

Rong Tian

Finding What Feeds the Heart

Jaclyn M. Jansen

Metabolism research has seen a great burst of popularity in recent years: scientists and doctors are investigating its role not just in obesity and diabetes mellitus but also in cancer growth and heart disease. There was a time though, not so long ago, when the field was distinctly out of fashion. The basic biochemical mechanisms had been defined decades earlier, and researchers thought that metabolites had little more to offer.

But for a select group of dedicated researchers, like Rong Tian, Director of the Mitochondria and Metabolism Center at the University of Washington, numerous questions remained unanswered. At a time when it was decidedly unpopular, Tian focused her research on understanding how metabolism affects heart function. What she found has come to challenge our assumptions about how simple sugar, fat, and amino acids affect the body. More than just energy sources, Tian has produced evidence that these molecules act as signals, changing the way cells behave in critically important ways.¹⁻³

The heart consumes a tremendous amount of energy—at least 12× its weight in adenosine triphosphate each day. In healthy adults, fatty acids feed the heart, but glucose is the preferred energy source for both healthy fetal hearts and diseased adult hearts. Scientists have long wondered why the heart switches from one energy source to another. Tian found that neither substrate is toxic: the heart can be forced to use glucose or fatty acids with no ill effects. Rather, it is the flexibility to choose between the 2 sources that is essential.⁴⁻⁶

Tian's work has also contributed to our understanding of metabolic cardiomyopathy.⁷⁻⁹ A cellular energy sensor, known as adenosine monophosphate-activated kinase, is also a master regulator of metabolism. Mutations in the kinase result in an enlarged heart with arrhythmia, as well as a buildup of glycogen. Tian found that the mutations cause the kinase to lose its sensor function. This floods the heart with an overabundance of glucose that is then converted into glycogen, leading to arrhythmia.

Another major challenge in the field has been developing a therapy for mitochondrial dysfunction. Although this organelle is most commonly thought of as the power house of the cell, it can also switch to a suicide mission, causing apoptosis that is often found in the diseased heart. Tian found that the mitochondria are exquisitely sensitive to protein modification

by metabolites. Impaired mitochondrial metabolism alters the redox state, tipping the balance between manufacturing energy and cell death.¹⁰⁻¹² Her work is being translated into clinical trials.

In a recent conversation with *Circulation Research*, Tian described how her path through science has been a series of new and exciting discoveries. Her combination of hard work, passion, and optimism—as well as a willingness to take risks—has led her to become a leader in cardiac metabolism research.

Were You Interested in Science at a Young Age?

My mother was a biochemist so I grew up hearing about science. It wasn't anything exotic—I would see mice in her laboratory all the time. But I did grow up in China during the Cultural Revolution, so I wasn't exposed to much science outside of her laboratory.

What Was It Like Growing Up During the Cultural Revolution? Did You Receive Much of a Science Education?

Not really. In the early years, we didn't spend many days going to school. We would go to factories for a month, then the countryside. These were considered important experiences. We needed to know what it was like in the working class.

The Cultural Revolution ended during my last year of middle school. Everything changed then. I entered high school—it was only 2 years at the time—and it was serious learning. At the end of high school, I took a national

examination, much like the SATs, to enter college. During the Cultural Revolution, colleges were largely closed. I was fortunate that the Revolution had ended: I entered college in 1980, just 3 years after they reopened.

Did You Immediately Choose a Major in Science?

The Chinese college system at the time was more like European universities. Your specialization was decided quite early. I was selected to go to the West China University of Medical Sciences. It was a 5-year program, and at the end, I would be a doctor.

I was extremely lucky because the University decided to do an experiment. They took a small fraction of the students and wanted to try to educate us in English. This was really an amazing effort. Just 3 years before, colleges had been closed. Very few



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people had much contact outside of China, and they weren't even sure they could teach us in English.

We were taught by much older professors who went to school maybe 30 years before. We had no formal textbooks and obviously no internet at that time. It was extremely difficult and risky but our determination prevailed. Looking back, that experience was incredibly rewarding.

How Well Could You Speak English Then?

We did learn English in middle school and high school. They selected people that looked decent on the national exams. It was a program that had certain risks, but I was incredibly excited to go into this class. I was not quite 16 years old at the time.

That Seems Young. Was That the Standard Age?

During the Cultural Revolution there weren't many rules. We only had 10 years of education. I skipped a year because we moved twice, but nobody cared much if you could catch up because there really wasn't much taught at school.

Were You Happy to be in Medical School?

When I went to medical school, I wasn't sure I wanted to be a doctor, but my parents encouraged me, so I did. Then I started school, and I realized I actually liked medicine. I felt like I fit in very well.

The program took an extra year because we had to learn everything in English. Five out of those 6 years I was the number one student in class. I did work hard, but I felt like it clicked with me. It just wasn't too difficult.

I was sure that when I graduated, I would be a practicing doctor.

What Changed?

After graduation, the school offered me a spot in their master's program. I was only 21, and I felt too young to become a practicing physician. So I took the offer and I decided to pursue a master's degree in medical science, focusing on cardiovascular disease. Three months into the program I learned of another opportunity. The University was nominating students to participate in a national competition to study abroad and get a PhD.

I was nominated and selected to study in Denmark. This was exciting and terrifying—I didn't even know where Denmark was on a map!

What Did You Do Your Graduate Work on?

I was studying the pharmacology of ACE inhibitors and other cardiovascular drugs. It was an exciting time because we saw large clinical studies that suggested that ACE inhibitors could reduce mortality in heart failure.

When I graduated, I came to the US for my postdoctoral research. I had heard from some of my colleagues that Brigham and Women's Hospital at Harvard was where I should go. They said there were incredible opportunities there. So I headed to the US.

Had You Been to the US Before?

No, Boston was the first city that I visited in the US. I knew nothing about it. Again, it was a bit risky, but I was excited.

What Laboratory Did You Join?

I joined Joanne Ingwall's laboratory at Brigham and Women's Hospital, where I studied bioenergetics of the heart using NMR spectroscopy. When I first joined, I can remember asking her for advice. She told me that "Harvard is a good place to be from"—meaning that you start there but go somewhere else soon

afterward. I was there from 1993 to 2009, so you could say that it took me a long time to be "from Boston."

Why Did You Stay so Long?

Things worked out well. I was very productive as a postdoc for 4 years. Then I got my K award and R29 from the NIH. I was also funded by the American Heart Association. I was awarded nearly everything I could have gotten to transition to junior faculty. But my work was very dependent on the unique NMR facility so staying there was more productive.

You Had Been There so Long. Why Did You Leave?

My work was going well, and I was well funded. I looked at my career and realized that I could go like this for years. But I wanted to drive the field forward with a broader program.

An opportunity opened up at University of Washington, where they wanted to build a mitochondrial metabolism center. Again, it was a great opportunity, but it would definitely be a challenge. When I came here, it was all empty space, but now 7 years later, we have built this Center. We are recognized University wide as a source of expertise. Nearly, a dozen of trainees have graduated from the Center and are now principal investigators. My own laboratory has more than doubled in size. It has really worked out.

Do You Feel Like You Have Work–Life Balance?

That question always comes up. I think yes and no. Yes because I do think family matters most. I have 2 sons. One is a college junior, and the other is a high school senior. They are always my priority. When the boys were younger, most of my spare time was spent on driving them to their activities. In return, they spent some time traveling to my conferences with me. I have always enjoyed my family most.

That Explains the Yes Part of Your Answer. What About the No?

Unfortunately, there are only 24 hours in a day. There is no magic, and there is always something you have to give up if you want to spend so much time on work. Over the years, I've learned to delegate and use all the resources available to me. But the most important thing is that I love what I do. To me, this is not a job. This is fun and exciting.

What Do You Like to Do When You Are Off?

I like to travel and garden. Most of all, I love to cook. It runs in my mother's family from my grandmother to my own mother.

My time in Boston had turned me into a New England Patriots fan. It became an issue a couple of years ago when Seattle Seahawks played Patriots in Super Bowl.

Do You Have Advice for Young Investigators?

I think it is really important to love what you do. Even though my parents put me in medicine, I happened to like it. Students now have a choice, and they should do what they like to do.

The same was true for my study of metabolism. When I got started, no one thought metabolism was interesting. People said it was a dead end field. But I just had so many questions and there were no answers. I never ran out of ideas to write a grant or come up with projects. It was the passion that drove me all these years.

Did You Ever Regret Leaving Medicine and Pursuing Academic Science?

No. I enjoy what I do. My medical training enables me to conduct translational research, although I do not practice medicine.

What Lessons Would You Pass on to New Investigators?

Seize the opportunity to venture into the unknown and seek mentoring along the journey. I was lucky that I had an unbelievably supportive and wise mentor. Joanne taught me so much about science but also about my career and life in general.

Did You Have to Work Hard?

It is definitely hard work. There is really no easy way out. I tell everyone that hard work is required for everything. It doesn't guarantee that you will be successful, but without it you will never have success.

Are There any Other Qualities That Are Important for Success?

Hard work and passion are important, of course. But optimism is also really important. And with optimism comes confidence. There is no formula for success except that the first step is believing that you will succeed.

Disclosures

None.

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