

Possible new treatment for glaucoma

By LEE BOWMAN
Scripps Howard News Service
05-DEC-06

New research in mice is revealing in minute detail how glaucoma causes blindness and suggesting possible new treatment targets, including some that might be covered by existing drugs.

The findings, published online Wednesday in the Journal of Neuroscience, "give a whole new approach to thinking about glaucoma therapy," said Dr. Joan Miller, chief of ophthalmology at the Massachusetts Eye and Ear Infirmary in Boston and a co-author of the study.

Glaucoma affects an estimated 3 million Americans, and it is thought that an equal number of people have the condition but don't know it. Glaucoma is six times more common in people over age 60, and six to eight times more common among blacks than whites.

The primary risk factor for glaucoma is increased pressure in the eye, typically measured in eye exams with tests that deliver a puff of air. If glaucoma is diagnosed early, eye drops or surgery to lower pressure inside the eye can prevent further optic-nerve damage and halt vision loss. But it hasn't been understood how the increased pressure leads to optic-nerve damage.

Dr. Toru Nakazawa and Larry Benowitz of Children's Hospital Boston and Miller and colleagues found several things happening in mouse studies that may explain how pressure in the eye goes on to damage the optic nerve and gradually narrow patients' field of vision.

They discovered that increased pressure in the eye causes the buildup of an inflammation-inducing substance called TNF-alpha in the retina. This in turn activates cells that are part of the eye's immune system, which eventually start to attack cells that support the optic nerves.

Ultimately, this contributes to the destruction of retinal ganglion cells, the nerve cells in the eye that send visual information to the brain via the optic nerve.

"The end stage of glaucoma is a loss of retinal ganglion cells," Benowitz said. "We now have good evidence that TNF-alpha plays an essential role in this loss."

When an inflammatory substance was injected directly into the eyes of mice with normal pressure inside the eye, the same chain of events occurred. But none of this happened in mice that were genetically engineered to be unable to produce TNF-alpha, or its receptor cells, even when eye pressure was artificially raised.

The researchers were able to show, for the first time, that blocking TNF-alpha's action with an antibody prevented the loss of both the support cells and the optic-nerve cells when eye pressure was raised.

"In the clinic, lowering intraocular pressure is a reliable treatment for glaucoma, but sometimes it is hard to lower the pressure even after eye-drop treatment or surgery," said Nakazawa, now at Tohoku University in Japan. "Here we show that blocking TNF-alpha function may have a benefit as a nerve-protecting treatment."

Injectable drugs that inhibit TNF-alpha include Enbrel, Humira and Remicade. They are already in use to treat such inflammatory conditions as rheumatoid arthritis and Crohn's disease.

"These drugs have potent systemic effects, so we would want to develop a very safe long-term and local treatment," Miller said. "Theoretically, it might be possible to put slow-release TNF-alpha inhibitors just outside the eye, so you wouldn't have to have frequent injections."

On the Net: www.glaucoma.org