miRNA-based gene therapy for Parkinson's Disease

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Technology description

Summary

Accumulation of the protein a-Synuclein (aSyn) in dopaminergic neurons is believed to be a cause of the neuronal death that leads to Parkinson's Disease. While modulation of aSyn expression through RNA interference is a promising therapeutic approach, many existing nucleic acid constructs are exogenously derived and suffer from low potency, causing off-target toxicity or other side effects. This technology employs synthetic microRNAs (smiRNAs) to reduce aSyn accumulation in dopaminergic neurons. By leveraging the endogenous gene regulation system, this approach provides a highly efficient and targeted therapy for Parkinson's Disease.

Leveraging endogenous gene regulation mechanisms for a more potent therapy

miRNAs are naturally occurring short RNA strands that play a critical role in post-transcriptional regulation of gene expression. This technology employs synthetic miRNAs that structurally resemble endogenous miRNAs involved in regulation of aSyn expression. By taking advantage of existing endogenous gene regulation mechanisms in which the target sites permit specific access by miRNAs, the use of smiRNAs is likely to be more efficient than other, exogenously-derived RNA interference approaches, thereby reducing unwanted side effects. To further increase their potency and enhance uptake by dopaminergic neurons, smiRNAs can be conjugated with glycoproteins that target specific neurotransmitter receptors. These constructs can be delivered via intracerebral injection.

Significant reduction of aSyn levels in dopaminergic neurons following treatment with a smiRNA-glycoprotein conjugate has been demonstrated in a murine model.

Publications

Rhinn H, Qiang L, Yamashita T, Rhee D, Zolin A, Vanti W, Abeliovich A. "Alternative a-synuclein transcript usage as a convergent mechanism in Parkinson's disease pathology" Nat Commun. 2012;2:1084.

Application area

Treatment of neurodegenerative diseases such as Parkinson's Disease and Alzheimer's Disease

Rescue of dopaminergic neurons

Targeted reduction of pathological gene overexpression

Development of more potent miRNA-based gene therapies for other diseases

Advantages

Leverages existing endogenous regulation mechanism for more efficient miRNA-target interaction

Reduces likelihood of side effects related to introduction of toxic exogenous constructs

Has been validated in vitro and in vivo in a murine model

Provides methods to develop targeted gene therapies for other diseases

Institution

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