Docket #: S22-089

Viral gene transfer of mutant CRISPR/Cas9 to modulate human alpha-synuclein expression as a precision gene therapy for Parkinson's disease

Stanford researchers have developed a method to target and lower alpha-synuclein, a major protein constituent of Lewy bodies that accumulate in the brain in Parkinson's disease, using viral gene transfer of mutant Cas9 coupled with a small guide RNA targeting the promoter region of the alpha-synuclein gene.

Parkinson's disease is a common cause of morbidity in the aging population. A key feature of Parkinson's disease is the accumulation of a protein called alpha-synuclein, which aggregates into Lewy bodies and results in neuronal death. Alpha-synuclein gene mutations result in early onset and progressive disease, and lowering alpha-synuclein levels alleviates disease. Parkinson's disease has no cure, and current treatments aim to manage symptoms. There is, therefore, a significant need to develop novel therapies for Parkinson's disease.

Therefore, Stanford researchers devised a way to target alpha-synuclein and lower its levels in vivo using viral gene transfer of mutant Cas9 coupled with a small guide RNA targeting the promoter region of the alpha-synuclein gene. Viral gene transfer was achieved using an adeno-associated virus (AAV) vector carrying their specially designed guide RNA delivered intrathecally into the cisterna magna. With this approach, the researchers successfully downregulated alpha-synuclein in a humanized transgenic mouse model.

Stage of Development
Preclinical

Applications

- Gene therapy for Parkinson's disease

Advantages

- Novel Parkinson's disease modulatory treatment

Patents

- Published Application: WO2023178280

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