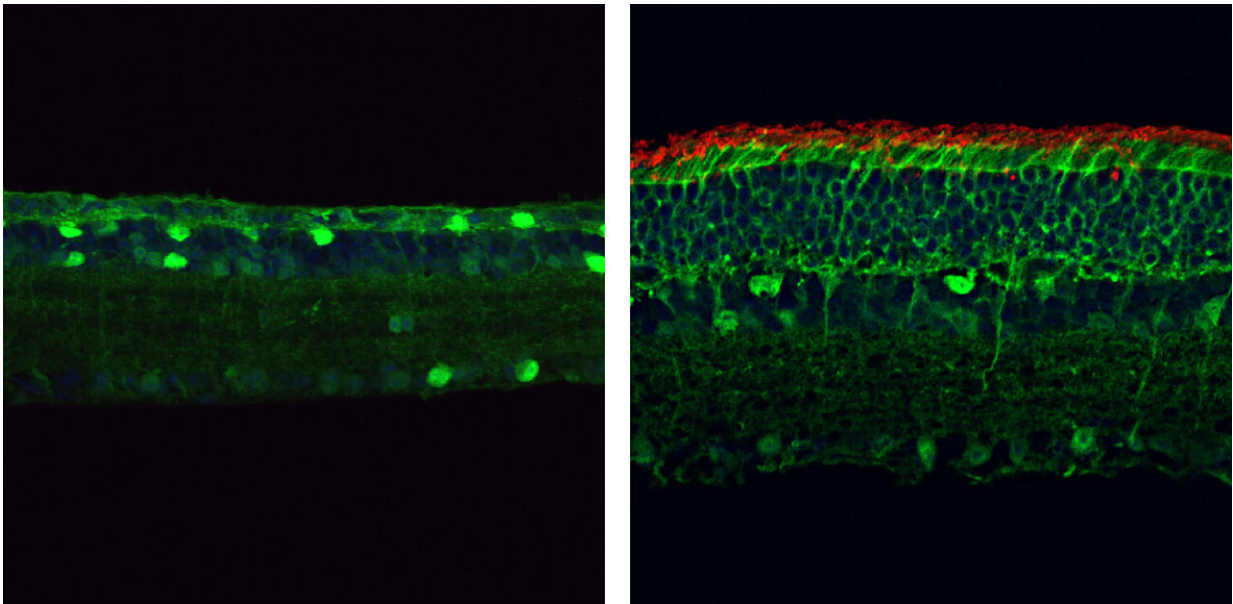


New gene-editing technique reverses vision loss in mice

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By the age of four months, the retinas of mice carrying a mutation in the gene encoding PDE6 β (left) are thin and lack rod photoreceptors (red). But mice who have had this mutation corrected through the PEsPRY system (right) have much thicker retinas containing numerous rod cells. Credit: © 2023 Qin et al.

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Researchers in China have successfully restored the vision of mice with retinitis pigmentosa, one of the major causes of blindness in humans. The study, to be published March 17 in the *Journal of Experimental*

Medicine, uses a new, highly versatile form of CRISPR-based genome editing with the potential to correct a wide variety of disease-causing genetic mutations.

Researchers have previously used genome editing to restore the vision of mice with [genetic diseases](#), such as Leber [congenital amaurosis](#), that affect the [retinal pigment epithelium](#), a layer of non-neuronal cells in the eye that supports the light-sensing rod and cone photoreceptor cells. However, most inherited forms of blindness, including [retinitis pigmentosa](#), are caused by [genetic defects](#) in the neural photoreceptors themselves.

"The ability to edit the genome of neural retinal cells, particularly unhealthy or dying photoreceptors, would provide much more convincing evidence for the potential applications of these genome-editing tools in treating diseases such as retinitis pigmentosa," says Kai Yao, a professor at the Wuhan University of Science and Technology.

Retinitis pigmentosa can be caused by mutations in over 100 different genes and is estimated to impair the vision of 1 in 4,000 people. It begins with the dysfunction and death of dim light-sensing rod cells, before spreading to the [cone cells](#) required for [color vision](#), eventually leading to severe, irreversible vision loss.

Yao and colleagues attempted to rescue the vision of mice with retinitis pigmentosa caused by a mutation in the gene encoding a critical enzyme called PDE6 β . To do this, Yao's team developed a new, more versatile CRISPR system called PE^{SpRY}, which can be programmed to correct many different types of genetic mutation, regardless of where they occur within the genome.

When programmed to target the mutant PDE6 β gene, the PE^{SpRY} system was able to efficiently correct the mutation and restore the enzyme's

activity in the retinas of mice. This prevented the death of rod and cone photoreceptors and restored their normal electrical responses to light.

Yao and colleagues performed a variety of behavioral tests to confirm that the gene-edited mice retained their vision even into old age. For example, the animals were able to find their way out of a visually guided water maze almost as well as normal, healthy mice and showed typical head movements in response to visual stimuli.

Yao cautions that much work still needs to be done to establish both the safety and efficacy of the PE^{SpRY} system in humans. "However, our study provides substantial evidence for the in vivo applicability of this new genome-editing strategy and its potential in diverse research and therapeutic contexts, in particular for inherited retinal diseases such as retinitis pigmentosa," Yao says.

More information: Huan Qin et al, Vision rescue via unconstrained in vivo prime editing in degenerating neural retinas, *Journal of Experimental Medicine* (2023). [DOI: 10.1084/jem.20220776](https://doi.org/10.1084/jem.20220776)

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