Elizabeth Murphy

Perseverance Pays Off

Jaclyn Jansen

For even the most accomplished researcher, the path to discovery is more often marked with failure than success. Rather than be deterred, Elizabeth Murphy, Senior Investigator at the National Institutes of Health Heart, Lung, and Blood Institute, sees each challenge as an opportunity to uncover new and unexpected insights into human biology. It is this sense of perseverance and optimism that has made her a successful scientist and a leader in cardiac research.

Murphy (who is better known as Tish among her peers) has dedicated her research to understanding the molecular changes that occur during and after a heart attack. Her early work focused on the ion changes that lead to cell death during ischemia and reperfusion. She found that an increase in sodium leads to a subsequent increase in intracellular calcium,[1–3] which triggers cell death pathways in the mitochondria.[4] Her work has helped to define many of the basic pathways that are responsible for cardiac cell death.

Recently, Murphy turned her attention to the mechanisms that protect cells from ischemia and reperfusion. Her lab focused on the effects of preconditioning: brief intermittent periods of ischemia and reperfusion that protect the heart from subsequent, more sustained attacks. Murphy and her colleagues identified several post-translational modifications and signaling pathways are activated during preconditioning.[5–7]

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Even with this success, her work took an unexpected turn. At the time, Murphy was like most researchers, using male mice exclusively to study ischemia reperfusion. For one set of experiments, a collaborator offered her female mice as well. When Heather Cross, a postdoctoral researcher in Murphy's lab, compared the males and females, she was surprised to find that males were much more sensitive to ischemia–reperfusion injury than female mice.[8]

Murphy and Cross were quick to follow-up on the unexpected result. They discovered distinct differences in how males and females respond to a heart attack. Now, the lab is working to define the role of estrogen and other estrogen-dependent signaling pathways in cardiac cell death.[9–12] Murphy's goal is to understand how these and other pathways protect the heart, in the hopes of identifying new ways to treat and prevent heart attacks.

In a recent conversation with *Circulation Research*, Murphy described how she has navigated her successful research career. She has been driven by a deep love of science and discovery—and perhaps even more importantly a relentless perseverance—that has allowed her to find unexpected opportunities along the way.

Where Did You Grow Up?

I grew up in a small town up in the mountains of Pennsylvania. My mother was a school teacher and my father ran a store selling beer. I'm the second of four children. When my older brother was born, my mother stopped teaching, and she didn't start again until he went to college. Most of the time that I was growing up she was home with us.

Being So Isolated, Did You Know Many Scientists?

There were no scientists in my family, and none in the town. A general practitioner was about the closest person to a scientist that I encountered. We were really in the middle of nowhere.

How Did You Become Interested in Science, Then?

Even though there were no role models for me in town, I was still very interested in science. Kids are naturally curious and science feeds into that. I was always looking for books in the library about experiments. I had also a basic chemistry set. When I got to high school, I was able to take science and biology classes. I realized that this was an interesting topic, and something I definitely wanted to pursue.

With No Role Models, How Did You Know How to Pursue a Career in Science?

When it came time to go to college, my mother encouraged me a lot. I think she was a typical 1950s mother who had enjoyed her

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career but spent much of her time at home with us. She encouraged me to apply to the University of Pennsylvania, so I did, and I was lucky enough to get in.

Was It a Culture Shock to Go to a Big City and Big University From Your Small Town?

Growing up, I didn't know anybody that had a PhD. Most people went to school fairly locally, even though we were only 100 miles from Philadelphia. People didn't venture to the big city very often.

When I got to Penn, it was completely different. For the first time, I was surrounded by lots of people who did know a lot about science. It was a culture shock going there, but it opened up lots of doors and opportunities. As an undergrad, you could work in a real science lab. It was my first true exposure to science, and it worked out very well.

Did You Always Know You Wanted to Do Research?

I knew I liked science, but I wasn't 100% sure what route to take. At the time, most of my classmates were interested in going to medical school. I went to see the Pre-Med advisor, and she suggested I try working in a lab. I didn't know how to find one. She picked up the phone and called her husband, Howard Rassmussen, who happened to be in a biochemistry lab, studying vitamin D metabolism and calcium signaling.

I spent two years and a summer in that lab. It was a wonderful experience, and I haven't left the lab since. I loved it so much that I decided to apply to graduate school. I ended up staying at Penn to get my PhD.

Where Did You Do Your Postdoctoral Work?

I met my husband during graduate school at the University of Pennsylvania in John Williamson's lab. He was an MD/PhD student in the lab with me. When it came time to move on to our next positions, we both found work positions at Duke. I did my postdoctoral work there with Mel Lieberman, a wonderful mentor, and my husband did his residency.

Was It Hard Dating Someone in the Same Lab?

Not at all! It was easy to meet, being in the same lab. We were on separate projects, and neither of us were supervisors, so there was no conflict of interest. Most of our lab mates were very encouraging of the relationship!

How Was Your Postdoc?

It was a wonderful experience. In graduate school, you are still learning—it can be a difficult time. You aren't really sure what you got yourself into! But then the postdoc is excellent. I had lots of independence and freedom to explore new areas.

I was also lucky to have a very supportive and encouraging mentor. Toward the end of my training, he recommended that I write an NIH grant, called the First Award at the time. It was funded, so I began to look for a job. My husband had moved on to faculty at Duke so I limited my search to something in the geographic area.

There is a branch of the National Institutes of Health in Research Triangle Park, North Carolina. They were just setting up a physiological NMR (nuclear magnetic resonance) lab run by the physicist Bob London. I had never done NMR, but I thought that it sounded interesting. Even though I couldn't take my grant along with me, I decided to join them anyway.

It was an exciting time. The lab was new with state-of-the-art equipment, and I had the opportunity to learn to use all it. I eventually got tenure there and moved into my own lab. Altogether, I was there for 20 years, and it was a wonderful experience.

Why Did You Move On?

About 10 years ago, my husband was recruited to Johns Hopkins. I contacted people at the Heart, Lung and Blood Institute at the NIH about a position. This was a good fit for me since I worked in heart research. There were many opportunities in Bethesda for collaboration with other researchers who were studying ischemia. So my husband and I made the move, and it's been very good. It's been a wonderful career.

Was It Difficult to Deal With the So-Called Two Body Problem, Limiting Your Job Search?

When I tell this story it sounds like I followed my husband around, but they were all good opportunities. If you look, you are likely to find good opportunities wherever you are—you only need to take advantage of them. For example, when I went to NIEHS (National Institute of Environmental Health Sciences), I knew nothing about NMR, but it turned out to be a wonderful experience. When you find an opportunity, you need to seize it and make it work for you.

So for us, the two body problem worked out. It wasn't much of a struggle. Maybe I would have advanced a little faster if I had looked across the country for a job. But ultimately there were plenty of opportunities in the area. If not, I'm sure my husband would have compromised. You have to find what works for both of you.

That's Good Advice. What Other Advice Do You Have for Young Investigators?

To be successful in science, you need to have good mentors. I had wonderful, supportive mentors throughout my career.

Particularly when you are first starting out, you really need to focus. It is important not to be spread too thin. Also, don't fall into the trap of thinking that you need to hit a homerun. Research is a process. You want to understand new mechanisms rather than trying to solve all the world's problems in one experiment. Focus and you will be successful.

I've also heard young investigators voice concerns about funding levels and worry about whether this is a good career. I would tell them that if you love what you do, you can make it work. Research is challenging, but I can't think of a more rewarding career. I enjoy the discovery and the surprises of research. You think you understand everything, but then a new discovery sets everything upside down. It is exciting and constantly new. I've never been bored, or felt like it was routine. I'm energized because there is always something new.

Perhaps my best advice is perseverance. If you love what you do, stay with it and don't be discouraged. You will succeed.

What Have Been Some of Your Biggest Challenges?

I like to think of challenges as a double-edged sword: your strengths are your weaknesses. The two body problem has given me some geographic limitations, but that has made me focus on looking for opportunities where I am. I've been able to make the best of where I am.

Have You Felt Any Challenges as a Woman in Science?

No, I haven't had any serious issues as a woman. I've had a number of supportive mentors, many of whom have been men. Even still, there aren't a whole lot of female role models in science, despite recent gains for women.

I'm part a group at the NIH group called Women Scientist Advisors. We are trying to understand why there are so few

women in leadership positions in science. We know that 50% of postdocs are female, but women only represent 30% of applicants for tenure track positions. Women just aren't applying, and we want to know why.

This is a subtle issue. None of the men that I work with are sexist or discriminating. For some women, it is life and family balance, and for others it might be a confidence issue. I think it is at least in part the lack of role models. There is a perception that the work-life balance isn't compatible. But I think research is more flexible than many other positions. You get to choose the days you do experiments, and you can analyze data at home.

How Do You Find Your Work-Life Balance?

I enjoy what I do. I find my research to be as interesting as almost any hobby. I do work long hours, but it doesn't seem like work. This is fun and exciting for me.

Research is like a mystery that needs to be solved. I become fixated on understanding my data. It is hard to know how many hours a week I work, but I enjoy what I do, so it doesn't seem like a job.

Of course, you do need down time, and it is important to get away and clear your mind. I like to run to unwind. And I also like to read for a break from work. Sometimes, the work can wait.

What Are Some of the Most Important Qualities to Be a Successful Scientist?

The most important thing is that you have to really enjoy doing research. I don't think it's for everybody. You have to have thick skin because a lot of your experiments don't work. And you have to be willing to deal with failure. I think only a quarter of experiments work well. That doesn't seem like great odds, but if you were a baseball player that would be a wonderful average!

You have to be really excited when things do work. You have to love the excitement of discovering something new. If you do, then there isn't a better way to spend a life. Enjoy what you do, be persistent, and don't get discouraged easily. Realize that failures can be an opportunity.

The NIH Isn't Like Most Other Research Institutions. How Does It Compare in Your Experience?

We don't write extramural grants, but we do get reviewed every four years. We write a report that is similar in many ways to a grant that someone at a university might write. The institute then brings in an external panel to do a sort of site visit. In some ways, it is fairer than the grant process since you get to meet the reviewers, and answer their questions directly. The process is different, but it still holds you accountable for your work.

Some people think that we are insulated from NIH budget cuts. In reality, our budget is cut the same percentage that external funds are cut. There is no place to hide!

We also benefit from a tremendous investment in core facilities. If you want to move into a new area, like proteomics or sequencing, the cores can teach you and your postdocs how to get into that area. It is an excellent resource that helps us move in new research directions when needed.

Scientists Wear Many Hats Today. What Are Some Other Roles You Play Outside the Lab?

As I said before, I'm part of the Women Scientist Advisors group at the NIH. Each institute has an advisor and we meet together to try to understand what the barriers are for women and why there aren't more women scientists, especially in leadership positions. That's been very fulfilling.

I'm also President of the International Society for Heart Research, which organizes meetings and provides mentorship opportunities for young people. It is fun and fulfilling to get people involved in the broader scientific community.

I'm also an editor/associate editor with a few different journals. It's incredibly rewarding—you interact with people throughout the world and read papers you might not normally see. I'm lucky to see science more broadly through these roles.

Disclosures

None.

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