A big part of the MS puzzle

Barancik Prize winner Katerina Akassoglou, PhD, studies links between the brain, immune system and blood-brain barrier.

by Vicky Uhland

Back in 1994, shortly after she began work on her doctorate at the University of Athens and Greece's Pasteur Institute, Katerina Akassoglou, PhD, made an important discovery. She and her fellow researchers found that mice that had certain types of immune system-regulating molecules in their brain developed mobility symptoms similar to those experienced by people with multiple sclerosis.

Scientists at that time didn't know much about how immune cells acted inside the brain, especially in people with MS. Most of the studies prior to Akassoglou's work focused on the role of the immune system in the body. The brain's immune system was a whole new frontier, with the potential for more treatment options and targets for MS therapies than previously thought.

"We were very surprised," says Akassoglou, the winner of the 2018 Barancik Prize for Innovation in Research. "We realized that we might be missing a big part of the pathology of MS."

The discovery was so groundbreaking that it set the course for Akassoglou's career. She realized that to understand MS and other neurologic diseases well enough to develop a cure, she needed to research how the brain, the blood-brain barrier and the immune system

interact throughout the disease course.

At the time, Akassoglou didn't know anyone with MS, and she viewed the disease mainly from a laboratory standpoint. But after she began her postdoctoral work at Rockefeller University in New York City, MS became personal to her.

Barancik Prize

The Barancik Prize for Innovation in Research was created in 2013 by the Charles & Margery Barancik Foundation and is administered by the National Multiple Sclerosis Society. The Baranciks have been major supporters of MS research projects for more than 20 years. They developed the Barancik Prize to recognize exceptional scientists who have demonstrated outstanding innovation and originality in MS research. Barancik Prize winners receive $100,000 that can be used at their discretion.

"I had the opportunity to interact with MS patients at events organized by the National Multiple Sclerosis Society, and it was truly transformational to meet them and see the belief and hope they had in our research," she says. "I developed a sense of urgency when I met with patients. I had the revelation that our work could really make a difference, and we had to hurry."

Stopping MS in its tracks

For the last two decades, Akassoglou has put that sense of urgency to good use, conducting a series of studies that are creating a new understanding of the origins of MS and pushing the boundaries of biomedical technology. She's developing an antibody that has the potential to not only halt damage to brain cells in people with relapsing-remitting or progressive MS, but also may repair MS-related nervous system damage.

This experimental therapy has the potential to "stop MS in its tracks," says Bruce Bebo, PhD, executive vice president of research for the Society. "Her relentless pursuit of a fundamental question in MS and the tenacity to translate this knowledge into potential therapies is why she is being recognized with the 2018 Barancik Prize."

"Katerina richly deserves the Barancik Prize because her work is pathbreaking and important. It's also a great example of the risk-taking science that the Baranciks and the MS Society are hoping to foster with this award," says Daniel Reich, MD, PhD, winner of the 2016 Barancik Prize.

Reich, who nominated Akassoglou for the 2018 prize, believes she could be "the most creative scientist currently working in the MS field. I rarely leave a conversation with Katerina without wondering whether I should change my own research focus based on her novel findings."

Is it in your blood?

After Akassoglou's research revelation in 1994, she set out to study what turns on the brain's own immune system in MS. She focused her studies on finding the link between the brain, the immune system and the blood-brain barrier. But she soon discovered that the technology she needed didn't exist. So she developed several cutting-edge imaging techniques that allowed her to see in real time how MS disease develops in the brain.

An international researcher

Katerina Akassoglou, PhD, was born and raised in Greece, the only child of a mechanic and a seamstress. She was the first in her family to go to high school, where a biology teacher piqued her interest in science. She went on to study at the University of Athens, earning with first-class honors a bachelor's degree in biology and a doctorate in biological sciences, specializing in neuroimmunology.

A truly international researcher, Akassoglou has worked at the University of Vienna, Rockefeller University in New York City, New York University and the University of California, San Diego. She's currently a senior investigator at the Gladstone Institutes, a professor of neurology at the University of California, San Francisco, and founder and director of the Center for In Vivo Imaging Research at the UCSF Gladstone Institute.

Akassoglou has written more than 85 peer-reviewed papers and has been awarded seven U.S. patents, with another nine pending. The Barancik Prize is the latest of numerous awards she's won over the last two decades. Akassoglou is one of two women to receive the Barancik Prize. (Laura Balcer won as part of a trio of scientists in 2015.)

"I have always promoted diversity in my lab, including women and underrepresented minorities in science," Akassoglou says. "I hope that winning the Barancik Prize underscores that the originality and impact of scientific discovery is not defined by gender, ethnicity or socioeconomic status. Scientific innovation can come from all genders and all ethnic groups as long as inclusive environments are in place in academia for innovation to flourish."

This helped her discover that a blood protein called fibrinogen is present in the brain very early in the disease. Fibrinogen, which helps blood clot, isn't normally found in the brain. But Akassoglou's research shows it can enter when there's a leaky blood-brain barrier, making clots called fibrin that start early, but can also last for long periods of time and promote damage in the brain.

"We've known for decades that the blood-brain barrier is leaky in MS, but we didn't understand what effect that had," Akassoglou says. In essence, it was a chicken-and-egg question: Was there more fibrin in the brain because of MS, or did fibrin play a role in promoting MS?

Through research partially supported by Society grants, Akassoglou has found answers to that question. She's discovered that fibrin can control communication between the brain, immune system and blood vessels. It can bind to receptors of the brain's immune cells, which can kill neurons and cause the inflammation that contributes to MS. And it hinders repair of myelin, the protective nerve coating that MS attacks.

"While others dismissed the idea that blood factors could be involved in the nervous-system damage that causes MS, Akassoglou saw this as an important clue," Bebo says. "Over the past several years, she doggedly pursued the hypothesis that the blood-clotting factor fibrin plays a critical role in MS."

Expanding the MS toolbox

Akassoglou was thrilled when she made the fibrin discovery. "We were very excited that we identified a new pathway not addressed by any existing MS medications," she says. "Strategies blocking the toxic effects of blood proteins could be very important tools in the toolbox of MS therapies."

Akassoglou and her research team have developed a unique antibody that can keep fibrin from finding the brain's immune cells and binding to them—without interfering with fibrin's vital role in blood clotting. Tests show this antibody has a huge effect on the course of MS in mice, including significantly decreasing the severity of their MS symptoms and reducing damage to neurons, myelin and inflammation.

The next step is to see if the antibody has the same effect in humans. Akassoglou co-founded a biotech company called MedaRed to research this and develop a medication using the antibody. If she's successful, there would then need to be years of safety and clinical trials before an actual drug could be available to people living with MS.

"If it pans out, the therapy could protect the nervous system from damage in both early and late phases of the disease, which could have profound impacts for stopping MS progression," Bebo says.

Vicky Uhland is a writer and editor in Lafayette, Colorado.

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