Washington University in St. Louis
Office of Technology Management

ANTISENSE OLIGO TO ENHANCE NEURONAL SURVIVAL IN HUNTINGTON'S DISEASE

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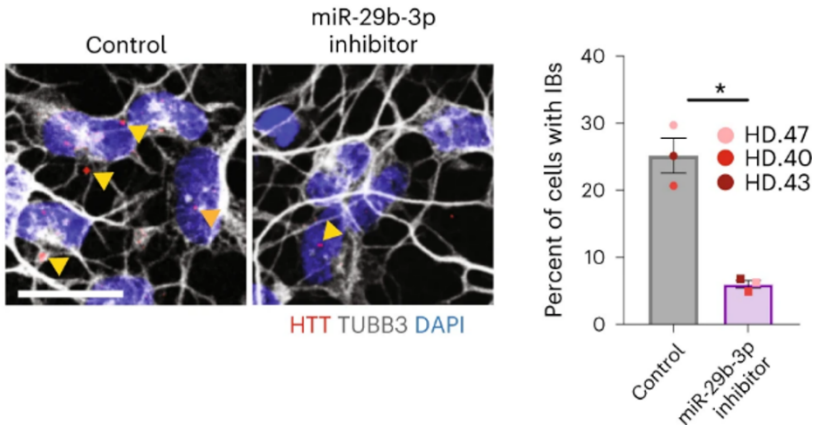
Technology Description

Researchers in Andrew Yoo's laboratory at Washington University have developed an antisense oligonucleotide targeting a miRNA (miR-29b-3p) as a treatment for Huntington's disease (HD). Inhibiting miR-29b-3p promotes neuronal survival by 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.



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 multiple patient samples, showing that miR-29b-3p promotes HD-MSN degeneration by specifically downregulating STAT3, a key regulator of autophagy and cell death. Promisingly, the miR-29b-3p inhibitor is able to increase/restore STAT3 in several HD-MSNs through its inhibition of miR-29b-3p.

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: Pending

Related Web Links: Yoo Profile & Lab