Editor's Note

Circulation Research Introduces Profiles in Cardiovascular Science

Roberto Bolli and the Editors

In keeping with our efforts to add a human/personal dimension to the content of the journal, we are pleased to announce a new feature titled "Profiles in Cardiovascular Science." Presented in an interview format, these articles will focus on the life, personality, and achievements of some of the most successful and influential cardiovascular scientists of our time—individuals who are veritable icons in cardiovascular science and serve as superb role models for young investigators. Unlike scientific manuscripts, these articles will be personal and reflective, featuring a blend of scientific, autobiographic, and intuitive content. Leading scientists will talk about their personal, as well as scientific lives, describing the circumstances, insights, and emotions surrounding their seminal discoveries. This new feature will allow them to reflect on the decisions, events, and personal attributes that contributed to their success.

The purpose of Profiles in Cardiovascular Science is to offer a new perspective on the process of scientific discovery and career development, one that is rarely found in scientific journals. These interviews will provide the readers with an intimate look at the lives of prominent investigators: how they embarked on their scientific journeys, how they made their major discoveries, the habits and beliefs that facilitated or hindered their work, and their motivations and personal challenges. Importantly (from the editors' point of view), we will encourage them to offer advice to our young investigators who are beginning their research careers. We hope that through these interviews, the readers will appreciate how scientific breakthroughs actually happen and the personal qualities and behaviors that most contributed to these exceptional careers. This feature will be available in both print and electronic versions.

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Jeffrey Robbins
Does Not Do Discouragement

Ruth Williams

Jeff Robbins' climb through the ranks as a top scientist has been rather unique in that he has accumulated only friends, rather than enemies, and in fact, he is universally praised for his integrity, benevolence, mentorship, and generosity of spirit. But another word always comes to mind when discussing Jeff: pixie. The dictionary definition is "playfully impish or mischievous; prankish" and anyone who has spent any significant amount of time around Jeff, or been given for a ride in his 1997 Ferrari 550 Maranello, would understand the reference. This personal characteristic carries over to his science and the almost magical ways he makes mischief in the heart by transgenesis. Always unpredictable but consistently rigorous, Jeff either gets credit or blame for helping to shape our field and its attitudes. However, his childlike wonder and enthusiasm at the way things work always shines through.

—Mark Sussman & Jeff Molkentin

For the past 20 years, Jeffrey Robbins has been picking apart the protein mechanics of the heart. To get at these cardiac nuts and bolts, Robbins, who is Professor of Pediatrics, Chair of Molecular Cardiovascular Biology, and Executive Co-Director of the Heart Institute at Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, established gene-targeting techniques in the mouse and other organisms.[1–3] His transgenic tools have unraveled the functions and failings of cardiac proteins, such as myosin, desmin, troponin, and more, and have provided insights into diseases, such as cardiomyopathies, hypertrophy, and heart failure.[4–8]

Robbins has been dedicated to science and experimentation since childhood, but did not enter the field of cardiovascular biology until he was turning 40. This is perhaps due to the fact that he took an unfamiliar research route to the heart—one that included studies of paramecium, homing pigeon behavior, spinach photosynthesis, mycoplasma membrane ultrastructure, goat globins, and chicken skeletal muscle.

Robbins discussed this winding scientific path in a recent interview with *Circulation Research*, explaining how variety keeps him on his toes and keeps him happy. Another key to Robbins's scientific happiness is his robust resistance to discouragement. Nothing, it seems, has ever swayed him from his chosen career, not failed exams, a burned down bathroom, nor even an arrest.

The opinions expressed in this Profile in Cardiovascular Science are not necessarily those of the editors or of the American Heart Association. E-mail ruth.williams@absw.org.uk

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Testing the Limits

Where Did You Grow Up?
In a suburb outside New York City, Westchester county, in a little town on Long Island Sound called Mamaroneck. I lived in apartments my entire life. My parents were certainly not wealthy. For a long time they struggled financially. I had two brothers, one older, one younger, and we all shared one bedroom.

Not a Luxurious Upbringing Then, But a Happy One?
I would say so. I'm a firm believer that you can make yourself happy or unhappy, no matter where you are. I was always pretty happy.

Where Did the Interest in Science Come From?
I always liked taking things apart, and I always liked asking questions. I drove my parents crazy. They bought us the Encyclopedia Britannica, which was a really big deal, and I

just started reading it. I came across this article that said air weighed something.

So, one day I convinced my mother I was sick, but really I had come up with this experiment. My father had this hair tonic, which was flammable. The idea was I would go into the bathroom, seal it off, weigh the hair tonic, and weigh three rolls of toilet paper. I did this and then soaked the toilet paper in the hair tonic and set it on fire. I wanted to collect all the ash to see whether or not I could measure the combustion, but it all floated up to the ceiling and went everywhere. It wasn't pretty. That day, I learned that there are two parts to an experiment. One is conceptualizing and the other is execution—the execution was a little flawed. I got pretty beaten up that night.

What Was Your Parents' Retribution?

I used to build model planes, so they took all my models away. I also had to pay for the repainting of the bathroom with my paper route money, and I was never allowed to stay home sick from school again, unless someone was with me.

It Didn't Put You Off Science Though?

No, it didn't. In fact, while I was at high school, I managed to get myself into a lab at Albert Einstein College of Medicine to work as a volunteer—lots of the universities in New York offered these Advanced Placement courses.

What Were You Studying?

I was trying to grow paramecium. Actually, that was another debacle. They were using these centrifuges in the lab, and so I came up with the idea that a washing machine might make a good centrifuge. I tried purifying three gallons of paramecium culture in our washing machine—that didn't work out.

Your Poor Parents

Yeah, they were pretty tolerant, I guess. Boy, that machine really stunk after the experiment. I put in place this mesh that supposedly would catch the paramecium, and I duct-taped it to the bottom of the washer so that it wouldn't crumple up. I thought I would be able to scrape the paramecium off of the mesh. Unfortunately, the mesh crumpled anyway, so the paramecium got into the waste water and the washer overflowed and flooded the apartment below us.

Pushing the Limits

Where Did You Go to College?

I started out at Stony Brook. That was a state university. My parents couldn't afford to send me to a private institution. My girlfriend went to Boston University, and, you know, kids that age really think below the belt. So, I managed to get myself into a lab as a volunteer with this guy who studied the homing mechanisms of pigeons. He was a pilot and had access to a private plane, and he would fly up to Boston every weekend to release his pigeons. He was looking for a lab volunteer to fly up to Boston with him to help. So, I got free rides back and forth to Boston.

For the second year, I transferred to the University of Rochester, and my girlfriend (wife to be) also transferred there. I was able to get into a lab there as a volunteer, too. I was studying the photosynthetic complex p700 in spinach. That led to my arrest.

Huh?

I was in the middle of an experiment during Thanksgiving, and they closed the dorms. I really had to finish this experiment, and I was living hand-to-mouth, so I decided to stay in the dorms anyway. I would go around taping open the locks. Security knew that there was someone in there, but they couldn't catch me. I was always one step ahead. But then, I was taking a shower and the door to my dorm room blew shut. There I was in a towel with no clothes and I couldn't get back into my room. I had to call security and say, "busted." They wanted to make an example of me, so they arrested me and kicked me off of campus.

Did You Manage to Finish the Experiment?

I did. I had isolated the p700. It was in the freezer. So, I was able to deal with it after Thanksgiving. I worked in that lab for 2 years. Then, as a junior, I went over to the medical school and worked in a lab studying mycoplasma membranes. I thought that was really cool. Back then, they had just come up with the Singer membrane model. It was great stuff. Plus, we could use the electron microscope!

I got my first federal grant in that lab and have had federal funding ever since—over 40 years.

That Was Quite a Mix of Projects—Paramecium, Pigeons, Spinach, and Mycoplasma. How Did You End Up in Cardiology?

That's a good question. I didn't get into cardiology for a good while after that. I took a postdoc position with Jerry Lingrel in Cincinnati, and my project was to isolate the globin genes. About two thirds of the way through, I heard about this new technology that Tom Maniatis had developed out at Caltech and I just called him and asked if I could come to his lab for a couple of weeks and learn. He said, yeah, sure. Three months after getting back, I had the globin genes and a job offer from the University of Missouri College of Medicine.

I moved to Missouri. I was very happy, having a great time. I rose through the ranks, got tenure, became an associate professor, and then left. I was recruited back to Cincinnati. Everyone thought I was crazy because I was going back to an untenured position.

What Prompted That?

I was worried about getting too fat and happy. I'm very uncomfortable being comfortable. There I was, tenured at a state university—a job for life—and I looked at my older colleagues and it wasn't clear to me that they had kept their edge, or enough intensity. Maybe they weren't scared enough. I wanted to be scared again. So, I went back to Cincinnati, and it was about 4 or 5 years later that I decided to go into cardiovascular research.

How Did That Come About?

I was studying chick muscle myosin, but I was looking around, thinking I don't want to just isolate genes my entire life. I want to ask what's going on at the protein level, what

is the cause and effect, what are the structure function relationships, and how do you ask those questions in the whole body? I needed to do genetics.

I was sitting with a good friend and he said, well if you're going to do genetics and you want something mammalian, do mice. At the time, there was this new business of gene targeting and transgenics. I said, what about the heart? He said, that sounds good. We went to a text book and looked it up and found that the mouse heart has four chambers, just like humans—that was in 1990.

That's how I got into cardiology.

Never Settling

What Happened Next?

Richard Jackson, who had recruited me to Cincinnati University, left and joined a major drug company. He offered me a very lucrative position at the company, and I was thinking seriously about taking it. The university had also offered me various positions, but I didn't really see it as a place where I wanted to build a career. At that point, Children's Hospital offered me something very different. They said, come and build whatever you want—we don't know what we want you to build, but we trust you.

Fantastic!

I could start from scratch. And they gave me money to recruit. I was fortunate in my choice of recruits, and over the years, we've built a very small but very focused division—the molecular cardiovascular biology division—that has national and international stature. My faculty is great.

What Has Been the Highlight of Your Career?

I think the success of my faculty. They are all leaders in their fields. That's pretty cool. I've reproduced myself biologically with my kids, and now I've reproduced myself scientifically with my faculty.

And What Was Your Lowest Point?

When I failed my graduate qualifiers. Normally, qualifiers are taken at the end of the second year. But I was on the fast track, and they let me take it at the end of my first year. I found out later—after I got my PhD—why I'd failed them. They had decided that they were going to use the exam to take me down a peg. They said, you didn't really fail them, we just thought that you needed to be slowed down a little bit. That was painful!

Did It Work?

Oh yes, I'm very modest and retiring.

What About Scientific Low Points? Any?

When an experiment doesn't work, it is not a low point. It is telling you something. Negative information is still information. It is either telling you that you did the experiment wrong, you're asking the wrong question, or your hypothesis is a negative hypothesis.

I've had at least three postdocs that have had every single tool that they need for success, except they get discouraged. I tell all my postdocs, if you get discouraged, this is the wrong business.

Any Other Advice?

You've got to ask interesting questions. Also, if one experiment works and gets you a paper, doing that same experiment 50 different ways is not going to make a career. You can't be afraid to change. If you can't reinvent yourself every 4 or 5 years, it is going to be very difficult to be successful.

Are You Still Happily Uncomfortable?

Oh, yes, very uncomfortable. With this new job as Executive Co-Director of the Heart Institute, I've had to learn about clinical practice, patient services, return on investment, meshing the research enterprise with the clinical enterprise. This is making me very uncomfortable, so that's good. I'll stay interested for the next 10 years.

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