Elizabeth McNally: Taking on Inherited Cardiovascular Disorders

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Elizabeth McNally’s love of the research laboratory first bloomed as an undergraduate. While working a summer job in the genetics laboratory of Leslie Leinwand at the Albert Einstein College of Medicine, McNally worked on the quest to find genes that cause muscle disease. The impact was so profound that it has shaped the focus of her career ever since. If one looks at the home page of the McNally laboratory based at the University of Chicago, it says simply, “We study the genetics of heart and muscle disease.”

Now a board-certified cardiologist, McNally is an expert in the genetics of rare, inherited cardiovascular disorders and muscle diseases like muscular dystrophy.

Q. What do you find most compelling about your biomedical research work in these inherited disorders?

EM: It probably comes down to those 5 really great days I have enjoyed in research over the last 25 years! I describe these as the exquisite moments when I looked at something and instantly knew it to be true. I had an idea, reviewed experimental test results of that idea, and knew immediately that the idea was correct. These moments are so good that they sustain me and keep me going. In fact, I’m just about ready for another one.

All joking aside, this means that I’m obviously a believer in perseverance, persistence, and hard work. I think most scientists are. We are remarkably good at failure. In fact, we don’t know what failure means. That is the nature of experimentation. You have an idea, do an experiment that doesn’t come out quite the way you thought, and you adjust. You take steps backwards on the way to taking steps forward, but it is still the process of moving forward.

It helps that I am an information junkie. It is really exciting to me to find something new, a totally new piece of knowledge that people didn’t know before. But you need thick skin and conviction of your ideas.

Recalls McNally of her introduction to laboratory research, “In Dr Leinwand’s laboratory, we had cloned some of the very first and most important genes for the function of skeletal muscle, and so we decided to search for the genes from patients with muscle disease to see if we could find any changes in them.” Although the tools to perform this type of research in earnest were still a few decades away, she was struck by how intriguing it would be to diagnose people with disease on the basis of their genes. She adds, “Even though that was decades ago, that is still what I do, only now we can get the genetic answers.”

Q. How did your mentoring relationship with Dr Leinwand influence your research career?

EM: I was drawn to work with her because she was doing what I liked: genetics. When I started as a summer student with her, she was one of the few people doing what was then the most cutting-edge molecular biology. This was when molecular biology and human genetics was in its infancy. I was attracted to the fact it was the latest, greatest cool science. Working with her was so fruitful because of all the opportunities available, and I wanted to work on them all.

Today, Elizabeth McNally, MD, PhD, is a Professor of Medicine and Human Genetics at the University of Chicago. As a physician-scientist who earned her academic credentials in a combined MD/PhD program at the Albert Einstein College of Medicine, McNally has her feet planted firmly in 2 worlds: cardiovascular genetic research and patient care. She is both Director of the Institute for Cardiovascular Research, a clinician who takes care of patients, and Director of the Cardiovascular Genetics Clinic, a clinic she founded to diagnose and treat people at risk for or with rare inherited forms of cardiovascular disease. Her accomplishments in both fields earned her the elected presidency of the American Society for Clinical Investigation (ASCI).

Q. What do you see as the most important qualities to be a successful physician-scientist?

EM: They are fundamentally different trainings. To be a scientist, you are really trained to pick a problem and drill...
down to a very, very detailed analysis of that problem. As a physician, you are often thinking about a big picture. A patient has many things going on. You have to think about how all of it integrates into the physiology and function of that individual person. Learning to know at what level to approach different problems is probably the biggest challenge. It means figuring out what magnification to use on a problem.

As soon as she became exposed to research as an undergraduate, McNally knew she wanted to include research in her career. Says McNally, “I remain a firm believer in the value of hands-on research in the undergraduate experience—to offer students the opportunity to get the bug for research before they go to medical school, because they tend to want to stay with it.” For that reason, McNally’s Chicago laboratory hosts several undergraduates at any given time.

Q. How do you think your colleagues would describe you?
EM: They would think I work hard. I do work very hard and spend a lot of hours, but I think they feel like what we’re doing as a laboratory is important, so I think they feel motivated by that.

In the course of her PhD work, also with Dr Leinwand, McNally determined the first complete sequences for the cardiac myosin genes.1 As a postdoctoral fellow at Children’s Hospital in Boston and Harvard Medical School, she worked with Louis Kunkel to define additional genetic defects in muscular dystrophy and cardiomyopathy.2–5 “People come to us because they know a disorder runs in their family. Sometimes we see people because somebody died in their family, and they want to know what their risk is,” she says. “Now, more often than not, we can diagnose these genetic cardiovascular disorders.”

McNally and her colleagues are also interested in determining the mechanisms by which genetics determine patient outcomes. In a typical family with an inherited heart or muscle disease, they will all have the same mutation; however, some family members have mild disease, others more severe. She is interested in learning what genetic modifiers lead to differential genetic expression and therefore patient outcome. She explains, “The team has found an interesting genetic modifier that regulates TGF-β, a key regulator of growth and development, and is on the path to finding more.”6,7 “In humans, her laboratory is now starting to do this by sequencing large panels of cardiovascular disease—causing genes in people.

“Used to be that we were in a genetic universe but did not know where the edges were in terms of understanding the genetics of inherited cardiovascular disorders,” she explains. “Now I feel like we know where the edges of the universe are. We just do not know, yet, all the stars within.”

McNally’s roles in advocating for progress in basic cardiovascular research extend beyond her work in Chicago. For the past 6 years, she has been an associate and consulting editor for Circulation Research, serving her colleagues in the areas of genetics and heart development. As a mentor of young scientists, particularly women and minorities who have not traditionally pursued careers in cardiovascular basic research, she views her laboratory as fertile ground where “young and energetic people” can excel. But she concedes that attracting students into basic research requires constant tending. “You must go out of your way to pull these brilliant young minds into the laboratory, to expose them to research and let them see your enthusiasm and excitement. If you have it, odds are they will too.”

Q. What advice do you have specifically for women interested in a career in cardiovascular research science?
EM: I think cardiovascular research science—and I speak also on cardiovascular medicine, because I do both—is still very much a male-dominated world compared to other disciplines in science. Genetics has more women in it; cell biology, too. Occasionally, you are going to bump up against glass ceilings, but ignore them. Move forward with your work. Just do a good job at what you do, and it tends to work out.

Dr McNally is hoping her enthusiasm as ASCI president will lead to advancing the cause of basic cardiovascular research in the political circles in Washington, DC. “We have to make our case very strongly to people in Washington to understand the importance of basic research to technology development in this country,” she says. “Most of the biomedical progress that has happened in the private sector—imaging, pharmaceuticals—all of that had its origins years ago in biomedically funded research from the National Institutes of Health. I think many people in Washington on both sides of the aisle know that investing in science is the most critical thing we do.”

Q. What motivates you during all those long days?
EM: The patients do. Any day you feel like you’re having a bad day, all I need to do is be with one of these patients, especially a young person who was born with one of these genetic diseases through no fault of their own, and this is the state they are in. It is incredibly motivational to want to come up with something to help.

For this reason, advocating for research funding has been the largest part of Dr McNally’s role as ASCI president. “I continue to do all I can—in the laboratory, with patients, in my role as ASCI president, as a private citizen—to advance basic research in cardiovascular disease,” she says. “Every day, I see firsthand the difference it makes in people’s lives.”

References
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