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Disease that causes blindness in children tied to new gene

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Northwestern Medicine and University of Wisconsin-Madison (UW) scientists have identified a gene that causes severe glaucoma in children. The finding, published in *The Journal of Clinical Investigation*, validates a similar discovery made by the scientists in mice two years ago and suggests a target for future therapies to treat the devastating eye disease that currently has no cure.

"This work shows us how a genetic mutation causes a severe form of glaucoma called primary congenital glaucoma, which afflicts a significant portion of children enrolled in institutions for the blind worldwide," said principal investigator Dr. Susan Quaggin, chief of nephrology and hypertension at Northwestern University Feinberg School of Medicine and Northwestern Memorial Hospital.

The gene, TEK, is involved in the development of a vessel in the eye called Schlemm's canal, which drains fluid from the anterior portion of the eye. In glaucoma, this vessel can be defective or missing, creating pressure buildup that can damage the optic nerve and cause vision loss. In previous research, Quaggin's lab showed that deleting the gene in mouse models led to glaucoma, but the scientists didn't know how mutations impairing the gene affected humans.

After publishing that research, Quaggin met Dr. Terri Young, a pediatric ophthalmologist and chair of Opthalmology at the UW. Young had identified mutations in TEK in some of her patients, but didn't know the significance.

"It was more than coincidental," Quaggin said. "Our meeting led to collaborations with ophthalmologists and geneticists from around the world who identified more mutations in this gene in children with this form of glaucoma. It was one of those eureka moments that sometimes happens in science."

Altogether, the team found TEK mutations in 10 unrelated families with children who have primary congenital glaucoma. All of these children did not have mutations in other genes known to cause glaucoma.

The scientists then demonstrated that the TEK mutations identified in children impair the vascular signaling pathway important in Schlemm's canal formation—the same way they do in mice. Findings made in animal models do not always translate to patients, but it appears that this important eye vessel functions very similarly in mice and humans.

"We don't know how other genes associated with glaucoma cause this disease," Quaggin said. "With TEK, we know exactly what's going wrong, which means we've identified a pathway that could be a great new therapeutic target for severe glaucoma and even more common forms of the disease."

In ongoing research, Quaggin's group is developing an eye drop that repairs the TEK pathway to fix the faulty vessel. The scientists are also exploring whether TEK pathway mutations play a role in adult-onset glaucoma.

Provided by Northwestern University