

A Race Against Time: One Couple's Very Personal Fight Against a Fatal Disease

After being diagnosed with the same fatal disease that ended her mother's life, Dr. Sonia Vallabh '02 and her husband left their careers to dive into medical research in hope of finding a cure.

Photo credit: Maria Nemchuk



In front of Dr. Sonia Vallabh '02 and her husband, Dr. Eric Minikel, there is a mountain to climb. It appeared without warning in 2010, when Vallabh lost her mother, Kamni Vallabh. It was a loss that devastated her and her family but also marked a critical and monumental change in their lives. It was a long and painful year for the Vallabh family after Kamni became sick. They could only watch as her undiagnosed condition progressed and her suffering worsened, ending on life support. It wasn't until December of that year that doctors determined a preliminary diagnosis after finding signs of prion disease in her spinal fluid.

Prions are misfolded proteins that form toxic pockets in the brain. They are the cause of rare and often fatal neurodegenerative diseases; in the U.S., the most common form of prion disease, Creutzfeldt-Jakob disease, takes the lives of about 500 people per year. Prion disease can be inherited, can arise spontaneously, or in very rare cases, can be acquired. But once the symptoms begin, it's an irreversible and aggressive process in which prions rip through healthy tissue, leaving gaps behind.

After Kamni's passing, her family learned that she had succumbed to a subtype of prion disease called fatal familial insomnia, and Vallabh was told that she stood a 50% chance of inheriting the disorder. She asked to be tested, and in a feature written by *Wired* reporter Kelly Clancy, Vallabh recalled the plain-spoken words of the doctor's results:

"The same change that was found in your mother was found in you."

It is obliterating news, particularly for someone so young, with what should be a long life ahead of her. But Vallabh received the news with little shock — in fact, she said she felt calm. She now understood what she faced, and she came to a decision.

There was work to be done.

Vallabh and her husband left their successful careers in law and engineering to study science and medical research, fully committing themselves to the search for a cure. It began modestly; Vallabh signed on for more science courses and enrolled in a night class in biology at Harvard's extension

school. But this soon became a full-fledged dive into medical research inside the Broad Institute of Massachusetts Institute of Technology and Harvard, and the pursuit of a PhD.

There is little time for the long and arduous process that comes with medical research and drug development. Fundraising for research was also an unexpected, frustrating and formidable challenge. As one path forward, the couple launched their own nonprofit, Prion Alliance, with the focused goal of raising funds through donations to support prion disease therapeutic science. There is opportunity to donate on their website, prionalliance.org.

Most damning was learning that the promising research that had initially inspired so much hope ultimately faced dead ends. They had known it wouldn't be easy, but their disappointment was heavy and their "naivete" — as she described — "was mortifying."

But their goals began to take new shape as they confronted one critical truth: They could not wait until the disease presented itself in a patient. With the rapid progression of the disorder, there would not be sufficient time to test a developing treatment. Unlike diseases such as Alzheimer's or Huntington's disease, the progression of prion disease happens, on average, over the course of five months from first symptoms to death. The other diseases have a 15- to 20- or in some cases 25-year diffuse course.

And so, they turned to targeting the proteins before they misfolded and stopping the prions from appearing in the first place.

"We can't wait to intercept people on that incredibly steep downhill. We have to catch them at a point where there's still a meaningful quality of life left to preserve," she said.

Inside the Schreiber lab at the Broad Institute, Vallabh and Minikel conduct their research on the development of therapeutics for human prion diseases. Their projects include searching for molecules that can reduce the amount of prion protein in the brain, and working to identify biomarkers to track disease progression and drug activity in living patients.

Vallabh had just successfully defended her thesis when she

spoke with WRA's Communications & Marketing Office. It's a significant mile marker in the career of any scholar, but she felt more as though she had checked something off a long list of to-dos.

"We're really just going to try and roll right forward with our same momentum," she said, graciously accepting congratulations but making it clear that she's ready for the next task.

Minikel and Vallabh's work, in part, harnesses existing research from Ionis Pharmaceuticals, which developed the synthetic DNA-based drug modality antisense oligonucleotides (ASOs). If Minikel and Vallabh can show evidence that ASOs, when injected, can change the levels of prion protein in their mouse patients — and in doing so, impact their survival — their research can move forward into potential clinical trials. This is no small feat, but Vallabh reports that there's sufficient data and a growing confidence that this could be a real gateway for her team.

"Prion diseases are such extreme cases, where doing a conventional clinical trial with symptomatic patients might actually be impossible, so we have an opportunity to fast track our work," she said. "There's an opportunity to do something different and really just pivot to total prevention and try to identify people based on risk, treat them with this drug that should lower prion protein in the brain and should, therefore, delay onset and reduce risk."

They have engaged scientists at the Food and Drug Administration (FDA) on one potential path forward. They hope to show that an ASO reduces levels of the disease-causing protein in the brains of at-risk individuals. If they are successful, their data could potentially support an application for provisional approval of a drug.

"The FDA has been very supportive," she said. "So now, one of our big mandates in the lab is to gather the data that continues to support that strategy and prove that, yes, we can measure this biomarker; yes, it's stable over time in the absence of drug; and yes, in the context of treatment it's telling us something meaningful about the activity of the drug."

Inside their lab, husband and wife must balance the practical and meticulous grind of medical research and the ebb and flow of an overwhelming sense of urgency and purpose.

"I feel like [that intensity] does set us apart from a lot of people we work with," she shared. "We have amazing allies, but I think we're on a little bit of a different wavelength. Yes, it can be really exhausting, and the way we're personally invested in this isn't something we can ignore. Honestly, I think one of the hardest things about our job is the fact that we approach it in such a goal-oriented way, and that's really different than how a lot of scientists approach their work. We know so many people who really have a more exploratory range for what they're doing and can just go where the results take them. We don't have that luxury."

But there's a brightness in their lives that she said keeps her

and her husband grounded — a new love named Daruka, their daughter, who was born in July 2017. Through in vitro fertilization with preimplantation genetic diagnosis, their child was born without the dangerous genetic mutation.

"I would say having our daughter has actually been a really wonderful way of helping us maintain balance in our lives," she said. "She really helps us unplug, and every day she lets us think about something completely different — at least for a little while."

When she reflects on the tremendous change she and her husband have experienced, in their careers and overall in their lives, she remarked that she does not feel that they, themselves, are completely different people. When they first transitioned into science, it wasn't clear that the pair should work in the same lab, rather than divide and conquer. But choosing to work side by side was the right choice. Each new obstacle has been easier to face with him in her corner and in their lab.

"It's been amazing to have the chance to work together on something that we both care so much about," she said. "Before we ever transitioned into science, we were really focused on how to have a good life together and how to build work lives that would support that. And now that has a whole new level of meaning to us. Every minute of every workday is in support of having that good life together."

It's not often that she reflects on her time at Reserve. (With so much on her plate, this is no surprise!) But she was delighted to consider today's students and what she might tell them, if she had the opportunity.

"I'd have to lead with the idea that life is full of surprises," she said. "You have no idea what you're going to end up needing your brain to do for you. It's interesting, because I'm doing something I never thought in a million years I would be doing for a living. In fact, science didn't come easily to me in high school. I thought I should follow my natural strengths, but I think I would tell students not to assume that you know what you'll end up doing. Reserve is full of overachievers, and I think most of us naturally want to gravitate toward our strengths and play it a little safer. But it's been kind of cool to realize that it's possible to find a path outside what you think you're good at, and that we can forge ahead and make a difference if we have to."

A conversation with Vallabh about her work includes profuse and heartfelt appreciation for the support she has received from her family, friends, mentors and colleagues. She made special mention of her father, who after initial concerns about taking on such an overwhelming challenge, has provided encouragement without pause.

When asked what her mother's reaction might have been had she known her daughter's future, there was laughter in Vallabh's voice.

"I certainly think she would have been proud of my degree from Harvard!" she said. "But yes, I think if she could have known, then she would have been very proud."