failure. "When one of my students gets a rejection letter, I can show them five or ten of my own," he says. "The academic environment should be more open to failure stories."

Drew reminds young researchers that even the chairs of their departments — scientists who seemingly have it made — do not always get their grants funded or their papers accepted. It would be telling, he says, if everyone published a 'shadow CV' of all their rejections to go along with the standard CV that lists successes.

Researchers can also help to ease their distress by making an effort to stop comparing themselves with colleagues in their lab or department. "Comparisons won't make you happy, so don't do it," Anseel says. Instead, he says, researchers should set their own personal standards of achievement and then do their best to meet them.

Metcalf has mostly won her battle over her sense of inadequacy, although her career has had its ups and downs. After she earned her PhD, she took a postdoc position in the United States that she quit after only six months, an outcome that made her feel even more like a scientific impostor. "I had a low sense of self-worth," she says. But she pushed through it, quickly found another post and went on to have a successful career that included research trips to the Antarctic and a highly sought-after faculty position at Lincoln University in Christchurch, New Zealand.

"You can trust the system to have put you in vaguely the right job. If you're invited to give a talk, you're ready."

Yet her troubles didn't end. In 2011, she lost her faculty job after an earthquake damaged much of the city. Instead of taking that setback as a sign that she needed to abandon science completely, she shifted from research to outreach. She is now the national coordinator of the Participatory Science Platform, a New Zealand government programme that promotes research collaborations between scientists and communities. "Anyone who knows me knows that I was meant for this job," she says.

As part of her duties, Metcalf has had many chances to speak to young people with different backgrounds and career aspirations. Many of them are already experiencing the symptoms of impostor syndrome, which gives her an opportunity to inspire by example. "My story really resonates," she says. "I've had my battles. You just have to keep fighting." ■

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TURNING POINT
Louis Picker

Louis Picker is not afraid to break with convention. Trained as a pathologist, he was on the front line when the AIDS epidemic emerged in the 1980s. He is now combining his interests in immunology and viruses to pursue an unusual HIV vaccine at Oregon Health and Science University (OHSU) in Portland — a project that was considered a fool's errand by many when he began.


OHSU

How did you get started in research?
I had always wanted to be a scientist. I started an MD–PhD programme at the University of California, San Francisco, but found it much too slow, rigid and hierarchical. I left that programme, but did a year of research there. Ultimately, I decided to become a pathologist specializing in immunology. It's astonishing how much biology you can learn from looking at hundreds of biopsy slides and by performing autopsies every day. I got a feel for the immune system that you couldn't get by doing graduate research on a mouse.

Describe your first AIDS autopsy.
I was a pathology resident at Beth Israel Hospital in Boston, Massachusetts. The devastation left by AIDS stuck with me. I decided to learn more about the disease so that I could do something about it one day. I had the opportunity to move into HIV research in the mid-1990s and haven't looked back since.

What led you to HIV-vaccine research?
Early in my career, I worked on a flow-cytometry-based assay to measure specific T-cell responses to viral infection in humans. I chose to work with cytomegalovirus (CMV), a virus that infects around 50% of adults in the United States and triggers a T-cell response that lasts throughout a person's lifetime. These factors enabled me to test the specificity of the assay. After studying CMV-specific T cells, I hypothesized that CMV could be exploited to create a vaccine that stimulates an immediate immune response to a variety of pathogens. By incorporating bits of HIV into the vaccine, we could prime T cells to hit the intruding virus early and hard. Our data in non-human primate models show that the vaccine stops infection with the simian counterpart of HIV in slightly more than half of recipients.

What does the next year hold for you?
We will move into clinical trials with our potential HIV vaccine. We are also exploring the use of unconventional viral vectors to manipulate the immune system against tuberculosis, malaria, hepatitis B and cancer at a level heretofore unappreciated.

Why did you choose research over more-lucrative private practice?
I knew that if I wanted to make a difference — and to pursue the CMV-based vaccine while others focused on conventional antibody-led approaches — I had to do lab-based experiments. As a pathologist, I would never have had access to patients. The best way to do relevant science was to test my ideas in a non-human primate model. The job I took at the OHSU was one of two possibilities I had at the time to do that type of work.

How easy was it to pursue your idea?
I was fortunate to have negotiated a start-up package at the OHSU that gave me the leeway to gamble. Either I'd make it or break it. I was warmly welcomed by researchers in the HIV field, which I appreciated. But it took me a while to feel that I fit in. Self-doubt was a powerful driver for me.

How risky was your decision?
To be honest, it helped that I had an MD. I knew I would always be able to get a job as a physician, so the degree allowed me a little more freedom in the early years. In the first crucial years while I was establishing myself, I figured I could always return to pathology. Most people with PhDs don't have that option.

What makes a great scientist?
You have to be a little bit of a lunatic. But your out-of-the-box thinking also has to be right. ■

INTERVIEW BY VIRGINIA GEWIN

This interview has been edited for length and clarity.

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