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Anthony Bretscher

Tony Bretscher offers himself as an example of the classic late bloomer. He describes himself as a mediocre physics student who scraped through Cambridge University to slink home in 1971, jobless and rudderless, to brood. Bretscher grew up near Oxford in a seriously overachieving family. His father, a physicist at the Research Establishment for Nuclear Energy, was formerly a member of the British delegation on the Manhattan Project. His mother was a natural mathematician. Of his four older siblings, two were successful biologists, including oldest brother Mark, who in 1971 was already an internationally known cell biologist at the MRC Laboratory in Cambridge. Tony Bretscher remembers vividly the defining moment in his professional life: "My brother came up to me one day," he recalls, "and told me in so many words that I wasn't as stupid as my paper credentials suggested. He said he wanted me to try doing Biology for a PhD, a subject which I'd never taken in my life."

So, Tony Bretscher, with the help of brother Mark, enrolled in the Department of Genetics at the University of Leeds. Having quickly read two biology textbooks cover-to-cover as preparation, he arrived in the bacterial genetics lab of Simon Baumberg and was soon happily at work on the isolation of promoter and operating mutations that affected the arginine biosynthetic pathway. "I loved it. I absolutely loved bacterial genetics, and this was before cloning," recalls Bretscher. Despite his near total lack of background, Bretscher finished his doctorate in less than three years.

The former Cambridge failure is now Professor of Cell Biology in the Department of Molecular Biology and Genetics at Cornell, where he has been since 1981. He runs a double track lab, a yeast genetics side exploring the actin cytoskeleton's role in secretion, and a cell biology side looking at membrane-cytoskeleton linking proteins. He also dedicates considerable service to the ASCB, as an Associate Editor of *Molecular Biology of the Cell* and a recently elected member of Council. Scientifically, Bretscher is best known as the discoverer (and namer) of ezrin in 1983, the first of the ERM family of proteins that include radixin and moesin and is emerging as critical to cross-linking actin filament networks to the plasma membrane in a variety of cell types. Named for Ezra Cornell, the founding patron of the University, ezrin occupied Bretscher's early career. "It was a minor protein that I thought might have a regulator function. It had an interesting localization that turns out to regulate actin attachment, but it was five years of hard slog."

Ezrin came out of Bretscher's work with Klaus Weber on cell polarity at the Max Planck Institute in Goettingen, Germany. "Klaus taught me everything I know about cell biology," says Bretscher. It was a major shift from the developmental bacterial genetics he'd been doing during his first post-doc at Stanford, working on cell-cell interactions in Dale Kaiser's lab.

Klaus Weber simplifies his own role in Bretscher's cell biology education. "Basically, I gave him globally what I wanted him to know and let him get on with it," says Weber. The area that interested Weber was the "brush border," a bristling hedge of finger-like microvilli present on the apical end of the distinctive epithelial cells that line the gut. Weber asked his new post-doc to take a closer look at the microvilli. "Clearly the microvilli were actin bundles but what kind of proteins made them and how did they assemble? I asked Anthony to purify the microvilli and out of that work, together we came up with villin and fimbrin (the cross-link filaments that hold the bundles together). People know Anthony for finding ezrin and the ERM family but it should also be known that he found villin," says Weber.

Bretscher took the brush border problem with him when he returned to the United States in 1980 for his first faculty appointment at UT Southwestern Medical School in Dallas. It didn't work out, says Bretscher, but things went better at Cornell. There, Bretscher devoted himself to the cell biology of ezrin and the ERMs but he missed his old genetics perspective. "I figured that the only way to really understand actin was to do a genetic analysis of actin and its binding proteins. To do that, I had to learn yeast," says Bretscher. In the summer of 1986, he took the Cold Spring Harbor summer yeast genetics course and returned to the lab to set up a genetics track. Today, half of his cell biology lab pursues the ERMs while the yeast half explores the actin cytoskeleton's role in secretion and organelle segregation.

David Reczek did his doctorate and a post-doc with Bretscher on the ERM side of the lab before joining Genzyme in 2000. He notes that Bretscher's parallel focus has given Bretscher a dual identity in the yeast genetics and cytoskeletal protein fields. Says Reczek with admiration, "Tony refuses to give up one or the other aspect of his research and he's done quite well in both and in getting funding for both." Reczek describes Bretscher as a superb advisor with "endless confidence in the ability to learn what was needed and to make a difficult protocol work. He kept saying, 'Give it one more shot. I'm confident you'll figure it out.' Tony is just very passionate about what he does; he's been doing it for a long time and yet he maintains that passion."

Klaus Weber concurs. "Anthony is totally unpretentious," Weber continues. "He's person-ally so likeable, so friendly, and so helpful a colleague."

Moving to Cornell also led Bretscher to another passion. On his first day there in 1981, Tony met his future wife, Janice, who was then a new graduate student on her first day there. Today the Bretschers have two daughters, Heidi, 16, a high school sophomore, and Erika, 11, a sixth grader. His family, Tony Bretscher tells one and all, is his number one interest and his number one activity. They share his wild delight in hiking, biking, and paddling around Ithaca and at their cabin upstate on a lake in the middle of the Adirondacks. The latest addition to their fleet of canoes, sailfish and kayaks is "Daphne," a wooden kayak that Bretscher built from a kit in his basement woodshop.

ASCB member William J. Brown says he came to Cornell's Molecular Biology and Genetics department and has stayed there for 18 years, largely because of Tony Bretscher. Off campus, Brown admires Bretscher's woodworking skills, including the "fair number of real cool woodworking tools" that Bretscher has managed to accumulate in his basement in recent years. On campus, Brown admires the way Bretscher interacts in the department. Brown remembers the years when Bretscher plugged away on ezrin and the ERM family at a time when membrane cytoskeletal cross-linking proteins were not fashionable. But most of all, Brown admires Bretscher's skill at balancing home and lab. "I've heard a lot of people in science talking about finding that balance," says Brown, "but I've watched Tony and he has some- how managed to figure it out."