

Christine Seidman

Many scientists master either basic research or clinical practice, but a career combining the two is not for the faint-hearted. With her unique approach to research, Christine Seidman blazed a trail in cardiovascular science.

Outside a snowstorm was raging, but that was not going to stop Christine 'Krocket' Seidman. She had made the trip to Buffalo, New York, on that day in November 2000 in search of 20 members of a family afflicted with dilated cardiomyopathy, a condition that weakens the heart muscle and disrupts efficient blood flow.

Christmas gifts of poinsettias for the family members covered the back seat of the rental car, which Krocket drove through blinding snow. She went from house to house—six in all—in a 30-mile radius of the Buffalo suburbs. At each house, she and her assistant, nurse Barbara McDonough, drew blood, gathered records and explained the study. Ten hours later, they were finally finished. "Krocket was committed in finding the family members," says McDonough. "Nothing keeps her from getting results."

It's that combination of determination, dedication and pure heart that friends and colleagues say has helped Krocket become a preeminent cardiovascular geneticist.

"Krocket is an unusual person," says Dan Roden, professor of medicine and pharmacology at the Vanderbilt University School of Medicine. "You have to be a very good clinician with a good understanding of patients and the phenotypes you see, and [then] bring it to the bench and answer questions using basic science," Roden says. Many scientists can do one or the other well, he adds, but few can master both.

Krocket and her husband, molecular biologist Jon Seidman, are credited with discovering many of the genetic causes of cardiac disorders. In 1986, they first identified several families with inherited hypertrophic cardiomyopathy, a disorder in which the heart muscle thickens and significantly increases heart mass. Using linkage analysis, they found that mutated genes encoding sarcomere proteins in heart muscle cause the disorder. The findings were published in the early 1990s.

"At the time it was a real first, a big first," says Peter Libby, chief of cardiovascular medicine at Brigham and Women's Hospital. "It was one of the first molecular defects that was uncovered in cardiovascular disease."

In the 1980s, scientists thought that metabolic defects caused hypertrophic cardiomyopathy. But the beauty of molecular genetics is that scientists do not need to fashion a hypothesis, Krocket says. "You use genetic tools to define what are the possible disease genes," she says. When their mapping studies led the Seidmans to a region that contained specific cardiac proteins, she says, they knew they had hit the bull's-eye.

As a young girl in Long Island, New York, Krocket says she always dreamed of being a doctor. She met Jon in an introductory biology class at Harvard and married him two years later. The couple moved to Madison, Wisconsin, where Jon was doing doctoral work in molecular biology at the university there. Krocket, meanwhile, received a medical degree from George Washington University and completed a residency at the Johns Hopkins Hospital, where she cultivated a life-long love of research.

After a year at the US National Institutes of Health, she went to Massachusetts General Hospital to complete a fellowship in cardiology. By that time, she says, she was frustrated that treating patients for heart failure only led them back to her with worsening symptoms. In her

naiveté, she says, "I thought if we just knew the real problem with the heart muscle and fixed it, maybe life would be better for everybody."

Shortly thereafter, she joined Jon's lab at Harvard Medical School and, in 1984, became one of the first scientists to clone an atrial natriuretic factor. "Jon and I started working together with that and never stopped," she says. The duo's most recent success is the discovery of a mutation in a transmembrane protein known as phospholamban that inhibits the reuptake of calcium ions during heart muscle contraction and causes chronic stimulation of the heart.

"Our collaboration is a prototype for fellows and students in the lab to learn that you have to work together," Krocket says. "You have to get away from who did it first and who did what and realize the fun of it is to bring different elements to the same complex problem and make a more important discovery because of it."

Krocket says her husband is the "brilliance" behind their association, and that the two bring different perspectives to the table: as a physician, she looks at interactions between organs, whereas he homes in on the cellular interactions. Jon says Krocket is better at the details than he is, and is "a very good communicator and a people person."

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Watching the Seidmans work together is almost like theater, says Libby. "You are able to be a spectator to how their brilliant minds work and you are also entertained by their affectionate but no-holds-barred sparring," Libby says. "It is a great deal of fun."

The Seidmans' partnership inevitably extends beyond work, but Krocket says that's an added perk. "It is fun to be able to have a good idea over the weekend and talk to your closest scientific collaborator right then and there before you forget it," she says. The only downside, she adds with a laugh, is that their three children did not always enjoy the scientific talks at the dinner table.

Family, Krocket says, is as dear to her heart as is science. Nights and weekends are spent at home with her children, now 22, 17 and 11. She likes to cheer on her children at hockey and swim-team events and take moonlight strolls with her 11-year-old son. "No matter how much that experiment didn't work and the grant didn't get funded and the paper got rejected," she says, "you go home and nothing matters when you get that welcome."

Krocket's dedication to family extends beyond her own to those she studies in her research. "Unlike for a lot of bench researchers, there is often a human face associated with the work I do," she says.

Krocket is committed to the families she is working with, says McDonough, who has often witnessed Krocket's dedication firsthand. "She always feels it is worth going the extra mile for them."

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