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## Treatment Of Inherited Retinal Disease

Tech ID: 32368 / UC Case 2020-637-0

### BRIEF DESCRIPTION

Researchers at UCI have developed a method of treating inherited retinal diseases, such as Leber congenital amaurosis (LCA) and retinitis pigmentosa, by gene therapy of the RPE65 nonsense mutation. This method uses base editor-mediated genome-editing by viral delivery and lead to improved patient treatment through enhanced editing of single base pairs and reduced off-target genomic editing.

### SUGGESTED USES

Gene therapy: This therapy can treat the inherited retinal diseases Leber congenital amaurosis (LCA) and retinitis pigmentosa.

### FEATURES/BENEFITS

- Long-lasting:** Base-editing directly alters the genome in RPE cells, which allows a non-diminishing therapy that should last a patient's lifetime.
- Precise:** By using adenosine-base editing and precise single-guide RNAs, this therapy minimizes undesired insertions and deletions effects and does not cause double stranded-breaks.
- Versatile:** This base-editing technology can be translated to nearly any mutations, such as loss-of- or gain-of-function for genes of any size, since only the point mutations will be directly corrected.
- Safe:** This therapy can be delivered by AAV or nanoparticle delivery for safely expressing the cassette without genome integration.

### TECHNOLOGY DESCRIPTION

Leber congenital amaurosis (LCA) constitutes approximately 10% of childhood inherited blindness cases, and most LCA patients have severe visual impairment and become legally blind due to progressing retinal degeneration. RPE65 encodes a critical enzyme in the retinal pigment epithelium, and loss-of-function mutations in RPE65 is one of the common causes of inherited retinal diseases, making this gene an important target for therapy.

Recently, the FDA approved the first gene therapy for LCA patients with biallelic mutations in RPE65; specifically, treatment involves delivering a full-sized functional copy of RPE65 that is expressed in an adeno-associated virus (AAV) vector. Although this AAV-mediated delivery has proven to enhance visual sensitivity for the first year, LCA patients often continue to suffer further retinal degeneration and undergo a relapse in visual sensitivity after one to three years. Moreover, the FDA-approved AAV gene augmentation is limited to solely correcting loss-of-function mutations in small-sized genes.

UCI researchers have improved the current method of LCA therapy by using an adenosine base-editor and single-guide (sgRNA) cassette. Adenosine base editing has the advantage of being more precise than traditional CRISPR editing because adenosine deaminase will directly change single bases within the genome. This newer base editing approach also reduces the chance of undesirable gene insertions and deletions because it does not make double stranded DNA breaks. This treatment approach can be adapted to a variety of inherited retinal diseases, both loss-of- and gain-of-function mutations, because the sgDNA can

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### INVENTORS

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### OTHER INFORMATION

### CATEGORIZED AS

- » **Medical**
  - » Delivery Systems
  - » Disease: Ophthalmology and Optometry
  - » Gene Therapy
  - » Therapeutics

### RELATED CASES

2020-637-0

target small- and large-sized genes.

## STATE OF DEVELOPMENT

Researchers have tested the single base-editing therapy on in vivo mouse LCA-models and demonstrate successful correction of homologous RPE65 nonsensemutation. Future directions involve adapting the successful mouse sgRNA to human sequence and testing any off-target and visual phenotypic effects in clinical settings.

## PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20230190893	06/22/2023	2020-637

## RELATED MATERIALS

» Suh, Susie et al. "Restoration of visual function in adult mice with an inherited retinal disease via adenine base editing." Nature biomedical engineering vol. 5,2 (2021): 169-178. doi:10.1038/s41551-020-00632-6 - 10/19/2020

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

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