Point of View
THE EYE RESEARCH INSTITUTE UNIVERSITY OF WISCONSIN–MADISON
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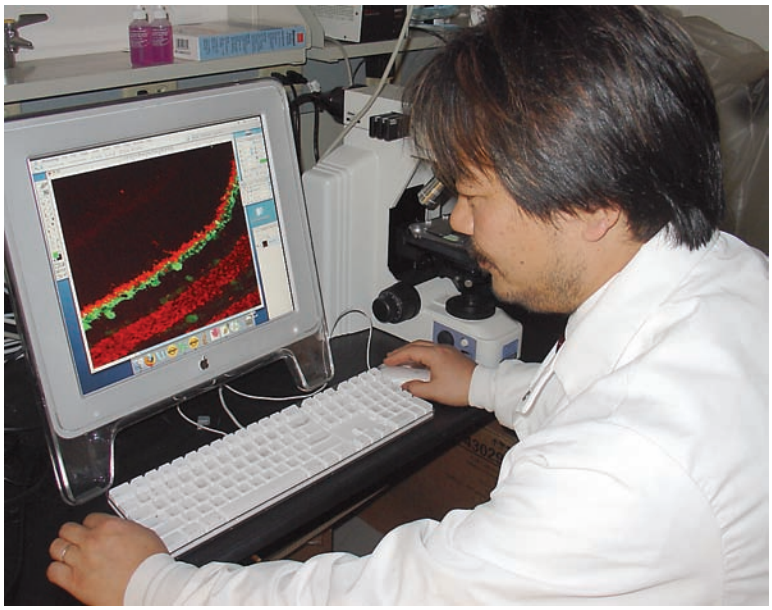
Curiosity as a Career

Children often want to be doctors or firemen when they grow up. But as a young student in Japan, Akihiro Ikeda spent his free time reading biographies of famous physicists and other scientists. "I pictured the researchers sitting in a room alone, reading and learning wonderful things. There was something very intriguing to me about their curiosity and dedication."

Like those physicists, Ikeda liked to ask "Why?" "My parents never gave me a direct answer," Ikeda laughs. "They encouraged me to find answers for myself."

Ikeda, now an assistant professor in the Department of Genetics and member of the Eye Research Institute, set out to find answers through scientific training and the development of an independent research program.

"I spent three years in a physiology laboratory as an undergraduate, learning about how one small change in a gene could alter the entire *phenotype* of an organism — the outward, observable structure. I worked on introducing a gene that caused obesity in a rat, which caused it to gain weight while eating a normal amount of food."



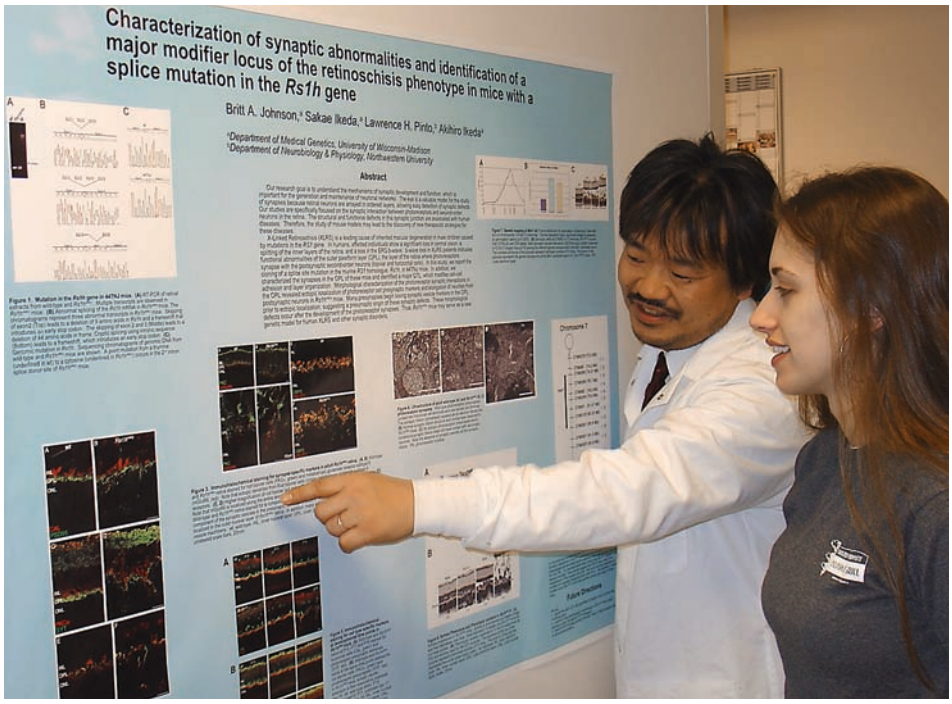
Images of the retinal layers in a mouse with retinoschisis are carefully analyzed by Akihiro Ikeda, PhD.

Intrigued by these genetic studies, Ikeda stayed in the same laboratory to complete a PhD in Veterinary Physiology, then pursued post-doctoral studies at the Jackson Laboratory in Maine. There he studied another type of obese rodent, the "tubby" mouse, which developed retinal degeneration in addition to gaining weight. Because of this surprising finding, he became curious about the connections between nerve cells, called synapses. "My post-doctoral training introduced me to the retina of the eye, which is nerve tissue that can be viewed easily. The retina is a well-organized structure — we can see all of the layers beautifully and look directly at the differentiation of cells and cellular interactions. It makes a great research model."

Ikeda's UW laboratory has set a goal of understanding the synapses between nerve cells in the retina, which he believes will reveal the mechanisms underlying human diseases contributing to blindness.

In particular, Ikeda works with a mouse model of *retinoschisis*. Retinoschisis causes splitting of the retina into two layers, resulting in progressive loss of central and peripheral (side) vision. There are two forms of the disease in humans. The juvenile form is an inherited (genetic) condition that affects primarily boys and young men. Although the condition begins at birth, symptoms do not typically become apparent until the first years of grade school. There is also an age-related form of retinoschisis, and this type can affect both men and women and is not a genetic condition.

"The mouse with retinoschisis was developed by the Tennessee Mouse Genome Consortium, a center that develops mouse models of human genetic diseases. It is a perfect model for our studies. Is the retina still splitting? We can look into the eye to directly see the effects that modifying a gene has on retinal structure. Does the retina work better? We can perform the same electrophysiological tests that human patients undergo to learn about the neuronal



Ikeda and graduate student Britt Johnson discuss details of a poster outlining their studies of mutations affecting neural connections.

activity following the genetic mutations we create."

But good questions leading to promising findings are not enough. Young investigators in the first stage of their careers — like Ikeda — must compete for grant funding. During this critical time, supplemental funds are required to support lab personnel and allow for the initiation of pilot studies. One of the goals of the Eye Research Institute is to support new faculty as they establish their laboratories, and as an Institute member, Ikeda was assisted in finding sources of funding.

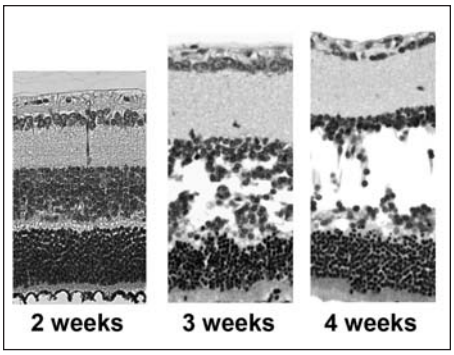
An application to the Retina Research Foundation (RRF), guided by the Eye Research Institute, garnered him the RRF Rebecca Meyer Brown Pilot Project award, intended to support junior scientists in their preliminary investigations. Houston ophthalmologist Alice R. McPherson, MD, an alumna of the University of Wisconsin Medical School, is RRF's founder and President. "I am grateful to Dr. McPherson and to the RRF," says Ikeda. "The research findings supported by the Rebecca Meyer Brown Pilot Project formed the basis for a National Eye Institute (NEI) grant application which will be funded this spring.

> ***The important thing is not to stop questioning. Curiosity has its own reason for existing.***
>
> *Albert Einstein*

Without the RRF support, the NEI grant could not have been as successful."

The award from the RRF was used to support Britt Johnson, a graduate student in Ikeda's lab. "Britt has been imaging the changes in retinal structures," explains Ikeda. "She makes high-resolution photos of the ultrastructure of the synaptic interactions using confocal and electron microscopy. These images give us a close-up look at what is happening in the retinal layers and provide clues as to which genes maintain normal structure instead of what is observed during retinoschisis."

What is the hardest part of his work? Ikeda laughs, "For a kid that always asked 'why,' it might be surprising that the hardest thing is figuring out the right questions to ask. What experiment



This cross-section of retinal layers in a two-week-old mouse with retinoschisis looks relatively normal, but as the mouse ages, the layers show the characteristic splitting.

will help me test this hypothesis? What is important about this finding? Why does this neuronal defect cause the cells to die? Keeping the questions coming is a challenge."

And what excites him the most? "New ideas and new results. When we find something new, I go home and can't sleep at night. I keep thinking, 'It might be this…how can we test it?' I may ultimately be disappointed, but even finding one answer after asking one hundred questions is enough to keep me going."

"When I became a researcher, my goal was to discover something significant. There is great satisfaction in the creation of knowledge and in believing that the knowledge can be applied to cure diseases and make a difference." It's early in his career, but with his outstanding training and questioning mind, Akihiro Ikeda has a promising path before him.

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