

Newly developed chemical restores light perception to blind mice

February 19 2014



Progressive degeneration of photoreceptors—the rods and cones of the eyes—causes blinding diseases such as retinitis pigmentosa and age-related macular degeneration. While there are currently no available treatments to reverse this degeneration, a newly developed compound allows other cells in the eye to act like photoreceptors. As described in a study appearing in the February 19 issue of the Cell Press journal *Neuron*, the compound may be a potential drug candidate for treating patients suffering from degenerative retinal disorders.

The retina has three layers of [nerve cells](#), but only the outer layer contains the rod and [cone cells](#) that respond to light, enabling us to see the world. When the rods and cones die during the course of degenerative blinding diseases, the rest of the retina remains intact but unable to respond to light. Even though the innermost layer's nerve cells,

called ganglion cells, remain connected to the brain, they no longer transmit information useful for vision.

Dr. Richard Kramer of the University of California, Berkeley and his colleagues have invented "photoswitch" chemicals that confer light sensitivity on these normally light-insensitive ganglion cells, restoring light perception in blind mice. An earlier photoswitch required very bright ultraviolet light, making it unsuitable for medical use. However, a new chemical, named DENAQ, responds to ordinary daylight. Just one injection of DENAQ into the eye confers light sensitivity for several days.

Experiments on mice with functional, nonfunctional, or degenerated rods and cones showed that DENAQ only impacts [ganglion cells](#) if the rods and cones have already died. It appears that degeneration in the outer retina leads to changes in the electrophysiology in the inner retina that enables DENAQ photosensitization, while the presence of intact photoreceptors prevents DENAQ action.

The selective action of DENAQ on diseased tissue may reduce side effects on healthy retina, exactly what is desired from a vision-restoring drug. "Further testing on larger mammals is needed to assess the short- and long-term safety of DENAQ and related chemicals," says Dr. Kramer. "It will take several more years, but if safety can be established, these compounds might ultimately be useful for restoring [light sensitivity](#) to blind humans. How close they can come to re-establishing normal vision remains to be seen."

More information: *Neuron*, Tochitsky et al.: "Restoring visual function to blind mice with a photoswitch that exploits electrophysiological remodeling of retinal ganglion cells."
dx.doi.org/10.1016/j.neuron.2014.01.003

Provided by Cell Press

Citation: Newly developed chemical restores light perception to blind mice (2014, February 19) retrieved 31 March 2023 from <https://medicalxpress.com/news/2014-02-newly-chemical-perception-mice.html>

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