the focus."

Returning home reawakened her love of the Canadian wilderness and her skills as an avid backpacker. During her recent stay in Toronto, Quarmby took her first extended canoe trip through Ontario's watery Algonquin Provincial Park. Quarmby's other great interest is her 19-year-old son, Jacob Sheehy, who after a gap year backpacking through Eastern Europe, has just enrolled in Computer Science at Concordia University in Montreal.

Quarmby is also an artist, a "closet painter," as she puts it, who after 25 years of painting abstract canvases for personal amusement and close friends, stepped out in public last summer with a show at a Toronto gallery. That led to her first commercial sales. Naturally, Quarmby has never had a painting teacher and belongs in no school of art but her own. ■

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Additional runners up will receive smaller cash prizes. A "Celldance Festival 2006" Winners' Reel will be posted for free, open-access downloading at www.ascb.org and deposited in the soon-to-be-launched ASCB Image & Video Library.

The contest is open to ASCB members and ASCB member applicants only. Entry deadline is September 30, 2006. For further details on how to enter (and the fine print in full), go to www.ascb.org/index.cfm?navid=128.