ANTISENSE OLIGO TO ENHANCE NEURONAL SURVIVAL IN HUNTINGTON'S DISEASE

Oh, Youngmi, Yoo, Andrew
Richards, Jennifer

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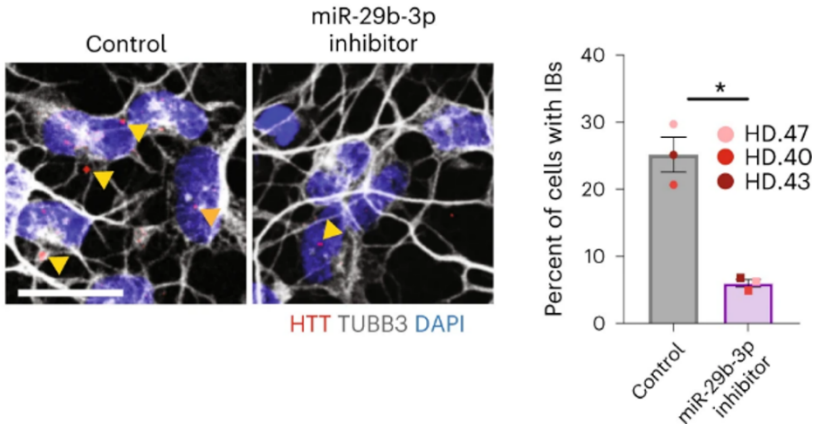
Value Proposition: *Novel antisense oligonucleotide (ASO) directly targeting a microRNA-mediated mechanism responsible for autophagy reduction and neurodegeneration in Huntington's disease (HD) improving patient outcomes in pre-HD subjects.*

Technology Description

Researchers at Washington University in St. Louis have developed an antisense oligonucleotide (ASO) inhibiting a miRNA (miR-29b-3p) as a treatment for Huntington's disease (HD) by promoting neuronal survival and rescuing neurons from degeneration. MiR-29b-3p is an age-associated miRNA significantly upregulated in post-onset HD medium spiny neurons (MSN). Increasing miR-29b-3p results in significant decreases in autophagy activity and induces neuronal degeneration in pre-HD-MSN.



Figures: Images (left) and quantification (right) of HD-MSNs. Inhibition of miR-29b results in significant reduction of cells with IBs, alleviating neuronal degeneration.

Stage of Research

Researchers have validated this invention using multiple MSNs reprogrammed from patient fibroblasts, showing that miR-29b-3p promotes HD-MSN degeneration by downregulating STAT3, a key regulator of autophagy and cell death. Promisingly, the miR-29b-3p ASO increases/restores STAT3 in HD-MSNs.

Publications

Oh, Y.M., Lee, S.W., Kim, W.K. et al. Age-related Huntington's disease progression modeled in directly reprogrammed patient-derived striatal neurons highlights impaired autophagy. Nat Neurosci 25, 1420–1433 (2022).

Applications

- Treatment for Huntington's Disease.

Key Advantages

- Effective rescue of HD-MSN from neuronal degeneration.
- miR-29b-3p/STAT3 interaction is identified to be specific to humans.

Patents

US Non-provisional patent application pending - Application #18/348,263

Related Web Links: Yoo Profile & Lab