UNMC research traces glaucoma, often associated with aging, to earliest days of development

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Pooja Teotia, left, a post-doctoral scholar, and Iqbal Ahmad, a professor in the department of ophthalmology and visual sciences at the University of Nebraska Medical Center, have opened new ways to study glaucoma.

UNMC

Glaucoma is known as a disease of aging, the kind that creeps up on people and slowly robs them of vision. But a researcher at the University of Nebraska Medical Center has traced the roots of a common form of the eye disease to a much earlier time, literally the earliest days of human growth and development.

The discovery, published recently in the journal Stem Cells, may offer opportunities for earlier diagnosis of the disease as well as new treatment options.

Iqbal Ahmad, a professor in the ophthalmology and visual sciences department at UNMC, said there are several forms of glaucoma, which ranks as the second-leading cause of blindness and affects approximately 3 million people in the United States and

some 60 million worldwide.

All forms, said Ahmad, who led the team of researchers, have one thing in common: Cells inside the eye known as retinal ganglion cells, which extend from the retina and give rise to the optic nerve, begin to degenerate. The optic nerve carries visual messages from the eye to the brain.

The condition typically comes on with little notice and few symptoms, creeping up so slowly that patients often don't notice until their optic nerve is compromised and, with it, their vision. The loss begins on the periphery. Many unconsciously compensate by turning their heads.

"That's why they call it the silent robber of vision," Ahmad said.

High pressure inside the eye is a risk factor for glaucoma, he said. But in some cases, patients with normal eye pressures suffer optic nerve degeneration. Such cases were one of the factors that led Ahmad and his team to look to the early days of development.

Ahmad said the team hypothesized that the retinal ganglion cells, which form during gestation, were somehow vulnerable — or even flawed — from the start in those who develop glaucoma.

To study them, however, they had to go back to those early stages of development. So the researchers took blood from adults with primary open angle glaucoma, which affects 90 percent of glaucoma patients, and reprogrammed the blood cells back into an earlier state, known as induced pluripotent stem cells. Such cells, by definition, have the potential to differentiate into a number of different cell types, from bone to heart, with the right programming.

The team figured out how to make them differentiate into retinal ganglion cells in an unlimited supply they could use for research. Pooja Teotia, a post-doctoral scholar in Ahmad's lab, played a crucial role in the work.

The stem cell model was based on a gene variation known to be associated with primary open angle glaucoma. About 40 percent of Caucasians have at least one copy, said Dr. Shane Havens, a glaucoma specialist at UNMC's Truhlsen Institute who is familiar with Ahmad's work. More than 99 percent of people of African descent have it, which partially

explains why African-Americans have higher rates of glaucoma.

Ahmad stressed that the process did not involve the use of embryonic stem cells. Research based on embryonic cell lines has been controversial because the original cells were derived from human embryos. “The ethical dilemma we used to face has been circumvented,” he said.

The researchers then compared the retinal ganglion cells derived from the glaucoma patient’s blood with those from a healthy adult who didn’t have glaucoma. The glaucoma patient-derived cells differed in form, function and gene expression.

“They even looked different,” Ahmad said. “The nerves that came out of the young retinal ganglion cells looked much weaker and smaller than the normal retinal ganglion cells. At the functional level, they were not behaving normally.”

Ahmad said the team is excited about the next steps. Being able to study the abnormal cells in a dish is giving the researchers “an amazing amount of information” about what might have gone wrong at the molecular level as well as along the intricate signaling pathways in their development.

Both offer the potential for earlier diagnosis and for new treatments. Ideally they would be able to identify patients who might develop the disease decades down the road and treat them before degeneration occurs.

Havens said treatments for glaucoma currently involve lowering eye pressure with medication, lasers or surgery. But that often comes after people have lost a significant portion of the optic nerve.

About 2 percent of people in the United States have glaucoma, but about half of them don’t know it.

“This would allow us to start earlier in patients who are at risk,” he said.

Ahmad said the researchers also are working to see whether they can correct abnormalities in the cells and to determine whether they would find their way and connect with the brain. If that works they may be able to transplant them into patients who already have the disease and reverse the degeneration.

"We're seeing some encouraging signs," he said.

Havens said the work, particularly the stem cell technique involved, also has broader implications for the study and treatment of other diseases, such as Parkinson's disease, that involve the nervous system.

"It's exciting work, for sure," he said.

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Complete eye exams urged, especially for the most at risk

The only sure way to diagnose glaucoma, according to the American Academy of Ophthalmology, is with a complete eye exam. A glaucoma screening that checks only eye pressure is not enough to find glaucoma.

So when should someone have an eye exam? According to the group, adults with no signs or risk factors for eye disease should have a comprehensive medical eye evaluation at age 40, if they haven't had one already. After age 40, the recommended interval is:

» Age 40 to 55, every two to four years

» Age 55 to 64, every one to three years

» Age 65 and older, every one to two years

For those at higher risk of certain diseases, including African-Americans and Hispanics who are at higher risk for glaucoma, comprehensive eye exams should be considered:

» Under age 40, every two to four years

» Age 40 to 54, every one to three years

» Age 55 to 64, every one to two years

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