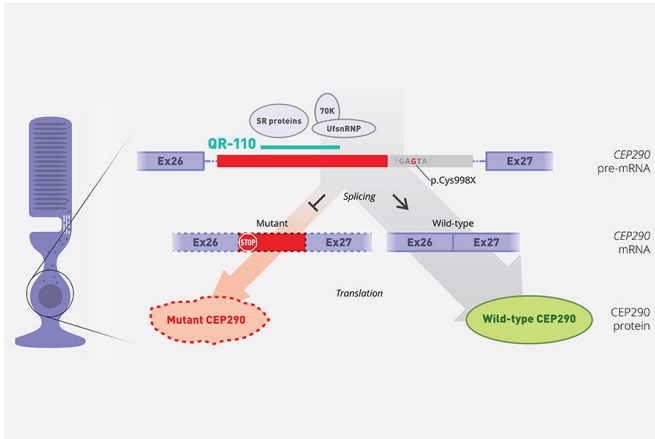


Injection improves vision in a form of childhood blindness

17 December 2018



QR-110 Mechanism of Action: In wild-type cells, splicing results in correct transcripts and therefore normal functional protein. In cells carrying the p.Cys998X mutation a cryptic splice site is also recognized. Thus two types of transcripts are produced: a mutant transcript, and a wild-type transcript. When QR-110 is present, the recognition of the cryptic splice site is blocked, and the production of wild-type transcripts is favored. Credit: Perelman School of Medicine at the University of Pennsylvania

A new treatment for patients with a form of congenital retinal blindness has shown success in improving vision, according to results published today in *Nature Medicine* led by researchers at the Scheie Eye Institute in the Perelman School of Medicine at the University of Pennsylvania.

The treatment was designed for patients with CEP290 mutations and a diagnosis of Leber congenital amaurosis (LCA). CEP290 acts as a gate between two compartments of photoreceptor cells—a type of sensory neuron in the retina that converts light into signals that provide vision. Primary photoreceptor blindnesses—such as those caused by CEP290 mutations—are the most common form of LCA and they are currently not

treatable.

In this clinical study at sites in the United States and Europe, participants received an intraocular injection of an oligonucleotide—a short RNA molecule—created to reduce the mutant CEP290 protein levels in the photoreceptors and restore retinal function.

"It was very dramatic to see one of the patients improve from only being able to differentiate light or dark to reading many letters on an eye chart at two months following the first injection," said lead author Artur V. Cideciyan, Ph.D., a research professor of Ophthalmology. "So, we performed a thorough interim analysis of all results from all patients."

Ten patients received at least one injection into their worst-seeing eye. At three months after the first injection, half of the patients showed improvements in visual acuity, measured by the ability to either read letters, or distinguish direction of black and white bars.

The most basic functions of photoreceptors are to receive and then signal light. This aspect of vision was tested in patients by presenting flashes of light in the dark and measuring the dimmest flash intensity detected. Treated eyes could detect on average more than six-fold dimmer lights three months after the injections compared to before. The results were highly statistically significant. Evaluations with two colors of flashes suggested that it was the cone photoreceptors used for daytime vision that were improving with the treatment.

"This therapy to repair the [genetic defect](#) in LCA10 is a breakthrough in treatment strategy and will open the door for [clinical trials](#) in other patients with this condition and other similar conditions that are currently untreatable," said Samuel G. Jacobson, MD, Ph.D., a professor of ophthalmology and co-

lead author of the study.

All patients enrolled so far into the study had two different CEP290 mutations. The p.Cys998X mutation causing a splicing defect was common in all patients and was specifically targeted by the oligonucleotide.

"We performed an extreme form of personalized medicine where we targeted not just a specific gene but a specific mutation in a gene," said Cideciyan. "It is gratifying to see [clinical evidence](#) supporting the action of this oligo predicted from basic science. In the future, we hope to evaluate patients carrying two identical splicing mutations to determine whether the efficacy of the injection might be even greater."

The authors note that the clinical trial is ongoing to measure safety and efficacy of the injections long-term and the effects of further doses.

More information: Artur V. Cideciyan et al, Effect of an intravitreal antisense oligonucleotide on vision in Leber congenital amaurosis due to a photoreceptor cilium defect, *Nature Medicine* (2018). [DOI: 10.1038/s41591-018-0295-0](https://doi.org/10.1038/s41591-018-0295-0)

Provided by Perelman School of Medicine at the University of Pennsylvania

APA citation: Injection improves vision in a form of childhood blindness (2018, December 17) retrieved 16 May 2021 from <https://medicalxpress.com/news/2018-12-vision-childhood.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.