Kathy Griendling: A Modest Molecular Biologist

Ruth Williams

The production of reactive oxygen species by NADPH oxidase was an activity thought to be exclusive to phagocytes of the immune system. While working on angiotensin II signaling in vascular smooth muscle cells,[1,2] however, Kathy Griendling discovered that these cells had NADPH oxidase activity, too.[3,4] A few years later, with the help of collaborators, the identity of this smooth muscle cell enzyme—a homolog of phagocyte NADPH Oxidase called Nox1—was discovered.[5]

Since then, a whole family of Nox enzymes have been identified and investigated for their roles in vascular pathologies, such as hypertension, atherosclerosis, and restenosis. In what is now an enormous field of research, Griendling's work remains preeminent.[6]

Despite her scientific breakthroughs and being an unquestionable leader in her field, Griendling is uncomfortable in the spotlight. She describes herself as introverted and confides to *Circulation Research* that the thought of being interviewed and profiled is "very embarrassing." Reluctantly coaxed from her office, she spoke to us about her scientific career and work ethos, and also about her recently discovered, and rather unexpected, passion.

Where Did You Grow Up?

In Pennsylvania, in a small town named Yardley, about an hour north of Philadelphia. It was a suburb, but it's in Buck's county—world-renowned for its beauty—so, I was very much into outdoor pursuits. I had lots of animals, including two horses, and spent a lot of time on the farm where they were kept.

When Did Your Interest in Science and Medicine Begin?

I really liked science in school. There was never one subject that I was clearly better at than others, but I thought science was very interesting, so when I went to college, I decided to do a double major in biology and math.

Where Did You Study?

I went to Penn State University. The reason I went there was because that was what I could afford. I had applied to MIT and was offered a place. But, at the time, my father had lost his job, and MIT is a private school, out of state, with very high tuition, so it was no longer an option.

Figure. Kathy Griendling, with family, in front of the Arenal volcano in Costa Rica.

With Your Double Major, Did You Ever Consider a Mathematics Career?

No. It's too dry. In my junior year of college, I took a course in physiology, and I just loved it. I thought it was the best subject for understanding how things worked, to understand the links between bodily systems; for example, why your blood pressure goes up when you become stressed.

So, You Were Spurred to Do a Physiology PhD?

Yes, I had started applying to some graduate schools, and then my advisor encouraged me to shoot higher. So, I applied to Johns Hopkins and went down there for an interview. They offered me a slot, and I agreed. I really didn't think about that decision as much as I should have, or would do now.

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Probably, if I'd known then what I know now, I might have chosen another school, because there was only one person in the physiology department at Hopkins, Bill Milnor, who did cardiovascular work. He was a great mentor, but it wasn't a strength of the department at that time.

When I'm mentoring young scientists now, I tell them to really look at their options carefully.

Why Did You Focus on Cardiovascular Biology?

No particular reason. I just found it fascinating. Dr. Milnor was interested in hemodynamics, and I found that interesting because it was a cross between math and physiology. Unfortunately, a lot of the work he did was on dogs. I remember at one point being in his office in tears because we had to work on these animals. He said, "But think of all the children who will benefit from this," and I sobbed, "I don't care, what about this dog!"

What Did You Study?

Pressure/force relationships and the development of contraction in isolated blood vessels. Around the same time, Furchgott came out with his seminal finding that endothelium releases relaxing factors. I had been working on something very similar using acetylcholine to treat vessels. Some days, I would get a contraction and some days, relaxation. I had a really hard time figuring out why. It turned out that it depended on whether I dissected the vessel face up or down. If it was face down, the endothelium was rubbed off, and I saw exactly what Furchgott saw—contraction. If only I'd been a little smarter…

Where Did You Go for Your Postdoc?

Here, I gave a little more thought to what I should be doing. My first postdoc was at UPenn. I studied force/contractile relationships with Ellen Fuller in collaboration with Robert Cox. Then, for my second postdoc, I decided that I wanted to have more experience with cellular and molecular mechanisms.

Ellen was a friend of R. Wayne Alexander, a cardiologist who did research in molecular biology, at The Brigham and Women's Hospital in Boston, and she told me to call him. I was afraid to do that, but eventually I did. He said he didn't have any positions. I said, "OK, well thank you anyway," and he said, "Wait! Don't hang up!" We talked for a few more minutes, and I explained that I had an NRSA fellowship grant, and he told me they are moveable. So, that was that. I moved with my grant to Boston.

I began working on signaling in smooth muscle cells after angiotensin II stimulation, figuring out what signals were generated. That turned out to be something I really liked—it was like a puzzle.

There was also a more personal reason why I was happy to move all the way to Boston. I had started to correspond with a very good friend from my PhD days at Hopkins who had decided to study medicine at Harvard. He's now my husband. So, it was definitely a good move, professionally and personally.

You Stayed in Boston Just Two and a Half Years?

Yes. Wayne received an offer to move to Emory as Chief of Cardiology, and he took several of his fellows with him as faculty. I was one of those. I remember standing in his office and asking, so who are we joining at Emory? What are they working on down there? And he said, actually, we're creating a basic research program in the cardiology division.

So, we started from scratch, and it was my first faculty job. So, it was a bit of a struggle to begin with—writing grants and so on—but Wayne is great to work with, extremely creative, and we had a very productive relationship for many years.

Luckily, my husband was able to come to Emory, too. He short-tracked his residency at Harvard and joined us as the first Research/Clinical Fellow in Cardiology.

How Did Your Important Work on NADPH Oxidase Come About?

Wayne was interested in angiotensin II signaling, and we observed that there was a very large increase in the cell's level of a lipid called phosphatidic acid. We were trying to figure out why. In the literature, there were only two known roles for phosphatidic acid. One was in calcium flux and the other was in neutrophils where it activated NADPH oxidase. We started to look and, sure enough, found that there is NADPH oxidase activity in muscle cells that is increased by angiotensin II. Ultimately, the pathway had nothing to do with phosphatidic acid, so that was just a bit of serendipity.

Although we could detect NADPH activity in the muscle cells, we couldn't find the catalytic subunit. We tried and tried, and eventually, I went to talk to Dave Lambeth, an expert on neutrophils and NADPH oxidase, here at Emory. We used to meet often, and one day he came to my office and said, we have something you might be interested in. He had found a homolog of the neutrophil oxidase and wondered if this was what we were measuring. Sure enough our cells expressed it.

Was This Your Proudest Achievement?

Career-wise, yes, because it really—I don't know how to say this—it really opened up a whole field. I can't keep up with the literature on it these days, there is so much. But it certainly wasn't just me. There were other people who made major contributions, faculty and very talented fellows, not just here at Emory, but elsewhere.

Life-wise, my proudest achievement is my family. I have 5 children and a great husband who takes half of the responsibility. We are very flexible with each other's careers. The only tough time is when we both have a grant deadline.

My oldest daughter is finishing her PhD in aerospace engineering at Georgia Tech. My second child graduated from Emory with a degree in History and Classical Civilization, so his interests are nothing like his parent's. The third one is a mechanical engineering major at Georgia Tech, the fourth one just started at Berry College in Northwest Georgia, and wants to become a vet, and the last one is 16 and still at home. She's a junior and interested in medicine but is not too happy that she's the only one left at home. I also have a new grandson by my oldest daughter and her husband.

Do You Have Any Advice for Young Women Scientists Who Want Families?

Probably the message that young women scientists need to hear is that it is absolutely possible to have a career and a family. You just have to keep your priorities straight. My career probably didn't advance as fast as some of my colleagues because I sometimes chose family over work, and I think you have to be aware that you may be confronted with that choice. But, it is absolutely worth the sacrifice, if you even want to call it a sacrifice, to have the joys of a family and not just a career. In the end, a family makes a much bigger difference in the world.

Any Other General Advice for Young Scientists?

I tell my fellows, you will get out of your fellowship what you put in, so if you want to succeed, you have to work hard. I do expect people to work hard. I work hard myself. Science is not an easy career. You have to be self-motivated.

Also, I think mentorship is extremely important in your career, and if you make good connections with a mentor early on, it can dramatically influence how your career progresses. A lot of science is serendipity, so you can't always predict who is going to make a discovery, but you can be prepared for it when it happens by working hard and finding a good mentor, listening to advice, and being proactive about your career.

My other job here is Vice Chair for Faculty Development, so you've got me on a subject I'm very passionate about.

How Did You Get That Role?

I never thought I would enjoy such a role. I thought I was too shy, and I just wanted to sit in the lab and not talk to anybody. But, I was asked to serve on a faculty development committee and, after two years, was asked to take over as Chair. I started to think about what we could do with faculty development, and I got rather excited. I convened the committee, and we wound up meeting every month and coming up with a whole host of programs. We have a fully fledged mentoring program, a career development day once a year, we do CV review sessions, and provide grant review advice. We've created an awards program to recognize all the different types of roles within the department. Before that, we had only had teaching awards, but now, we have research awards, mentoring awards, and clinical service awards.

I am a very introverted person, so getting out there and being friendly and speaking to strangers is very hard, but it has been very rewarding. I found that I really liked spending time with people and trying to help them through obstacles in their career. In 30 minutes, I can make a difference in somebody's career and get him or her on the right track.

Have You Had Any Obstacles in Your Own Career?

Every time I had a child, it was hard to come back. There is such a strong pull to want to stay with them. Besides that though, I really haven't had many difficulties: I have been very lucky. I'm sure there were some setbacks with research, but I have blocked them out.

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