SOUTHWESTERN NEWS

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MICE SHOW FUNCTION OF GENE THAT CAUSES TWO TYPES OF BLINDNESS

DALLAS-July 9, 1999-UT Southwestern Medical Center at Dallas scientists have used genetically altered mice to help explain two types of human blindness, one that occurs in children and another that develops in approximately one in four adults over 65.

Stargardt's disease affects about one in 20,000 children over age 6, and age-related macular degeneration (AMD) develops in approximately one in four adults over 65. Both disorders affect central vision, which enables reading, driving and face recognition. The work is a major step toward finding treatment for these macular-degenerative illnesses, in which cells in the center of the retina-the macula-die.

The research, published in today's issue of *Cell,* describes a UT Southwestern study of mice that the investigators developed by inactivating the *ABCR* gene, which produces Rim protein (RmP). This study identifies the molecule transported by RmP in the retina's photoreceptor cells. When a mutation occurs in *ABCR,* then RmP dysfunctions and cannot perform its transporter role.

"Our research revealed, among other things, the biochemical change in patients with Stargardt's that makes vision more difficult when coming from sunshine into a dimly lit room," said Dr. Gabriel Travis, associate professor of psychiatry and an investigator in the Center for Basic Neuroscience at UT Southwestern. This symptom is called delayed dark adaptation, an early sign of the illness, which is the most common form of juvenile macular degeneration.

Because the genetically engineered animals lack the *ABCR* gene, RmP also is missing. In normal mice, RmP inhibits accumulation in the retinal pigment epithelium (RPE) of lipofuscin, a brown pigment generally associated with aging. The buildup of lipofuscin poisons

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the RPE, which then cannot perform its role of keeping photoreceptor cells healthy. The unhealthy cells begin to die, causing blindness. The lipofuscin accumulation seen in the rodents is identical to what is observed in humans with Stargardt's and AMD.

"Although the mouse retina does not contain a macula, our studies offer a possible explanation for vulnerability of the macula in several human blinding diseases," Travis said. "We observed complete inhibition of lipofuscin accumulation when mutant rodents were raised in total darkness. This observation suggests that patients with Stargardt's disease and some forms of AMD could slow the progression of their blindness by wearing sunglasses and avoiding bright light."

If researchers can discover methods to inhibit lipofuscin accumulation in retinal pigment epithelial cells, new treatments for Stargardt's disease and AMD may be possible. Currently no treatments or cures are available for Stargardt's, and only a small percentage of AMD cases can be treated with lasers. Once a patient is diagnosed with Stargardt's, there is rapid progression to legal blindness.

Other researchers involved in this study were Dr. Jian Weng, assistant professor of psychiatry; Dr. Nathan Mata, a postdoctoral fellow in psychiatry; Dr. Sassan Azarian, instructor of psychiatry; and Dr. David Birch and Radouil Tzekov of the Retina Foundation of the Southwest, Dallas. Birch is a UT Southwestern adjunct professor of ophthalmology.

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