Targeting Oxidative Stress for Parkinson’s Disease Therapy

Adeno-Associated Virus (AAV) Vector-Mediated Knockdown of NADPH Oxidase1 (Nox1)

Parkinson’s disease (PD) is a progressive neurodegenerative disorder characterized by the aggregation of α-synuclein proteins and the progressive loss of dopaminergic neurons. Oxidative stress is a major contributing factor in the pathogenesis of PD and has been linked to both α-synuclein aggregation and subsequent dopaminergic neuron death. The NADPH oxidase family (Nox), a specialized reactive oxygen species (ROS) generation system, is activated in dopaminergic neurons under stress conditions and has been associated with many neurodegenerative diseases, including PD and Alzheimer’s disease.

Technical Summary

UCF researchers have identified Nox1, an isoform of the Nox family, as a crucial mediator of oxidative stress and consequent dopaminergic neuron death. To inhibit Nox1 expression and activity, a selective adeno-associated virus (AAV) vector targeting system was developed against Nox1. The AAV vector expressing RNA interfering molecules against Nox1 (Nox1-specific shRNA) was stereotaxically injected into the substantia nigra of PD animal models. Knockdown of Nox1 significantly reduced oxidative stress, α-synuclein aggregation, and dopaminergic neuronal death in the treated animals. Inhibition of Nox1 represents a potential new therapeutic target for PD therapy and other α-synucleinopathies-based neurodegenerative diseases.

Applications

• Selective AAV vector targeting system to reduce the expression and activity of Nox1

Benefits

• Decreases Nox1 protein levels, oxidative stress, α-synuclein aggregation, and dopaminergic neurodegeneration
• Targets an upstream source of oxidative stress
• Demonstrates activity in in vitro and in vivo PD models

Technology #32897

• US Patent 9,394,544

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