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Healing Blindness in Mice

Delivering light-sensitive proteins to the retinas of blind mice restores some vision.
By Emily Singer

Viruses can deliver light-sensitive proteins to specific cells in the retinas of blind mice, allowing rudimentary vision, according to new research. Although previous studies have shown that the light-sensitive proteins can be beneficial, the delivery methods were not practical for humans. The viral-delivery method is similar to ones already used in human gene therapy.

The new light-sensitive proteins were active for the length of the study, about 10 months, suggesting the treatment would work long-term. In addition, the therapy appeared safe; the proteins, which were derived from algae, remained within the eye, and they did not trigger inflammation.

"In my opinion, the biggest step forward in this paper is the use of viral delivery techniques, the same delivery techniques that would have to be used should the technique move on into human treatment," says [Thomas Münch](#), a researcher at the University of Tübingen, who was not involved in the study but has done similar research. Recent gene-therapy studies, which used similar viruses to deliver different proteins, have shown preliminary success in treating a rare genetic form of blindness in patients. But the current approach could be applied to a much broader group of people because it could restore light-sensitivity to the retina regardless of the cause of degeneration.

To restore vision, [Alan Horsager](#), a researcher at the University of Southern California, and collaborators capitalized on [optogenetics](#), a type of genetic engineering that makes neurons sensitive to light. They used a specially designed virus to deliver numerous copies of the gene that makes a protein called channelrhodopsin to the eye. The protein forms a channel that sits on a cell's membrane and opens when exposed to light. Positively charged ions then rush into the cell, triggering an electrical message that is transferred to other cells in the retina.

The gene was modified so that it became active only in specific retinal cells called bipolar cells. In a healthy eye, these cells are activated when adjacent photoreceptor cells detect light. The researchers hope that making the bipolar cells directly responsive to light in an eye stricken by retinal degenerative diseases, such as retinitis pigmentosa or macular degeneration, could enable the altered cells to replace photoreceptors that have died off. Horsager cofounded a startup called [Eos Neuroscience](#), along with MIT neuroscientist Ed Boyden, to commercialize the approach.

The optogenetics approach is conceptually similar to the retinal prosthesis, in which implanted electrodes stimulate the retina in response to light captured by a camera. ([One such device](#) was recently approved for clinical use in Europe.) But researchers say that restoring light sensitivity to individual retinal cells should enable more fine-grained vision than direct electrical stimulation, which activates many cells simultaneously. "Although the retina is a fairly thin and small piece of brain tissue, it is extremely complex," says Horsager. "If we are going to interface with tissue, we want to do it in a circuit-specific and precise way."

In a water maze test in which the correct direction to swim was illuminated with light, the treated animals found the escape route much more quickly than their untreated counterparts. In very bright light, they performed almost as well as normal mice. The research was [published online](#) last week in the journal *Molecular Therapy*.

While the findings are promising, it's not yet clear at what resolution the animals can see. The task requires general sensing of light, rather than fine-grained detection. Horsager predicts that a human patient given a similar treatment "would be able to walk outdoors and hopefully sense light and navigate the environment to some degree."

The researchers plan to tinker with the therapy further before moving into clinical studies. They are exploring other proteins that might provide greater light sensitivity, as well as proteins that would turn off activity in another subset of cells in the retina. The ability to turn some cells on and others off in response to light would theoretically orchestrate a response that is more like that of the normally functioning retina. Because light signals undergo significant processing in the retinal circuits before being transmitted to the brain, the more closely scientists can mimic the activity in the intact retina, the better the resulting vision is likely to be.

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