Altering eye cells may one day restore vision

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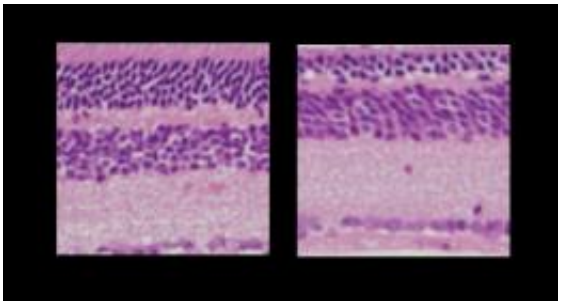

The light-sensing cells of the eye are the top purple and pink layers in these images. The cells on the left have been reprogrammed to make them less vulnerable to the degenerative effects of retinitis pigmentosa. As a result, more have survived compared to the untreated cells in the right image. Credit: Joseph Corbo, MD, PhD

(Medical Xpress)—Doctors may one day treat some forms of blindness by altering the genetic program of the light-sensing cells of the eye, according to scientists at Washington University School of Medicine in St. Louis.

Working in mice with retinitis pigmentosa, a disease that causes gradual blindness, the researchers reprogrammed the cells in the eye that enable night vision. The change made the cells more similar to other cells that provide sight during daylight hours and prevented degeneration of the retina, the light-sensing structure in the back of the eye. The scientists now are conducting additional tests to confirm that the mice can still see.

"We think it may be significantly easier to preserve vision by modifying existing cells in the eye than it would be to introduce new stem cells," says senior author Joseph Corbo, MD, PhD, assistant professor of pathology and immunology. "A diseased retina is not a hospitable environment for transplanting stem cells."

The study is available in the early online edition of Proceedings of the National Academy of Sciences.

Mutations in more than 200 genes have been linked to various forms of blindness. Efforts are underway to develop gene therapies for some of these conditions.

Rather than seek treatments tailored to individual mutations, Corbo hopes to develop therapies that can alleviate many forms of visual impairment. To make that possible, he studies the genetic factors that allow cells in the developing eye to take on the specialized roles necessary for vision.

The retina has two types of light-sensing cells or photoreceptors. The rods provide night vision, and the cones sense light in the daytime and detect fine visual details.

In retinitis pigmentosa, the rods die first, leaving patients unable to see at night. Daytime vision often remains intact for some time until the cones also die.

Corbo and others have identified several genes that are active in rods or in cones but not in both types of photoreceptors. He wondered whether turning off a key gene that is activated only in rods could protect the cells from the loss of vision characteristic of retinitis pigmentosa.

'"The question was, when retinitis pigmentosa is caused by a mutation in

a protein only active in rods, can we reduce or stop vision loss by making the cells less rod-like?" he explains.

The new study focuses on a protein known as Nrl, which influences development of photoreceptors. Cells that make Nrl become rods, while cells that lack the protein become cones. Turning off the Nrl gene in developing mice leads to a retina packed with cone cells.

To see if this rod-to-cone change was possible in adult mice, Corbo created a mouse model of retinitis pigmentosa with an Nrl gene that could be switched on and off by scientists.

"In adult mice, switching off Nrl partially converts the rod cells into cone cells," he says. "Several months later, when the mutant mice normally had very little vision left, we tested the function of their retina."

The test showed a healthier level of electrical activity in the retinas of mice that lacked Nrl, suggesting that the mice could still see.

Corbo now is looking for other critical development factors that can help scientists more fully transform adult rods into cones. He notes that if complete conversion of rods to cones were possible, this therapy could also be helpful for conditions where cone cells die first, such as macular degeneration.

More information: Montana CL, Kolesnikov AV, Shen SQ, Myers CA, Kefalov VJ, Corbo JC. Reprogramming of adult rod photoreceptors prevents retinal degeneration. *Proceedings of the National Academy of Sciences,* online January 14, 2013.

Provided by Washington University School of Medicine in St. Louis