Kathleen J. Green

People used to say annoying things about intermediate filaments, such as calling them the poor relations of the cytoskeleton—a description that still provokes Kathleen (Kathy) J. Green, an adhesion researcher and professor of Pathology at Northwestern University's Feinberg School of Medicine in Chicago. "When people say things like that, I always point out that this is not a good attitude," Green explains in measured tones. "I know several people who really struggled in [NIH] study sections because reviewers would say that the data were not there that intermediate filaments did anything beyond contributing to tissue integrity."

The data are there now. Intermediate filaments have taken their rightful place in the cytoskeleton hierarchy along with actin and microtubules. Green contributed to the data through her patient work on desmosomes, the intercellular junctions that anchor intermediate filaments to the cell surface and support cell-cell adhesion. Desmosomes are thus major players in embryogenesis, cell differentiation, and wound healing.

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The Green lab and others in the field have tracked defects in desmosomal and other adherens junction proteins in unexpected clinical directions, including oncogene regulation, autoimmune disorders, and most recently cardiomyopathies. The obvious hypothesis, Green explains, is that loss of function in these adhesion molecules weakens the heart muscle in response to mechanical stress. That factor may contribute, but new evidence indicates that aberrant signaling could also be a key factor, says Green. "The loss of some of these junctional proteins may lead to redistribution of signaling molecules. That could alter the differentiation of heart muscle and replace it with fibrofatty tissue. So it could be that it's not totally a question of mechanical integrity."

Nailing Desmosomes

Putting a basic research problem into a wider clinical context is classic Kathy Green science, says John R. Stanley, Dermatology department chair at the University of Pennsylvania in Philadelphia. Stanley began collaborating with Green in the early 1990s on pemphigus, an autoimmune skin-blistering disease thought to involve desmosomal defects. "I'm a physician-scientist," says Stanley, "so the good thing was that I could look at it from the disease point of view and Kathy knew the Cell Biology point of view. As we started collaborating, she got more interested in pemphigus, and I got more interested in the biology of desmosomes. Kathy characterized the structure of the desmosome in a way that really nailed it down," Stanley explains. "People always thought it was adhesion, but this defined function. If you interfere with function [of the proteins], then you interfere with adhesion."

Stephen I. Katz, director of the National Institute for Arthritis and Musculoskeletal and Skin Diseases at the National Institutes of Health, agrees that Green has been a longtime force in generating scientific knowledge on keratinization as well as adhesion molecules. According to Katz, "Kathy is one of those triple-threat people. She's an outstanding Ph.D. scientist who can think in clinical terms. She's an outstanding teacher and a very good administrator."

She's also a great mentor, says Andrew Kowalczyk, a former postdoc now on Emory University's Cell Biology faculty. "Now that I'm trying to run my own laboratory and get my own funding, I have a completely different appreciation of Kathy," he says. The pure biological problems surrounding the desmosomal–cadherin junction drew then-postdoc Kowalczyk to the Green lab. "It wasn't until I was in Kathy's lab for some time that I began to recognize the importance of desmosomes in clinical science," he admits. "She introduced me to the skin biology community. She got me interested in clinically relevant problems and active in societies, including the ASCB, where I could become connected to the broader community that's tackling similar problems."

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"Kathy characterized the structure of the desmosome in a way that really nailed it down," says John Stanley.

Kathy Green comes from the dry upland valleys of southern California, where her mother's family were farmers and citrus growers. Her mother's generation, though, also cultivated education. "On my mother's side, they were all basically teachers of one sort or another. So I was always drawn to academia," Green recalls. Her father was a self-made man, a teenage emigrant from Arkansas who built a successful sandblasting business in the San Bernardino valley town of Redlands. The company was so successful that it drew her mother out of the classroom to run the office—but education remained a priority. Green remembers, "I always liked science and liked observation, but I also enjoyed English and did well in things that required writing."

Biology won out at nearby Pomona College. A big influence was her Genetics and Developmental Biology professor, Larry Cohen. "He was the first person who showed me what it was like to be a scientist," Green recalls. "I remember him coming back from a Keystone meeting all excited. Here was this professor from a small liberal arts college, and he was telling us about the latest things he'd heard at the lectures and about interacting with colleagues at the meeting." It was her first glimpse of a global scientific culture, Green explains, which still delights her.

Everything a Biologist Could Want

Green picked Washington University in St. Louis for graduate school because of its innovative "umbrella" interdisciplinary program that allowed her to tailor her own curriculum in Cell and Developmental Biology. Her thesis advisor was David Kirk, an immunologist who had changed research directions to study cell morphogenesis through a new model organism, *Volvox carteri.* A multicellular relative of the more famous unicellular *Chlamydomonas, Volvox* had everything that a cell biologist could want—differentiated cell types, primitive light-sensing eye spots, and specialized intercellular bridges during embryogenesis. Moreover, *Volvox* finished cell division with a contortionist's trick: The cleaving daughter cells must turn themselves inside out to station their flagella outside the spheroid. This inversion process fascinated Green. "I guess you could say that my interest in the cytoskeleton and cell attachment derived from *Volvox.*"

To get up to speed on the cytoskeleton, Green took the summer Physiology course in 1981 at the Marine Biological Laboratory in Woods Hole, MA. There she met Northwestern's Bob Goldman, one of the pioneers of intermediate filaments and current ASCB President-Elect. Green hit it off immediately with Goldman and with his longtime research associate and wife, Anne Goldman. In 1982, Green moved to Chicago to join the Goldman lab as a postdoc.

But something equally important did not happen that first summer at Woods Hole. Thirty-four of the 36 students in the physiology course took a one-week workshop on gene sequencing taught by a hot-shot postdoc from MIT named Rex Chisholm. Green was one of the two who didn't. "I figured I could pick it up later," Green remembers. In any case, Green explains, that first summer both she and Chisholm were "otherwise involved." Several years later back in Woods Hole, Green and Chisholm were not; they married in 1984.

Sequence of Events

By then, Chisholm had moved to Chicago to take a faculty post at Northwestern's medical school and set up his lab just down the hall from Goldman's. In 1986, Green finally took Chisholm's sequencing course. Green stayed in her husband's lab long enough to learn sequencing and develop an intriguing cDNA library of bovine desmosomal genes. Switching then to human desmosomes, Green founded her own lab in Northwestern's Pathology department in 1987.

Today Green and Chisholm live in a downtown high-rise apartment on Chicago's "Gold Coast." Their existence is intensely urban—walking to work, shopping, and entertainment. "I liked St. Louis," Green recalls. "It's a great city, but Chicago is an order of magnitude greater." The couple are longtime supporters of Chicago's Steppenwolf Theatre Company and try to work their travel schedules around their season tickets.

They both travel far and often on science business, but Green contends that having collaborators and peers in distant places is one of the great benefits of the research life. Green and Chisholm are both extremely active in the ASCB. Chisholm chairs the Public Information Committee, and Green was just elected to a three-year term on the ASCB Council.

The couple indulges their nonurban, nonscience side once a year at the Green family summer house near Hebgen Lake in southwest Montana. Life at the summer house is "roughing it," notes Green, only in the sense that hot water is limited, TV reception is more so, and the Internet connection is dial-up—all of which suit Green and Chisholm immensely. Back in the city, they like to do gourmet cooking. "Rex really enjoys doing complicated recipes," Green explains. "He's into starting from the freshest ingredients. He doesn't do leftovers. Me, I like looking to see if I can put together something new from what's there. I like to be creative with the reagents in the refrigerator." ■

—John Fleischman