Long Partnership Culminates in Support for Genetic Disease Research

By Jennifer Walker

In 1977, Becky Stirn, age 24, began to see sparkles in the peripheral vision of her right eye. At home in California, she was diagnosed with pseudoxanthoma elasticum (PXE), a rare inherited genetic disease that affects connective tissues in various parts of the body, including the eye. That same year, Stirn came to the Wilmer Eye Institute to gain an understanding of PXE. She has gone on to become one of the longest-serving members of Wilmer's Board of Governors.

"There's something special about Wilmer's patient care, where empathy and sensitivity to patients are prevailing points of view," says Stirn, a former business executive primarily for the medical devices market.

It was four-plus decades ago that Stirn's retina specialist on the West Coast first referred her to **Victor McKusick, M.D.**, a medical geneticist at Johns Hopkins Medicine, and **Arnall Patz, M.D.**, and **Stuart Fine, M.D.**, at Wilmer, to learn more about PXE, which is caused by a mutation to the ABCC6 gene. In the eyes, this disease causes calcium deposits to build up on Bruch's membrane, the tissue that acts as a barrier between the retina and the blood vessel-rich choroid beneath it. These calcium deposits can cause small cracks to form in the membrane, creating space for the blood vessels to grow into the retina and potentially bleed, leading to central vision loss. Complications from the disease often occur later in life, but Stirn lost the central vision in her right eye in her 20s and began having impacted vision in her left eye at age 36.

In 1980, Stirn was invited to join the then newly created Wilmer Advisory Council (now referred to as the Wilmer Board of Governors), a group developed by Patz to give voice to the patient perspective. In her 44 years on the board, Stirn has given many talks to the Wilmer community about her patient experience, provided career mentorship to women at the institute and offered her expertise on licensing. Last June, she was honored

with Wilmer's Aida de Acosta Root Breckinridge Award, which was established by Wilmer Director **Peter J. McDonnell, M.D.**, the William Holland Wilmer Professor of Ophthalmology, to recognize women leaders who devote significant time and resources to the institute.

Stirn and her husband, Brad, who have been Wilmer donors for many years, most recently decided to support the work of **Jefferson Doyle, M.D., Ph.D., M.H.S.**, the Andreas C. Dracopoulos and Daniel Finkelstein, M.D., Rising Professor of Ophthalmology and co-director of the Wilmer Genetic Eye Disease Center, who is studying early disease processes of PXE. "There's been so little research on PXE, and even less when it comes to the eye," Stirn says. "Dr. Doyle brings together genetics and expertise in different ophthalmological subspecialties to think outside of the box about how to approach this disease."

In collaboration with **Shira Ziegler, M.D., Ph.D.**, in the Department of Genetic Medicine at Johns Hopkins Medicine, Doyle and his team are studying several PXE-related mouse lines to better understand what causes calcium to deposit in PXE eyes, the consequences of this calcification and therapeutic options that can target this process. Doyle and Ziegler are also interested in understanding how modifier genes influence disease severity as a way of developing new treatment strategies. They are studying ABCC6-deficient mice that have been bred into different mouse background strains, which markedly affects the severity of disease. They plan to use this information to understand what genes and processes alter disease severity to teach them how to slow disease progression. Doyle's ultimate goal with this work is to better understand what drives PXE eye disease to help develop specific therapies that can be used much earlier in disease progression.

Above: Brad Stirn, Becky Stirn, Jefferson Doyle

"At the moment, after a patient gets diagnosed with PXE, we watch their eyes for a couple of decades until they have a problem, and then we start trying to deal with the complications," Doyle says. "I'm interested in how we can prevent complications from ever developing. If we can understand the underlying disease process, we can try to develop novel therapies that we can use much earlier. "

With support from the Stirns, Doyle has been able to bring on an outstanding young graduate student to advance PXE research in his lab. "The potential of what we can gain in terms of understanding ocular disease in PXE at a much earlier stage and identifying therapies is enormous," he says. "It's been a real partnership with Becky and Brad, and their impact cannot be overstated." ●