Further development of a systemic gene therapy treatment for Parkinson’s

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Name of Fellow

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Institution
Funder

Parkinson's UK

Contact information of fellow
Country

United Kingdom

Title of project/programme

Further development of a systemic gene therapy treatment for Parkinson's

Source of funding information

Parkinson's UK

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€ 420,358

Start date of award

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5.5

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Neuroprotection | Gene therapy | Cell biology

Research Abstract

Gene therapy is one of the most promising tools for the treatment of Parkinson’s, however one

of the major challenges facing this approach is the development of a gene therapy vehicle for widespread delivery to the brain. We have developed a gene therapy vehicle based on targeted exosomes which we have shown are capable of selectively targeting the delivery of siRNA to brain resulting in gene silencing after intravenous administration. Alpha-synuclein aggregation plays a central role in PD pathology and increased expression or decreased degradation may be key features in its mechanism. Consequently an obvious initial target is alpha-synuclein. The first aim is to evaluate the efficacy of normal and modified siRNA delivery by RVG-exosomes to silence alpha-synuclein expression in mice. The second aim is to develop this system for long-term silencing within the brain using minicircles expressing shRNA (shRNA MC). As a model system we will target the fluorescent EGFP protein. We will optimise the sequences, constructs and electroporation conditions in SH-SY5Y cells over-expressing EGFP. Subsequently, we will evaluate the efficacy of long-term silencing by shRNA MC delivery by RVG-exosomes to silence EGFP expression in the brain of transgenic EGFP-mice. Finally, we will silence the expression of human WT and phospho-mimic S129D alpha-synuclein expressed in mice using shRNA MC. Alpha-synuclein silencing will be evaluated by qPCR, western blot and immnuhistochemistry throughout the brain. These studies will allow us to continue to develop this gene delivery vehicle and identify its suitability for use in the treatment of Parkinson’s.

Types:
Fellowships

Member States:
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Parkinson's disease & PD-related disorders

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