Docket #: S19-014

Gene therapy for optic neuropathies

Stanford researchers have developed a gene therapy that combines a retinal ganglion cell (RGC)- specific promoter with CRISPR gene editing to provide effective neuroprotection in optic neuropathies. Optic neuropathies are a group of optic nerve diseases characterized by the progressive death of RGCs and optic nerve degeneration. Optic neuropathy is the most common clinical cause of irreversible blindness. There is no effective neuroprotective treatment to prevent RGC/optic nerve degeneration. Genes involved in RGC signaling have been found to play roles in RGC/optic nerve degeneration and thus serve as potential gene therapy targets. However, before effective gene therapies can be developed a method to specifically target the RGCs is needed. To help meet this need, the inventors identified a promoter that specifically and potently sustains transgene expression in RGCs. They then developed a gene therapy method to treat optic neuropathy that combines this RGC-specific promoter with CRISPR gene editing targeted to the ER stress and/or UPR pathway. This technology provides a much-needed neuroprotective treatment for optic neuropathies.

Stage of research
The inventors performed a proof-of-concept study using a mouse optic nerve crush in vivo axon injury model. This study showed that combining the RGC-specific promoter with CRISPR gene editing of endogenous pro-degenerative genes in an AAV-mediated gene therapy increases survival of RGC somata and axons and promotes functional recovery.

Applications

- Gene therapy for optic neuropathies including:
    - Glaucoma
    - Optic neuritis
    - Optic nerve traumatic injury

Advantages

- Solves an unmet need- provides an effective neuroprotective method for treatment of optic neuropathy
- This technology provides:
    - Novel therapeutic targets
    - New RGC-specific promoter for use in gene therapy
    - New AAV-based gene therapy for neuroprotection
- RCG-specific promoter- reduces unwanted gene expression in other retinal cells

Publications

- Q. Wang, et al Mouse ɣ-Synuclein Promoter-Mediated Gene Expression and Editing in Mammalian Retinal Ganglion Cells *The Journal of Neuroscience* May 13, 2020.
- Huang, H., Miao, L., Liang, F. et al. Neuroprotection by eIF2a-CHOP inhibition and XBP-1 activation in EAE/optic neuritiss. *Cell Death Dis* 8, e2936 (2017).

Patents

- Published Application: WO2020176862
- Published Application: 20220133910
- Issued: 12,496,356 (USA)

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