# New glaucoma cause discovered

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Acute angle closure glaucoma of the right eye (intraocular pressure was 42 in the right eye). Credit: James Heilman, MD/Wikipedia

Northwestern Medicine scientists have discovered a novel cause of glaucoma in an animal model, and related to their findings, are now developing an eye drop aimed at curing the disease. They believe their findings will be important to human glaucoma.

A cure for glaucoma, a leading cause of blindness in the U.S., has been elusive because the basis of the disease is poorly understood.

In glaucoma, pressure builds from poor drainage of fluid from the anterior chamber of the eye, destroying retinal ganglion cells and eventually the optic nerve. The eye becomes like a bathtub that can't drain because the pipe is clogged. The clogged or defective vessel, known as Schlemm's canal, is part of the lymphatic system that is

essential for drainage in the eye.

The new study for the first time identifies the molecular building blocks needed to make the 'drainage' vessels, providing the necessary chemical tools to repair the eye's plumbing and restore normal drainage. Up until now, the molecular basis of the disease caused by an absent or defective canal was unknown.

The study will be published Sept. 9 in The *Journal of Clinical Investigation*.

"This is a big step forward in understanding the cause of the disease that steals the eyesight from 60 million people worldwide," said senior study author and Northwestern Medicine nephrologist Susan Quaggin, M.D. "This gives us a foothold to develop new treatments."

Quaggin is director of the Feinberg Cardiovascular Research Institute at Northwestern University Feinberg School of Medicine and chief of nephrology and hypertension at Feinberg and Northwestern Memorial Hospital.

"Our goal now is to grow new 'pipes' or vessels to cure the glaucoma," said Quaggin, also the Charles Mayo Chair of Medicine at Feinberg.

The findings are based on a new mouse model of glaucoma developed by Quaggin and Ph.D. student Ben Thomson, which is one of the first animal models of the disease. Quaggin expects the animal findings to be relevant in human glaucoma.

Quaggin is collaborating with Amani Fawzi, M.D., an associate professor of ophthalmology, and Xiaorong Liu, an assistant professor of ophthalmology, both at Feinberg, and Northwestern scientist Samuel Stupp to develop a nanofiber eye drop that activates regrowth of the

clogged vessel.

"We are developing a highly potent peptide nanostructure that has the capacity to interact with many receptors at the same time," Stupp said. "This will amplify the required signaling pathway for an effective therapy. The nanostructure is also being designed to have the necessary half-life to optimize efficacy." He is the Board of Trustees Professor of Chemistry, Materials Science and Engineering, and Medicine, and director of the Simpson Querrey Institute for BioNanotechnology.

"Just imagine if we could grow a bigger Schlemm's canal in anybody with glaucoma to lower the pressure in the eye," Quaggin said. "That's what we're hoping for with this new eye drop."

## The Source of Bad Eye Plumbing

The Northwestern study identifies a critical chemical signaling pathway for the healthy functioning of the Schlemm's canal and the substances necessary for its growth and development.

That pathway requires the chemical equivalent of a lock and key to open. The lock is a substance called Tie2 and the key is a growth factor called angiopoietin Northwestern scientists discovered if either the key (angiopoeitin) or the lock (Tie2) is missing in mice, they can't make Schlemm's canals and will develop glaucoma.

Both these substances are necessary to unlock the pathway to a cascade of events inside the cell that produce the canals.

"We really nailed that pathway as being critical," Quaggin said. "Now we know these two substances are key factors in the development of glaucoma, which wasn't known before."

The lock and key are likely to be involved in human glaucoma, Quaggin noted. "The mouse model is so similar to what we see in patients with glaucoma," she said.

The animal model of glaucoma now will enable scientists to study treatments as well as how glaucoma develops.

"Now we can understand how raised pressure leads to the damage of the neurons in the optic nerve," Quaggin said.

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