

CAREERS

POSTDOCS A lab head looks for trainees, not employees **p.553**

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DANIEL STOLLE



MEDICAL RESEARCH

Subject to reflection

Most scientists who study disease carry out their research with an eye to treating others — but a few have only to look at their own bodies to feel the need for a cure.

BY VIRGINIA GEWIN

Lukas Wartman always wanted to be a physician-scientist — but he never expected to be a research subject. Nor did he anticipate that his postdoc adviser would end up sifting through his genome for clues to treatment.

In 2003, during his final year of medical school, Wartman was diagnosed with the blood cancer acute lymphoblastic leukaemia (ALL). He went into remission after chemotherapy, relapsed one year into his clinical fellowship in oncology and then recovered following a bone-marrow transplant. In 2008, he started postdoctoral research in cancer genetics at Washington University in St Louis (WUSTL), Missouri.

At the time, his adviser, cancer researcher Timothy Ley, was carrying out the first whole-genome sequencing study of acute myeloid leukaemia (AML). When Wartman relapsed again in 2011, Ley and his colleagues sequenced his cancer genome, too. They found that a certain gene was overactive, which pointed them to sunitinib, a drug for kidney cancer that is known to reduce the gene's activity.

Despite having to cope with complications from a second bone-marrow transplant, Wartman continues to conduct cancer research, emboldened by his own illness. He focuses on AML, which produces symptoms similar to those of his cancer, but has a different genetic cause. Last December, Wartman published preliminary data on the suitability of a drug for

both AML and ALL in the American Society of Hematology journal, *Blood* (L. Wartman *et al.* *Blood* **124**, 5292; 2014).

Scientists such as Wartman, who research diseases that affect themselves or their loved ones, occupy a curious niche in the scientific enterprise. Their experiences can offer unique research insight, garner media attention and provide valuable connections to patient groups. And they are highly motivated to find a cure.

But their jobs are also fraught with the emotional — and sometimes ethical — challenges that can arise when researching something that resonates deeply on a personal level. Several of Wartman's peers and mentors encouraged him to leave oncology to free himself from thinking about cancer all the time. ►

► Those who come to know a disease as both patient and investigator can take steps to preserve their emotional health and research objectivity. These scientists need to be mindful of their motivations and realistic about their goals — and foster a broad and deep support network for times when research findings hit too close to home.

SOUL MEETS BODY

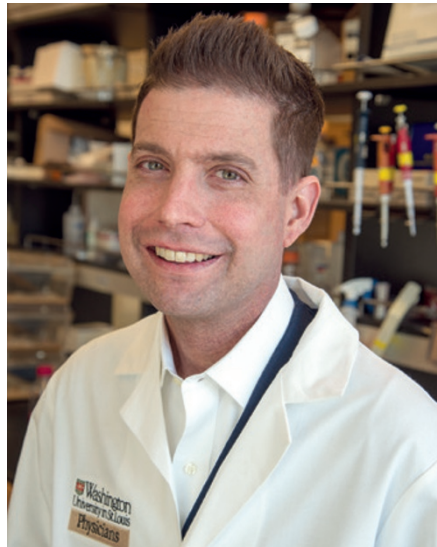
When a personal connection is involved, the drive to improve research into and treatment of a disease can be especially powerful. Geneticist Angela Christiano knows this first-hand: she jumped into her line of research after being diagnosed with an autoimmune disease called alopecia areata, which causes hair to fall out. As a postdoc, she had worked on dermatological diseases, but she began to look for another research focus when she moved into a tenure-track position at Columbia University in New York City. One day in 1996, her hairdresser pointed out a bald spot on the back of her head. After her diagnosis, she learned that frustratingly little was known about her condition.

And so she began a decade-long journey with patient-advocacy groups to establish a registry that now contains 3,000 serum and cell samples for genetics work. In 2008, she conducted a genome-wide association study and found seven genes linked to the disease. She also uncovered similarities between alopecia areata and other autoimmune disorders such as type 1 diabetes and coeliac disease.

Christiano launched clinical trials to test whether two drugs — one for rheumatoid arthritis and another for a bone-marrow disorder — could also combat alopecia areata. Last year, she published results showing that three patients treated with one of these drugs achieved near-full hair regrowth (A. Christiano *et al. Nature Med.* **20**, 1043–1049; 2014). Her emotional bond with the patient community fuels her work. “I give talks every year to the National Alopecia Areata Foundation patient conference. The year that I presented the genome-wide association study — and when I announced drug candidates for clinical trial four years later — they gave me a standing ovation,” she says. “We were all sobbing.”

A deep personal drive might be just what is needed in an understudied, underfunded field. Leonard Jason, a psychologist who directs clinical training, found his diagnosis of chronic fatigue syndrome (CFS) in 1990 to be life-altering, both personally and professionally. After an 18-month leave of absence from DePaul University in Chicago, Illinois, to recuperate, he delved into the CFS literature and realized a need for a better definition of the illness, a less-stigmatizing name and more-robust research on prevalence.

The field was riddled with questions — indeed, many physicians dispute whether CFS is even a genuine illness. “A number of folks had their careers destroyed by coming into this



Lukas Wartman studies the genetics of cancer.

area,” Jason says. Cognizant of potential career fallout and his susceptibility to overexertion, he focused on what the field needed most and what he could realistically achieve. He spent a decade on epidemiological studies that expanded estimates of the US patient population from 20,000 to 900,000. His work also showed that medical interns are more dismissive of the term chronic fatigue syndrome than of the more physiologically based name, myalgic encephalomyelitis (L. Jason *et al. Am. J. Community Psychol.* **30**, 133–148; 2002). “The key is to keep the focus on small wins,” he says. “I’ve been able to work with patients, researchers and government officials for over two decades on a variety of topics — from changing the name, to searching for biological markers.”

Jason might be one of only a few people with CFS conducting research on the condition, but that is not the case in other areas. “In type 1 diabetes research, there is an overrepresentation of people with the disease,” says Timothy Tree, an immunobiologist at King’s College London. And Tree is one of them.

Tree is driven by one specific question — why did he, and not his brothers, inherit the disease from their father? His need to answer that question, as well as whether he could pass it on to his children, keeps him going in the lab. “When the experiment goes wrong or funding gets turned down, having the disease gives me a reason to stay in it for the long haul,” he says.

Researchers in his position can offer practical perspectives, Tree says. For example, if a colleague suggests an idea for a therapy, he can give an informed opinion on how likely patients would be to comply. “It gives me a different kind of objectivity.”

Yet some people are concerned that such personal significance could compromise objectivity by introducing bias. “Bias can operate at a subconscious level,” says David Resnik, a bioethicist at the US National Institute of Environmental Health Sciences in Research

Triangle Park, North Carolina. And the results can potentially skew the work, he adds. “It might lead a researcher to make interpretations of data or study designs differently.”

Rebecca Dresser, a research ethicist at WUSTL, says that researchers who study their own or family members’ diseases can take precautions to safeguard against bias or perceptions of bias. “Consult with people who don’t have the same personal perspective — and get them on the team reviewing grants and research protocols,” she says.

But researchers such as Christiano and Tree say that they can put scientific integrity ahead of hope. If anything, Christiano says, having alopecia areata made her more cautious and conservative. “I’m the most demanding one on the team. I want to be triple sure about any findings before we go forward.” And Tree notes that his experience with diabetes has taught him how important it is not to oversell positive results. “As a patient, I know that people hang on to every word you say for hope.”

A FINE LINE

Balancing work and personal life is always important — more so when that work can have an impact on a scientist’s emotional state as well as productivity. “Having a bit of distance — between my own problems and the larger-scale problems we were trying to understand in the lab — definitely made things easier for me,” says Wartman. Of course, he does not directly study his own genome. “Tim and I sat down and had a serious discussion about whether or not even doing the genomics of AML would be too psychologically heavy for me to take on,” he says.

Wartman’s experience has strongly influenced his priorities. He benefited from the sequencing of his cancer genome, and feels a need to help others to gain similar insight. So he chose to devote his energy to the genomics tumour ward at WUSTL.

Each month, he and his colleagues invite cancer-care professionals to present cases. Together, they decide which diseases merit genome sequencing, bridging the gap between research and discovery genomics. “I spend a lot of my off hours getting this up and running,” he says.

But sometimes the pressure can become too great. Michael Dodd was on track to conduct his postgraduate research at the University of Oxford, UK, on a condition that afflicts his father called hypertrophic cardiomyopathy, in which the heart muscle thickens. He did not know that he, too, carried the underlying genetic mutation, until a year into his PhD programme when a genetic test came back positive. “It was quite a shock to find out, especially since, to this day, I don’t present any symptoms,” he says. At one point, his supervisor, Hugh Watkins, doubled as his physician.

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Dodd chose to shift his research focus elsewhere. “I sometimes found it weird to be in the lab,” he says. He was one of several patients who had the mutation, yet no symptoms, and so had MRI scans in their lab. “It was weird to see a bar graph, knowing I’m one of the points,” he says.

The research could be emotionally taxing. “It would feel odd to work on, for example, a mouse with the same genetic mutation as me, and wonder if I would respond similarly,” he says. But he did want to keep working on the heart, so he is now a postdoc studying the cardiac effects of diabetes, a disease that his grandfather had.

SPOTLIGHT SCARS

The emotional toll can be especially intense when media attention forces the scientist into the public eye. Wartman felt the landscape shift after a high-profile piece about him appeared in the *New York Times* in 2012. He is happy that patients find his personal perspective helpful, but regrets that the decision to share his story no longer rests with him. “It’s still not the easiest topic for me to talk about,” he says. “The last time I relapsed, I came close to dying. To rehash that on a regular basis is emotionally draining.”

Media attention can change one’s entire research career. Kay Redfield Jamison, a clinical psychiatrist and founder of a clinic for mood disorders at the University of California, Los Angeles, channelled her struggles with bipolar disorder into research on the illness’s wide range of effects — from enhanced creativity to a high risk of suicide. But when she wrote her autobiography in 1995, entitled *An Unquiet Mind: A Memoir of Moods and Madness*, she knew that her professional life would never be the same. She gave up her clinical practice. “You can’t say that you’ve been psychotic and nearly died by suicide and expect people to look at you the same way,” she says.

Now at Johns Hopkins University in Baltimore, Maryland, Jamison focuses on writing and public speaking. She credits a network of supportive friends and colleagues for helping her to navigate her career ups and downs. “Becoming a poster child for an illness is draining,” she says. “It becomes a disturbing part of your identity.” Still, it was worth it to reach others who were suffering. “That’s what good comes out of it.”

At the end of the day, that desire to aid others motivates many researchers to continue their work even though their own health is poor. “Leukaemia disrupted my career and goals and was a huge setback in my life,” Wartman says. “At the same time, if I can turn my own struggle into a story that helps other people, that has value.” ■

Virginia Gewin is a freelance writer in Portland, Oregon.

TURNING POINT

Roberto Kolter

Roberto Kolter set up his microbiology laboratory at Harvard Medical School in Boston, Massachusetts, in 1983. Postdocs worldwide hope to join his lab because of his career-targeted training philosophy, but with rare exceptions, he brings in only those who already have a fellowship.



Why do you accept postdocs only if they have their own funding?

I focus on those whom I believe have a fantastic chance of getting their own funding as a principal investigator. I think it’s unfair for me to interview those who have very little chance of getting their own funding, considering how competitive the academic job market is and how important it is to show independence.

What does your laboratory focus on?

I let the postdocs explore what they want to explore, as long as it is within the sphere of my interest. I’ve worked on starvation physiology, biofilms, signalling, experimental evolution, antibiotics and many other subjects.

Describe your training philosophy.

I train people to go on into academia, industry the corporate world or whatever they want to go into. We need to give them the experience that they require, including learning how to teach and learning how to manage. Postdocs are not just there to come to the lab so that principal investigators can get their next grant.

What stands out when you look at applications?

I have learned that networking works very, very well. If I know who trained that individual, and I know and respect them, then I’ll know a lot about how this postdoc will work in the lab. But that does not mean that if I don’t know the mentor I will close the door to the postdoc. They need to have also done their homework — they need to know how I train people and how they think they would fit in.

When have you made exceptions?

There are one or two cases where I was completely sure that they would get a fellowship, and they didn’t. But by then I had gotten so excited about the project we had co-developed that I chose to support them from my own funds.

How does your lab develop a research project?

The ideas often emerge from conversations that start about 18 months before the postdoc comes to work with me. It has almost always been my policy that incoming postdocs build their research projects and are free to take the

project with them once they leave, to help them to set up their own lab. That gives the postdocs who are leaving a good opportunity to establish themselves without having to compete with me and the people in my lab.

What careers do your postdocs pursue?

About half the 100 or more postdocs that have gone through my lab hold full-time academic jobs, of which running a research lab is a big component. Many people whom I take on as postdocs want a job in the biotechnology arena. The other 50% are dominated by those who choose to join a company. Those can range from start-up biotech companies to very well-established pharmaceutical or chemical companies. Others lead research groups at institutes or government labs, work as research associates, teach science or do other science-related work. Only two have left science.

Do they get permanent positions right away?

No one who has come through my lab has had to leave science because they could not get a job. Personally, I believe that I have failed a postdoc if I take them into my lab and they cannot get a job that they love when they leave. That usually means that they have to go on to do a second postdoc. There have been very few such individuals — fewer than five, in the 32 years I have had my own lab. So overall I rate my success rate in helping postdocs get their first job at about 90%.

What do you see as the role of a postdoc?

The meaning of postdoctoral training has been lost in today’s scientific community. As mentors, we need to really reconsider what we are training postdocs for. And that’s just it: it’s a training period, not a job. ■

INTERVIEW BY JULIE GOULD