Gene editing technique improves vision in rats with inherited blindness

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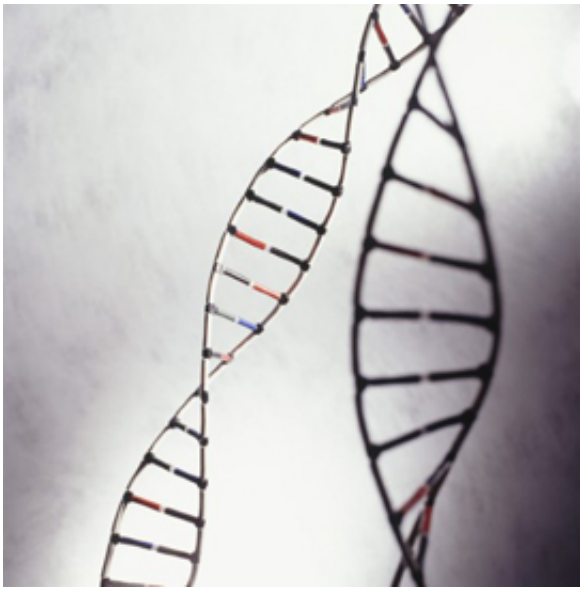

Credit: NIH

A new technique that has the potential to treat inherited diseases by removing genetic defects has been shown for the first time to hinder retinal degeneration in rats with a type of inherited blindness, according to a Cedars-Sinai study.

A research team at the Cedars-Sinai Board of Governors Regenerative Medicine Institute focused on inherited retinitis pigmentosa, a degenerative eye disease with no known cure that can lead to blindness. The researchers used a technique known as CRISPR/Cas9 to remove a

genetic mutation that causes the blindness disease. CRISPR/Cas9 is adapted from a strategy used by bacteria to fight invading viruses. Although the study involved rats, it is an important milestone because of its potential implications for humans.

"Our data show that with further development, it may be possible to use this gene-editing technique to treat inherited retinitis pigmentosa in patients," said Shaomei Wang, MD, PhD, a research scientist in the institute's Eye Program and associate professor of Biomedical Sciences. Wang was the senior author of the study, published in the journal *Molecular Therapy*.

Retinitis pigmentosa is a class of diseases in which patients experience night blindness in the early stages, along with atrophy and pigment changes in the retina, constriction of the visual field and eventual blindness, according to the National Institutes of Health. While rare overall, it is one of the most common inherited diseases of the retina, affecting about 1 in 4,000 people in the U.S. and Europe. CRISPR/Cas9, the technique that Cedars-Sinai scientists used to target retinitis pigmentosa, has been in use by genetic researchers for less than five years. In that time, it has transformed the science of genome editing by making the process easier, more dependable and less expensive.

The technique is adapted from a system that bacteria deploy to disable invading viruses. The bacteria first copy part of the invader's genetic code into a special sequence of ribonucleic acid (RNA), which acts a messenger to carry out the code's instructions. When the virus returns, the RNA binds to a protein called Cas9, guiding it to the matching gene in the virus. The protein disables the gene. By modifying this system, scientists can program Cas9 to turn selected genes on or off, or rewrite the genetic code. (CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeat, the type of DNA sequences involved in this process.)

In the study, the Cedars-Sinai researchers designed a CRISPR/Cas9 system to remove a mutated gene that causes photoreceptor cell loss in the eye. They injected this system into young laboratory rats that had been engineered to model a type of inherited retinitis pigmentosa known as autosomal dominant, which involves this mutated gene. After a single injection, the rats were able to see better compared with controls, as measured by optomotor reflex, which involves turning the head in response to moving stripes of varying degrees of brightness.

Clive Svendsen, PhD, a co-author on the study, said the effectiveness and consistency of these results may be improved by modifying elements of the CRISPR/Cas9 system and using new viral delivery techniques. In the future, after more research, he believes that reliable genome editing through this system may provide a means to correct a wide range of inherited diseases in patients.

"This is the first time CRISPR/Cas9 gene editing has been used to prevent vision loss in a living animal. It is a truly remarkable result and paves the way for more exciting studies and translation to the clinic in the future," said Svendsen, director of the Board of Governors Regenerative Medicine Institute and the Kerry and Simone Vickar Family Foundation Distinguished Chair in Regenerative Medicine.

Provided by Cedars-Sinai Medical Center