

Elizabeth M. Wilson-Kubalek

On the day that it all became too much, Elizabeth (Liz) Wilson-Kubalek was signing off on the doctoral thesis of a Stanford graduate student who'd done half of his thesis research in her lab at the Scripps Research Institute in La Jolla, CA. Wilson-Kubalek remembers thinking, "This is totally ridiculous. I can sign for a doctorate, but I don't have one myself."

In 2001, Wilson-Kubalek had a grant—a competitive R01 from the National Institutes of Health (NIH)—to pursue her novel idea of crystallizing proteins on lipid nanotubes to determine the 3D structures of the proteins by electron microscopy (EM) and image analysis. She had published more than 30 papers. But Wilson-Kubalek didn't have a Ph.D. She'd left her native Scotland at 18 with a minimal qualification as a medical laboratory technician. And yet she'd built a research career as an innovative electron microscopist who worked with many of the leading lights in protein structure, including Nigel Unwin, Jim Spudich, Roger Kornberg, and Ron Milligan. Still without a degree, there she was, certifying the work for someone else's Ph.D.

In despair, Wilson-Kubalek went to see Sandy Schmid, the chair of cell biology at Scripps. Schmid was wonderfully supportive, Wilson-Kubalek recalls. "Sandy said that she didn't see why I shouldn't be able to get into graduate school. And then I told her that I didn't have a bachelor's. Sandy said, 'Hmm. That makes it a little harder.'" But Schmid and Scripps dean Jeff Kelly figured a way to pull together a Scripps graduate school application for Wilson-Kubalek on the basis of her published work and outside recommendations.

Wilson-Kubalek was admitted to the Kellogg School of Science and Technology at Scripps in 2002. For the next three years, Wilson-Kubalek was a PI, a busy collaborator, and a full-time graduate student. It was a worrisome time for her friends and mentors, says David DeRosier, now emeritus at Brandeis. He first met Wilson-Kubalek in the mid-1980s, when she was doing

electron crystallography for Nigel Unwin at Stanford. DeRosier recalls, "For those of us who knew Liz well and encouraged her [to enroll in graduate school], we often wondered if this really was the best thing for her to do. It was just so much work. But, by golly, she did it."

Ruining the Bell Curve

Mark Yeager is Wilson-Kubalek's friend and former colleague from the Unwin lab. Now he is the director of research in the Division of Cardiovascular Diseases at the Scripps Clinic and a faculty member at the Scripps Research Institute. Yeager recalls running into Wilson-Kubalek on the Scripps campus, where she was teaching a basic seminar on EM techniques for new grad students and postdocs, while she was enrolled in a required fundamentals course. "I remember seeing her a couple of days before the exam. I knew that she'd enjoyed the course, but she told me she was very worried about her score. Well, it turned out that her score was so high that they had to pull her test out. Liz was ruining the bell curve," Yeager says with a laugh.

One would expect such achievement from a woman with a third-degree black belt in judo who used to compete internationally, says Yeager. "I think Liz is a wonderful model for all of us because of how she's managed to balance her life as a scientist, an athlete, a mother, and a mentor." Wilson-Kubalek finally "walked" at the 2005 Scripps graduate commencement.

The Road to Science

Wilson-Kubalek was born in Aberdeen, Scotland, moving at 12 with her family to Edinburgh. Neither her parents nor her teachers thought much of her academic prospects. When she left high school at 16, she enrolled in a technical college program in Edinburgh to qualify as a medical laboratory technician. Two years later, she took the most direct way out of Scotland, an airplane to Basel, Switzerland,



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where she'd landed a job, long-distance, in a private cytology lab.

She arrived with no other contacts and with schoolgirl French but no awareness that people in Basel spoke German. Yet Wilson-Kubalek recalls that flight as “one of the high points of my life. I never felt better than when I got on that airplane.” Until then, she says, “nobody ever thought I'd be doing anything.” In Basel, she began to change that expectation. Wilson-Kubalek made friends and learned Swiss German by joining a judo club. She picked up cytology in a flash—she had a knack for recognizing pathological cells, she says—and was soon put in charge of double-checking the work of other technicians. But routine slide reading grew boring. Wilson-Kubalek decided that she wanted to work in a research lab. At that point, she'd never seen one.

Spotting a posting at the University of Basel's Biozentrum for an X-ray crystallography job for which she was totally unqualified, she managed to talk her way into a tryout with Hans Jansonius. He gave her a three-month trial and quickly realized that she was a fast learner. In 1981, “Wilson, E.” made her first appearance in the scientific literature as a middle author in a *Journal of Cell Biology* paper describing a method of seeding protein crystals to grow out larger samples for X-ray crystallography.

By Degree

Jansonius became the first of a long line of mentors who urged her to get a formal education. But a Swiss university degree would have required proficiency in three languages, and the UK offered her no educational prospects either. Then former Jansonius lab members urged her to join them in San Francisco. Wilson-Kubalek fired off letters and took another plane ride into the unknown.

Her protein seeding expertise got her a job in Sun-Hou Kim's crystallography lab at the University of California, Berkeley. She loved Berkeley and American research, but marriage and visa trouble forced a brief return to Switzerland. It took the new couple two job hops to get back to California. Wilson-Kubalek headed for the Stanford campus with Kim's recommendation to seek out Nigel Unwin and learn EM.

Wilson-Kubalek blossomed in the Unwin lab, working on the nicotinic acetylcholine receptor. She quickly mastered EM basics and, at Unwin's urging, learned new techniques such as cryo-EM and developed her own tweaks to standard methods. Unwin did not treat her as a technician. He listed her on lab papers,

signed her up to do poster presentations, and sent her in his stead to give seminar talks at other institutions. For Wilson-Kubalek, giving a talk was not as hard as sitting through her introduction. “You know where they usually introduce the speaker by saying that she did her bachelor's here and her doctorate there? Well, they'd say, ‘Liz has a lot of experience,’” she recalls.

Then in 1987, Unwin left Stanford to return to the UK and a post at the Medical Research Council in Cambridge. Wilson-Kubalek's personal situation made following him impossible. To stay at Stanford, she worked out a time-sharing deal between Jim Spudich and Roger Kornberg. For Spudich, she worked on the structure of myosin II, a molecular motor in *Dicyostelium*. For Kornberg, she helped resolve the first structures of *Escherichia coli* RNA polymerase and yeast RNA polymerase by electron crystallography. In 1992, she moved to Pat O. Brown's Howard Hughes Medical Institute-supported lab, where she introduced the use of nickel-chelated lipids for 2D crystallization of histidine-tagged proteins. She demonstrated the feasibility of this approach by forming 2D crystals of HIV-1 reverse transcriptase on a nickel-lipid substrate.

Besides her creativity, Wilson-Kubalek's world-class bench skills have made her a valuable collaborator, explains Sidney “Wally” Whiteheart, now at the University of Kentucky. “If you look at all those papers she's published with various groups, the center of all these papers is Liz's ability to get the proteins to behave. That's all to her credit.”

A Decorated Nanotube

Although a successful collaborator, Wilson-Kubalek still found herself increasingly frustrated at Stanford by her nondegree status. In 1995, the situation came to a head with the breakup of her marriage and an offer from Ron Milligan, another Unwin lab veteran, to join his lab at Scripps. It was in Milligan's lab that she came up with the idea to “decorate” nickel-lipid nanotubes with histidine-tagged proteins.

The technique made Wilson-Kubalek well known in the community, according to DeRosier. “This method with lipids and nickel derivatives has been quite successful, and almost everybody knows her from that. She has quite an international reputation. If you call up labs in Europe or Japan, they'll know who Liz is.”

That public profile was already growing in 1998 when Wilson-Kubalek was pushed into giving the leadoff talk at a Tahoe Symposium

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when the featured speaker failed to appear. “That was kind of nerve-racking,” she recalls. In the audience was Sue Schaffer, then deputy director for the National Institute of General Medical Sciences at NIH. Schaffer sought her out afterward, wanting to know what Wilson-Kubalek’s lab was planning next. Wilson-Kubalek repeated her old story—she didn’t have a lab because she didn’t have a grant because she didn’t have a degree. Schaffer interrupted her: You don’t have to have a degree to apply for an NIH extramural grant, said Schaffer. You need institutional support for lab space and an appropriate title. And you need a good idea.

A Green Light

Wilson-Kubalek already had the idea. Back at Scripps, Bernie Giulia, who was then the chair of cell biology, gave her a title—staff scientist—and a green light. “If Sue Schaffer says you can do this,” Giulia declared, “then I think you can do this.” Her first application narrowly missed the funding cutoff, but the revision sailed through. Ironically, by the time her R01 was up for renewal in 2005, Wilson-

Kubalek was no longer the grant applicant without a degree. But the NIH funding climate was already changing, and when the application was denied, Wilson-Kubalek

decided not to fight it. Today, she is a senior staff scientist in the Milligan lab, where she enjoys collaborating with colleagues inside and outside Scripps. Most recently she has been working on kinetochore proteins with Arshad Desai of the University of California, San Diego (UCSD).

She lives in Cardiff-by-the-Sea, near La Jolla, where she now shares custody of her 12-year-old daughter, Kyla Wilson, with Kyla’s father, Gavin Meredith, a senior scientist with Invitrogen. “Kyla gets science from both sides,” Wilson-Kubalek explains. “Right now, Kyla wants to be an environmentalist. She wants to change the world.” Kyla, who has just won a coveted place in a special summer

science camp program at UCSD, may be on her way. “But Kyla’s not going to have problems like I did,” declares Wilson-Kubalek. “She’s had a proper education right from the start.” ■

—John Fleischman

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NAS Invites Nominations for Lounsbery Award

Intended to stimulate research and to encourage reciprocal scientific exchanges between the United States and France, the Lounsbery Award is given in alternate years by the National Academy of Sciences to a young American or French scientist in recognition of extraordinary scientific achievement in biology and medicine.

The award is scheduled for presentation in 2009 to a young American scientist. In addition to the award of \$50,000, a further sum is provided for the recipient to visit a laboratory or research institution in France.

For more details about the award and nomination process, visit www.nasonline.org, and click on “Awards.” The deadline is September 15, 2008. ■