Docket #: S22-219

HDAC4-mediated neuroprotection

Stanford scientists have developed a neuroprotective, adeno-associated virus (AAV) gene therapy vector that expresses a mutant form of HDAC4 or a fragment of HDAC4 with novel applications to retinal and neurologic diseases, including glaucoma and other retinal ganglion cell diseases.

Glaucoma, a leading cause of irreversible blindness globally, affects over 2.7 million individuals over 40 in the United States. Glaucoma comprises progressive degeneration of retinal ganglion cells. Degeneration of these nerves results in cupping, a characteristic appearance of the optic disc, and visual loss. Currently, glaucoma is treated by lowering intraocular pressure. However, this strategy is not always effective. Another possible way to treat glaucoma is by preventing neurodegeneration in glaucoma through neuroprotective HDAC4. HDAC4 is a Class II histone deacetylase (HDAC), a group of catalytic subunits of multiprotein complexes that alter chromatin structure and repress gene expression via binding to site-specific transcription factors. HDAC4 neuroprotection occurs in the nucleus and is mediated by preventing abortive cell cycle progression.

The current invention presents an AAV therapy that confers neuroprotection of retinal ganglion cells in glaucoma. The packaged vector is also useful for other retinal ganglion cell and central nervous system diseases and traumatic injury.

Stage of Development
Proof of concept

Applications

- Treatment for glaucoma and other retinal ganglion cell diseases to be injected into the eye by ophthalmologists.
- Treatment of non-ocular CNS injuries, including following trauma to the spinal cord.
- Treatment of other neurological disorders, including stroke.

Advantages

- A new AAV gene therapy vector that expresses a mutant form of HDAC4 or a fragment of HDAC4.
- Novel application of HDAC4 NT for the treatment of retinal and neurologic diseases.

Patents

- Published Application: WO2024010709
- Published Application: 20250179463

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