When the Eyes Fail

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Wayne State University researchers and colleagues, led by Zhuo-Hua Pan, Ph.D., professor of anatomy and cell biology in the School of Medicine, have reported a novel strategy for treatment of blinding retinal degenerative disease such as retinitis pigmentosa (RP). This National Eye Institute of the National Institutes of Health supported research was published in *Neuron*, a highly regarded journal which publishes reports of novel results in any area of the neurosciences.

**A search for a cure for retinitis pigmentosa**

Vision normally begins when rods and cones, also called photoreceptors, respond to light and send signals through other retinal neurons, inner retinal neurons or interneurons, and the optic nerve to the visual cortex of the brain where visual images are formed. The severe loss of photoreceptor cells caused by congenital retinal degenerative diseases results in partial or total blindness. These disease conditions affect one in 3,000 people worldwide. At present, no treatment is available for restoring vision once rods and cones, the normally light-sensitive cells in the retina, have been lost.

Dr. Pan and his colleagues took a novel strategy for developing a potential treatment of blindness caused by retinal degenerative diseases by genetically converting light-insensitive inner retinal neurons into photosensitive cells – thus restoring light-sensitivity to retinas that lack photoreceptors. Using a harmless virus, they introduced a gene encoding a light-sensitive protein from green algae, called channelrhodopsin-2 (ChR2), into surviving inner retinal neurons in mice that were genetically bred to lose rods and cones, a condition similar to
the blinding disease, retinitis pigmentosa, in humans. They found that the introduced ChR2 protein made the inner retinal neurons become light sensitive. What’s more, they found the ChR2 protein persisted for long periods in these neurons, and the neurons generated signals that were transmitted to the visual cortex of the animals’ brains.

“Our study demonstrates the feasibility of restoring visual responses in mice after they lose the light-sensitive photoreceptor cells,” said Dr. Pan. “It raises the possibility that this approach may be a potential strategy for the treatment of blindness caused by rod and cone degeneration in humans.”

“With this strategy, the investigators have made a paradigm shift in the field and opened the possibility of genetically modifying the surviving retinal interneurons to function as a replacement light-sensing receptor,” wrote John Flannery and Kenneth Greenberg of University of California, Berkeley, in a preview of the paper in the same issue of Neuron. “This publication is clearly a significant first step into this new field of re-engineering retinal interneurons as genetically modified ‘prosthetic’ cells,” they wrote.

“This innovative gene-transfer approach is certainly compelling,” said Paul A. Sieving, M.D., Ph.D., director of vision research at the National Institutes of Health. “This is a clever approach that offers the possibility of some extent of vision restoration at some time in the future.”

Dr. Pan and his colleagues are working to determine whether the light signals reaching the visual cortex can be perceived by the brain as useful vision. They are also making a number of technical improvements to better fit the need for vision restoration, for example, by selectively targeting ChR2 in certain populations of inner retinal neurons and using other similar light sensitive proteins to increase light sensitivity and restore both ON and OFF pathways in the diseased retina.

This research is providing many people with hope that one day there will be a treatment for restoring vision to those afflicted with RP.

About Dr. Zhuo-Hua Pan: Dr. Pan received his B.S. degree from the University of Science & Technology of China, his M.S. from the Institute of Biophysics at the Chinese Academy of Science, and his Ph.D. from the State University of New York at Buffalo. He joined Wayne State University in 1999.