## 2001

### Pamela Bjorkman

Crystallographers, they say, are the only people in biology who can declare, "I solved something." Pamela Bjorkman has solved her share of the bioactive molecules that drive all cell life, revealing through crystallography their precise structure and form.

Pamela Bjorkman's career started with her solution of a human class I histocompatibility antigen, HLA-A2, while still a doctoral student with Don Wiley at Harvard University. She continued as a post-doc at Stanford and then joined the faculty at CalTech, where she climbed quickly to full professorship. In recent years, her CalTech lab solved the structure of the neonatal Fc receptor (FcRn), both alone and complexed with its ligand, the Fc region of Immunoglobulin G (IgG). FcRn mediates the intercellular transport of IgG, and may be central to one of the great mysteries of mammalian life—how a mother transmits humoral immunity to her newborns. Bjorkman's lab also solved the structure of the protein HFE as a complex with transferrin receptor, which is mutated in the disease hereditary hemochromatosis (HH), the leading genetic disorder among Americans of European ancestry.

But Bjorkman insists that she is not just a crystallographer. Bjorkman's new work on FcRn has moved into cell biology, using real time confocal imaging to study its role in the intercellular trafficking of IgG.

Caroline Enns, a cell biologist at the Oregon Health Sciences University in Portland who is a longtime friend and a current collaborator on the transferrin receptor work, says that Bjorkman's refusal to stay in any one narrow territory is what makes her such a successful scientist. Says Enns, "I've known a whole bunch of crystallographers. Pamela is different. She's really interested in the biology as well, what these molecules do and how their structure and function relate."

Bjorkman discovered early that lab research was the best way to learn anything. The revelation came to her in sophomore biology class in public high school in Portland, Oregon. Until then, her experience had been all too typical—workbook lessons, prepared slides, and fill-in-the-label diagrams of cells. "In junior high, biology was just so uninteresting," she recalls. "They never showed us how scientific knowledge was acquired, they just made us memorize it. Even so, when I did become interested in facts, no one really steered me towards a career in research. This was at a time when if a girl was good at science, someone would say, 'Why don't you become a nurse?'"

"It never occurred to me that studying science was a way to do something interesting," she recalls. "In junior high, you were just told that you needed to eat protein but you really didn't know why. In high school, we started by understanding what a protein was. Suddenly I realized that you could get real answers to questions yourself. The next year I took chemistry, physics and math. I was lucky: my high school science teachers were really excellent."

Lab science appealed to her the most. Starting as a chemistry undergraduate at Willamette University in Salem, Bjorkman launched her research career with an Oregon Heart Association Fellowship to work in a lab at Reed College, helping to compare zinc/copper ratios in cadaver tissue from atheroschlerotics by nuclear activation analysis. She was first author on the resulting paper published a year later. By then, she'd already transferred to the University of Oregon in Eugene, for a chance to join a research lab. She quickly found the biophysicist Hayes Griffith and worked with him and his research associate, the late Patricia Yost, on spin label measurements of lipids in membrane systems. Griffith and Yost, Bjorkman says, not only taught her science, they taught her how to become a scientist. "My parents had no background in science and I hadn't been exposed to any of this," Bjorkman says. "Hayes and Pat sat me down and said, 'If you want to do research, you have to get a PhD.' They wrote down a list of places I should go for graduate school so I guess that's how I ended up at Harvard."

Bjorkman arrived in Cambridge thinking she would do further biophysical membrane studies. But at a retreat for new students, she heard Don Wiley talk about using protein crystallography to study proteins in influenza virus. "The idea that you could learn about how viruses work and possibly influence major public health issues through structural biology was something I'd never heard before. I was immediately hooked," she recalls. Looking back, she laughs at her choice. "Of all the things that Hayes and Pat told me I could do, the only area they told me that I should not do was protein crystallography. It was too expensive, they said, and if I wanted to get a faculty job doing protein crystallography, I wouldn't get hired because no one wanted to spend that kind of money to set up a lab." Fortu- nately, this proved not to be Bjorkman's case.

Hayes Griffith says that Pamela Bjorkman was the most determined undergraduate they'd ever taught. "The thing that distinguished Pamela was her determination. Pat always referred to her as the 'velvet tank.' She was gentle, very polite but very persistent. She also had all the makings of a great scientist." Moreover, Pamela had the luck, says Griffith, to pick protein crystallography just at the right moment.

“There was a revolution,” Bjorkman says of the early 1980s during her time at the Wiley lab. “People decided that structural biology was really important and suddenly everyone wanted to hire a crystallographer.” Moreover, Bjorkman says, crystallography is no longer the budget breaker it once was. “Today it pales in comparison to the costs of NMR or electron microscopy.”

Bjorkman returned West for her post-doc with Mark Davis at Stanford, trying to solve the structure of a T cell receptor. “That project never did succeed for us,” she says. “We ended up getting rotten crystals. But I did manage to learn molecular biology while I was a post-doc, which was useful for setting up my own lab later. I had decided that I didn’t want to just crystallize what other people could purify and it was becoming obvious that the way people were going to do structural biology was to express all the proteins. I learned what I needed to learn.”

As a junior faculty member at CalTech, Bjorkman soon won a Howard Hughes investigatorship. She now has a thriving lab of a dozen members.

Bjorkman’s only unhappy surprise arriving at CalTech in 1989 was that she was the first mother on the faculty: her husband, neurobiologist Kai Zinn and she had had their first child, Leif, five months earlier. “I had no idea that CalTech was that way [when I interviewed] and I didn’t ask. I didn’t know until I came here with Leif and noticed that there were very few other women professors and that none of them seemed to have children. Two or three months later another woman [on the faculty] had a baby; but for a long while, we were the only female professors with kids.”

Bjorkman claims membership in the generation of women who came of age during the feminist revolution. Bjorkman is still proud to call herself a feminist and can scarcely understand why younger women seem so uneasy with the word. Yet she says that until graduate school, she was oblivious to the subtle and not-so-subtle ways women in science are treated unfavorably. “Women are not so much deliberately excluded as they are not thought about,” she reflects. “It’s human nature for people to have friends like themselves, and when a question comes up of who to invite to a meeting or who should give a talk, you tend to think of your friends. If all your friends are white males, then you’ll tend to invite a white male. It’s the same thing for minorities in science. It’s this vicious circle. It’s almost impossible to create a normal atmosphere for women in science when they are in such low numbers, so it’s hard to imagine the situation will improve until more women are hired as faculty.”

Bjorkman says she is distressed by the younger generation of women who tell her that they are discouraged by the prospects of a life in science. “It seems very sad to that there aren’t more women going into science. They tell me that if they want to have children that they can’t possibly go into academic research and be a professor. I hear this over and over from young women students. So I say, ‘Haven’t you noticed that I have two kids?’ And they say, ‘Yeah, but I don’t want to be like you.’ I’m not sure what they mean by that, but I hear this all the time and the only thing I can say is that you can make it work without sacrificing time to be with your child.”

Leif Zinn-Bjorkman is now 12 and his sister Katya is 7. The kids share their father’s “obsession,” says Bjorkman, with rock climbing, hiking and backpacking. A year ago, the family rafted the Colorado River through the Grand Canyon and this summer they tackled some technical rock climbing in the Sierras. Bjorkman has taken the children with her to scientific meetings and conferences, generally bringing a babysitter. The kids have taken notes during her presentations and critiqued her afterward. Indeed Bjorkman thinks that academic research is the ideal profession for someone raising children. “You can set your own hours. If your child needs you— if the child is sick or wants you to go on a field trip with them— you can be there and catch up with your own work at night. I don’t see other careers as being that flexible, especially about taking time off during the day.”

Bjorkman’s greatest cause for parental concern these days is her son’s encounter with junior high biology, which is even duller than Bjorkman remembered. “I couldn’t believe what they had him doing— copying pictures of cells and memorizing what different compartments are and what they do. He could tell you that the mitochondria are the energy source but he wasn’t taught anything beyond that. Still at that age, I was bored sick by science, so maybe some of these kids will eventually discover that science is more than just reading textbooks and memorizing facts.” Of all the things that Pamela Bjorkman is in science, bored is the hardest to imagine.