New Leaders in Cardiovascular Science

Deepak Srivastava
Follows His Heart to Study the Heart
Ruth Williams

One percent of all births worldwide are to children with a heart malformation. To better understand what has gone wrong in these children and how to prevent or correct such malformations in others, Deepak Srivastava, the Younger Family Director at the Gladstone Institute of Cardiovascular Disease and Director of the Roddenberry Stem Cell Center at Gladstone, studies the biology of heart development.

He has identified several transcription factors, microRNAs, and other components that are essential for cardiogenesis in the mammalian embryo,1–5 but Srivastava’s work is relevant for heart problems affecting adults too. Heart failure after a heart attack is a major cause of death in men and women, and Srivastava is using the knowledge he gains from studying heart development to coax damaged adult hearts to regenerate. For example, his team has shown that, using a cocktail of developmental factors, heart fibroblasts—cells that form the rigid scar tissue after a myocardial infarction—can be converted into contracting cardiomyocytes both in vitro and in live mice.6,7

From caring for sick children, Srivastava is a physician at the Benioff Children’s Hospital in San Francisco, to regenerating mouse hearts, all of Srivastava’s career decisions and research interests have come down to the same basic principle, he told Circulation Research in a recent interview: do what you feel most passionate about, rather than what seems practical. This, he says, is the key to a happy career.

Where Did You Grow Up?
My parents, Satish and Rani Srivastava, immigrated to the United States from India when I was less than a year old, along with my 2 older sisters. My father was a scientist and he moved to the City of Hope Medical Center in Los Angeles as a faculty member and stayed there for 8 years. So I grew up in Los Angeles for my first 8 years, but then he was recruited to be a professor at the University of Texas Medical Branch in Galveston, and so we lived there for the rest of my childhood.

Were You Happy to Move to Texas?
Initially, I was not happy, but Texas turned out to be a great place. When we first moved, I decided that I was not going to like anything related to Texas. I never got any boots. I never got a hat. I avoided developing a Texan accent. But when I moved out of Texas in my twenties, I became nostalgic for it and found myself listening to Country and Western music. I even bought a pair of boots! Ultimately, I moved back to Texas after my clinical training and spent nearly a dozen years there, which was fantastic.

Did Your Father’s Career Fuel Your Own Interest in Science?
Although I was always interested in science and medicine, for a long time while I was growing up I did not want to be a scientist, probably because my father was one. It was not until late in college that I realized that was not a good reason to not do what I loved. I was, and continue to be, inspired by my father’s passion for discovery and my mother’s love of teaching. I got to see first hand the meaning of the saying, “Find a job you love and you’ll never have to work another day in your life.” That is how I feel about what I do now as a physician and scientist.

Was There a Particular Incident That Made You Change Your Mind?
I started out as an economics major at Rice University. It was the 1980s and I thought I would go to Wall Street and be an investment banker. But it was actually one discrete day that a friend of mine at Rice stayed up late with me and just kept asking questions about why I was making the decisions I was making. By 4 o’clock in the morning it was crystal clear that I should not go to Wall Street and make money for other people, but that I should do something good for mankind.

The next day I changed all my classes and my major and I never thought about it again. It was an epiphany.

Who Was Your Friend?
Her name is Ruth Farrar. She was an English major at Rice, and she remains a close friend. I often credit her for bringing clarity to my life at that time and thank her for inspiring me to follow my passion.

The principles of that conversation have guided most of my subsequent decisions. And they are the principles I advise young people to adopt too.
What Are They?
People often make major decisions in life based on facts and data of the current time, but during the course of an entire 40- or 50-year career, those facts and those data points will likely change. You then could find yourself having made a decision that no longer has the right foundation. But if you make your decisions based on what you are most passionate about, then typically that does not change over a lifetime.

So since that conversation, I have always followed what I was most passionate about with little regard to what seemed most sensible.

So Did You Have a Passion for Pediatrics?
Yes. I was actually interested in surgery when I was in medical school and thought I was going to be a surgeon. But then I did my pediatric rotation, which was mandatory, and I just loved it. I had never thought about pediatrics as a career, but I found it much easier to wake up at 4 in the morning and take care of an innocent child than when I was doing adult medicine. I also liked the fact that if you fixed one thing, the rest of the body was usually healthy and the child did well.

But there again I struggled with that choice because while I enjoyed pediatrics, it was the lowest paying subspecialty in medicine and was the least competitive. I had done pretty well in medical school and I was competitive, so I struggled with the logic of making that decision, but ultimately I followed what interested me most.

I also knew that I wanted to do science. Everybody advised me that between the quality of science being done in other specialties and that being done in pediatrics, there was a large gap. Rather than shy away, however, I decided I could maybe fill that gap.

When I started my pediatrics residency at University of California, San Francisco, I thought I would become an endocrinologist, in part, because it was a field more amenable to basic science. Again, this was not based on the fact that I loved endocrinology, but on logic. However, I kept being drawn to patients with heart disease. I liked the intensity of the situation, the gravity of it: life and death. Because the situations were so intense, it meant I quickly developed a close bond with the families I cared for, and I enjoyed those relationships tremendously. But there were few successful pediatric cardiologists doing molecular biology, so I struggled with that decision too. Again, I decided to do what interested me most and to make it work.

How Do You Make It Work?
I have benefited greatly from having dedicated and caring mentors. I did some research in medical school with Dr Brad Thompson, and we talked a lot about how cells acquire such distinct fates despite sharing a common genome—a major unanswered question. Cardiac defects in children are essentially problems of incorrect cell fate decisions, so there seemed to be a natural marriage of clinical and basic inquiry. Larry Shapiro, Abraham Rudolph, and Julien Hoffman, mentors while I was a pediatric resident, helped me solidify this idea. I decided to move to Boston to do a fellowship in pediatric cardiology, in part, because the chair of cardiology at Children’s Hospital was the world’s leading molecular cardiologist at the time. I did all my clinical training for the first 2 years and then started training in his laboratory. But then 4 or 5 months into the project his laboratory closed and I had to find a new place to train.

So You Were Homeless?
Yes. So I looked around the country because I had a specific project in mind, which was to identify the MyoD equivalent in the heart—that is, a single factor that could convert a fibroblast into a cardiomyocyte. I contacted Eric Olson, who had done a lot of beautiful work with myogenic transcription factors that could transdifferentiate a fibroblast into skeletal muscle cells, and he had an interest in moving into the cardiac area. I called him and told him what I wanted to do and asked if I could come to his laboratory. I had a research fellowship from the Pediatric Scientist Development Program, and they had to approve my transfer. After first expressing concern that Eric was too junior, being only 38 years old, they let me make the move. It quickly became clear that Eric’s laboratory was the best place I could have trained!

Eric was at the MD Anderson Center in Houston at the time and I joined him there for 2 years before he moved to Dallas. I started my own laboratory in Dallas in 1996 and stayed there until 2005.

After Dallas You Moved to the Gladstone. Why?
I had thought that I would stay at UT Southwestern for at least another 10 years. It is a fabulous institution. I received terrific mentoring there from not only Eric but also Joe Goldstein, Mike Brown, Helen Hobbs, Chuck Ginsburg, and many others. I also have a fondness for Texas and my parents still live there.

But I moved because the Gladstone Institute had just built a new building on University of California, San Francisco’s Mission Bay campus and had created an opportunity for a new director to come in and build a program in whatever direction they chose with tremendous resources and space. I was drawn to what Bob Mahley, Gladstone’s founder, had built as well as the culture of the place. I had trained in San Francisco and was fond of it, and my wife, who I met while I was a resident in San Francisco, actually grew up here, so it was a great fit.

Tell Me About Your Wife.
My wife’s name is Denise and she has been the foundation of my life for the past 23 years. When we met in 1991, she was a neonatal intensive care unit nurse at University of California, San Francisco and I was an intern. We started dating and fell in love and just before I moved to Boston I asked her to marry me—and she said yes! So we moved to Boston and Houston and Dallas and back to San Francisco together. She has been wonderfully supportive of the time that I have spent professionally and has done everything to ensure that I could do all the things that I feel most passionate about. She is a wonderful wife and I feel lucky to have her as my life partner and best friend.

Do You Have Kids?
We have 3: 13-year-old twins, Claire and Dillon, and a daughter, Sydney, who is almost 10 years. They are a tremendous source of joy and I believe they still think I am cool, but we will see how long that lasts! We have a lot of fun together.

How Have You Managed to Juggle Family Life and Scientific Career?
It is tough, and it requires one to be extremely efficient because the time with your children goes by really fast. Fortunately many people had warned me of that, including Eric, and so I have been conscious not to miss this critical and wonderful period of our kids growing up. On the weekends I spend a lot of time with them, almost all day. I do some work, but only when they are asleep.

When I am at work I am focused—I do not even eat lunch. But when I am at home, I am 100% focused on family. You really have to compartmentalize your life and not let one side seep into...
the other. It also helps that I am surrounded by talented people, in particular a fantastic executive administrator, Bethany Taylor, who has been a great partner in my professional life.

**You Obviously Work Hard. Do You Think Hard Work Is Important for Success in Science?**

To be successful in any venture, one has to be devoted and willing to give it all they have and that involves working hard and making sacrifices when needed. But if you are passionate about the mission you are on, it does not feel like you are working hard, you are just having fun accomplishing your goals. That is what I think we should all strive to achieve, no matter what line of work we choose.

**What Is the Primary Motivation for Your Work?**

There are 2 primary motivators for me. One is the urgency I feel in finding treatments for the patients I take care of. It is frustrating that we still have limited options and that kids and adults are still dying from heart disease with few options. We have to do better and have to do it soon.

The second motivator, which has grown as I have gotten older, is the pleasure that comes from training the next generation of scientists. I have been fortunate to have several brilliant people work with me and watching them develop their own independent laboratories or contribute in other ways to make discoveries has been extremely rewarding.

**What Has Been the Lowest Point of Your Career?**

That is a tough question for me as I have been unusually fortunate. I am an eternal optimist so I likely have had many adverse situations that I just failed to notice or have forgotten about! I suppose having to find a new laboratory in which to train could be considered a major hurdle, but it turned out well and I saw it as a new opportunity.

The biggest adversity I have probably had personally, however, is what many people have to deal with, and that is the poor health of loved ones. My father has heart failure, so that has been difficult, and my wife has recently developed a chronic illness called gastroparesis, which is essentially a disease where the nerves that innervate the gut, stomach, and intestines start to degenerate. She is in and out of the hospital a lot and it makes things a little more challenging. But she is a fighter and she is tough. She does a lot of martial arts and so that inner strength has helped. Our kids are also. It also helps that I am surrounded by talented people, in particular a fantastic executive administrator, Bethany Taylor, who has been a great partner in my professional life.

**What Has Been Your Proudest Career Moment To Date?**

My proudest moments are when my trainees have gotten their grants and gotten good jobs and make new discoveries. But within my own discoveries, the recent reprogramming work of fibroblasts to cardiomyocytes has probably been among my proudest achievements because it really reflects a long-standing question—trying to find factors that reprogram fibroblasts to cardiomyocytes—that has been a 20-year quest for me. It represents a culmination of all the work we have done with transcription factors, with signaling molecules, and with microRNAs. Going to the Nobel Prize ceremonies in Stockholm in 2012 with my friend and colleague Shinya Yamanaka, who I recruited to Gladstone, was not too bad either!

**With a Young Family and a Busy Career Do You Have Time for Any Hobbies?**

I love being on the water, so I do a lot of boating in this beautiful bay that we have here in San Francisco. I am also an avid tennis player. I am grateful to my father and uncle, Yogesh Awasthi, who together taught me how to play and inspired my love of the game as a child. I still play every week and that is my favorite thing to do outside of work. I grew up wanting to be a tennis player, actually. But quickly realized that I was not going to achieve the same growth spurt that my other colleagues had!

**Do You Play Tennis With Your Family?**

I had bought our kids’ racquets before they were born and have been playing with them since then. We have a lot of fun and have played as a family and together. It also helps that I am surrounded by talented people, in particular a fantastic executive administrator, Bethany Taylor, who has been a great partner in my professional life.

**Disclosures**

None.

**References**

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