OUTLOOK SCIENCE MASTERCLASS

you put the mouse in a difficult situation that it would have previously given up on, it now makes an effort to solve the problem.

Have you tested this in higher animals?

Not yet. Unfortunately, the technology that we use for mice is not directly applicable to humans. But I know researchers are working on how to replicate in humans something similar to what we did in mice and eventually we can expect that this will become possible. Hopefully, one day, our findings will lead to a new kind of therapy for depression.

I am a researcher from southern Africa, where investment in science is low. What career advice would you give to young scientists who come from countries that are not known for their science research?

When I was a student in Japan the 1960s, I became fascinated by molecular biology. But there was no molecular biology in my country. So I had to go to graduate school abroad. I was fortunate to have the opportunity to study in the United States and I stayed abroad, including in Europe. My antibody work was entirely done in Switzerland. I didn't have much of a relationship with Japan until very recently. But now, after many years, I try to help Japanese science.

For a while, you may have to be trained outside of Africa. Since you are young, if you really want to do science I think there will be a way for you to go abroad and receive training. Then you could go back to southern Africa and try to help science in your country; if you get good training your knowledge will become useful not only to you, but eventually also to the community in which you grew up.

What are your interests outside of science?

I do not have anything that interests me as much as science. But, later in my life I was introduced to music by my wife and our children. I go to concerts with them and I enjoy it. My daughter plays the violin quite well. My younger son played cello and piano. I am not sure what I will focus on if I stop working in the lab. Once in a while I wonder what I am going to do if and when I retire. Is there such a thing as retirement for me? I can't imagine it.

This interview has been edited for length and clarity.

Keikantse Matlhagela is an HIV

researcher and lecturer at the University of Botswana's Faculty of Medicine. Previously, she was a Fogarty Research Fellow at the Harvard School of Public Health.





Q&A Elizabeth Blackburn End-game winner

Elizabeth Blackburn shared the 2009 Nobel Prize in Physiology or Medicine with Carol Greider and Jack Szostak for their work on telomeres — the protective caps at the end of chromosomes — and for identifying the enzyme telomerase, which maintains telomere length. Now at the University of California, San Francisco, she offers Elena Tucker an insight into her life inside and outside academia.

Why did you choose to study the ends of chromosomes?

The driver for me was wanting to understand how life works, rather than solving a particular problem that afflicts humans. When I was finishing my doctoral work at Fred Sanger's lab in Cambridge, UK, DNA-sequencing methods were embryonic. At the time, in the early 1970s, it was hard to sequence DNA except at the ends of relatively short DNA molecules. That was just what was possible. Researchers had looked at the DNA of viruses such as bacteriophages, but I wanted to know what goes on inside the nuclei of cells with real chromosomes. I heard that Joe Gall at Yale University in New Haven, Connecticut, had discovered very short, linear chromosomes in the cell nucleus of the eukaryotic protozoan *Tetrahymena*, and I thought I might be able to sequence the ends of those with the limited technology available at the time.

How did your research get off the ground?

Once at Yale I started analysing the ends of the short *Tetrahymena* chromosomes. What I found was really odd. I had expected to see something similar to the single-strand overhanging DNA observed at the ends of bacteriophage linear DNA, but telomeres were

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different. They consisted of tandem repeats of a short sequence, and the numbers



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of these repeats varied between molecules and over time. This changeability was a really strong clue of enzyme involvement in maintaining them. Once I had my own lab at the University of California, Berkeley, I extended the telomere research to yeast, collaborating with Jack Szostak at Harvard Medical School in Boston, Massachusetts. We demonstrated that this changeability is not unique to one kind of organism, and that it might be universal to eukaryotes. So I started searching for a new kind of enzyme. That was when my then-graduate student Carol Greider and I discovered telomerase.

We also found that we could make cells quite miserable if we disrupted their telomeres. The molecular puzzles became more and more intriguing. Moving to the University of California San Francisco with its medical school has led me towards all sorts of systems-wide questions around human health and telomeres. I started collaborations to study how chronic stress can affect physiology, which I would never have dreamed of asking on my own.

Why did you decide to enter, and then exit, the start-up world?

Telomere length is not usually by itself diagnostic, but more a general measure of health. Because of the correlation between long telomeres and a long and healthy life, over the years people have realized that there may be some benefit in measuring the length of their telomeres. Our lab has been quite good at that ever since telomeres have been on the radar. We realized that one day, just as you might send off a DNA sample for sequencing, you might also send a sample to a company that

could measure your telomeres. I set up Telome Health with a couple of others, but when it started going in directions that I thought were not scientifically driven I gave away all my

"We found that we could make cells quite miserable if we disrupted their telomeres."

equity to the University of California — as did my co-founder Elissa Epel. All in all, the adventure of starting something and talking with people in the finance world was a positive experience. I learned to admire the skills that business people need, realizing that scientists have a lot to learn from their world.

What are the main unanswered questions involving telomeres?

I would like to know how a telomere really works. We have a parts list, so we know what it does in a static sense. But in live cells, telomeres are extraordinarily dynamic. They are complex little ecosystems that constantly have proteins arriving and leaving every second. I think we could learn a huge amount by studying telomeres in action, rather like researchers do by watching active ribosomes assemble proteins, in addition to knowing their structure. The second unanswered question is how we might be able to modify telomere maintenance to make human bodies more resilient, given the correlation between having long telomeres and living healthily and for a long time. I would love to see humanity achieve a situation in which, although we get old and decrepit and things go wrong, we can improve health in the elderly far more than is achieved today.

What happened during your time on the President's Council on Bioethics, which was established by former US president George W. Bush and disbanded by Barack Obama?

When you are a scientist, you are part of this community so you serve on a lot of committees, and sometimes they are National Advisory Commissions. I knew the Bush council had political implications when I joined. I kept being a nag about getting the science right in reports, and they threw me off! That got a lot of attention because it occurred in the context of other developments that spoke to the issue of the use of evidence in policymaking. There were many things at stake. For example, some in government at that time minimized the evidence for climate change. I do believe that although there might be other considerations besides scientific evidence in policymaking, politically impartial research should always be the bedrock of policy decisions.

Apart from your Nobel prize, you've received a UNESCO L'Oreal for Women in Science Award and been one of *Time* magazine's 100 most influential people. What achievement are you most proud of?

What I'm truly proud of is having done the science and I'm proud of the people who work with me — I'm proud that we've done these things together. The awards are really just symbols. But in the sense that symbols influence people in subtle ways, they matter. If I'm photographed receiving an award, the picture makes the point that there's a woman winning a science prize — that aspect of an award is important to me.

How has your experience of motherhood influenced your career and vice versa?

For years I honestly didn't think much about having children. People would often say "you'd better have a baby soon if you're turning 30", but I didn't listen. I became pregnant in my late thirties when my career was very much underway — I found out I was pregnant in the same week that I was promoted to full professor at Berkeley! I feel very lucky, but I don't think my path is necessarily a recipe for happiness that others should follow. Children can happen at any time, and the challenges will be different depending on where you are in your career.

When you were a child, did your interest in science make you feel different from your peers?

I always felt like a fish out of water. I had good friends growing up and we would do stuff that was normal in Tasmania, Australia, like swim after school and then eat disgustingly delicious meat pies slathered with tomato sauce. But I wouldn't yap to my friends about science. I would talk about Beatles songs. I wasn't afraid of being thought weird, though talking science seemed to come across as pretentious. No one was overtly nasty, but I did sometimes feel pushed away, and that was hurtful. Selfpreservation is a useful life lesson. I suppose I always knew that I was different. I was thrilled with the idea that I could go and do a PhD, and do it outside Australia to really expand my horizons.

This interview has been edited for length and clarity.

Elena Tucker is a Peter Doherty Fellow at the Murdoch Childrens Research Institute, Australia, where she studies the genetic basis of rare human disorders.

