Docket #: S21-363

Neuroprotective Gene Therapy for Glaucoma

The Hu Lab at Stanford has developed a neuroprotective gene therapy for treating glaucoma and other optic neuropathies. Their gene therapy AAV vector expresses NMNAT2 operably linked to a retinal ganglion cell-specific promoter (mSngc). NMNAT2 is an enzyme enriched in axons and critical for NAD+ synthesis. The researchers found that they can drive expression of NMNAT2 in retinal ganglion cells and increase NAD+ levels, which significantly protect the RGCs and optic nerves in two mouse models *in vivo*: traumatic optic nerve crush model and SOHU glaucoma model. This promising neuroprotective gene therapy has high translational potential. Currently, the lack of neuroprotective treatments for retinal ganglion cells and optic nerves is a central challenge for glaucoma management. The only available treatments act by reducing intraocular pressure, but fail to completely prevent the progression of glaucomatous neurodegeneration. Novel neuroprotective treatments are urgently needed.

Related Technologies
Stanford docket S21-382 describes repurposed neuroprotective agents and a novel therapeutic target for the treatment of glaucoma and other optic neuropathies.

See Stanford docket S19-014 for more on the Hu team's foundational work on neuronal ER stress and AAV-mediated gene therapy strategy.

Stanford docket S19-013 describes glaucoma animal models based on silicone oil-induced mild/chronic and severe/acute reversible ocular hypertension.

Stage of Development
Research *in vivo*.

Applications

- This AAV vector may be developed into gene therapy vehicle for clinical trials of glaucoma.
- Treatment for other optic neuropathies and optic nerve (ON) axonopathies, e.g., retinal ganglion cell degeneration, optic neuritis, ON traumatic injury and other ON-related diseases.

Advantages

- The decrease of neuronal NAD+ level has been linked to many neurodegenerative diseases, including glaucoma.
- Increasing NAD+ in neurons is a promising neuroprotection strategy.
- Current treatment methods include uptake of NAD+ precursors, which requires lifelong delivery.

Publications

- Fang, Fang, et al. "NMNAT2 is downregulated in glaucomatous RGCs, and RGC-specific gene therapy rescues neurodegeneration and visual function." *Molecular Therapy* (2022).

Patents

- Published Application: WO2023086770
- Published Application: 20240293581

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