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Light-responsive ligands activate retinal neurons to repair vision loss in blind mice

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Retinitis pigmentosa, age-related macular degeneration, and other retinal diseases lead to the deterioration of photoreceptors, the light-sensing cells in the eye. Eventually, this deterioration progresses to vision loss. Although there are several therapies in development to reverse retinal disease-related blindness, each is associated with safety concerns related to long-term stability. In mouse models of retinal disease, light-sensitive molecules known as photoswitches have been shown to restore light responses to damaged retinas. The ability to control the duration and application frequency of photoswitches, which are applied as a pharmacological therapy, makes them an attractive alternative approach to treating vision loss.

In this issue of the *JCI*, research led by Russ Van Gelder at the University of Washington describes diethylamino-azo-diethylamino (DAD), a third-generation photoswitch that is capable of restoring visual function in blind mice.

The design of DAD enables it to exist in charged and uncharged forms, which helps the light-sensitive molecule dissolve easily in solution and also ensures adequate delivery to retinal circuitry. DAD activates efficiently when exposed to blue or white light and rapidly reverts to its inactive form in darkness.

In mice, DAD application restored light responses primarily by photosensitizing bipolar cells, the retinal neurons that receive and integrate input from photoreceptors.

This preference for acting through bipolar cells give DAD distinct advantages over previously-developed photoswitches because taking advantage of existing retinal processing may enable better resolution of complex visual stimuli, such as movement.

More information: Laura Laprell et al, Photopharmacological control of bipolar cells restores visual function in blind mice, *Journal of Clinical Investigation* (2017). DOI: 10.1172/JCI92156

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