Development of in vivo gene therapy methods to treat Parkinson’s disease.

https://www.neurodegenerationresearch.eu/survey/development-of-in-vivo-gene-therapy-methods-to-treat-parkinson%c2%92s-disease/

Question
Principal Investigators

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Related
Institution

Lund University

Contact information of lead PI
Country

Sweden

Title of project or programme

Development of in vivo gene therapy methods to treat Parkinson’s disease.

Source of funding information

The Swedish Brain Foundation

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€ 108,814

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01/07/2015

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2.5

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Research Abstract

This project is based on the idea that to be a viable clinical option, gene therapy needs to be cell-specific
and regulatable, which optimizes efficacy and minimizes side effects.
My group has pioneered the development of cell-specific, disease auto-regulated lentiviral vectors for gene therapy (Jakobsson et al, 2003, 2004, 2006, Nielsen et al, 2009, Wettergren et al, 2012). The vectors offer a possibility to deliver a therapeutic substance to a specific cell type,

e.g. astrocytes, and have the transgene expression vary in accordance with the severity of the disease, in this case astrogliosis. Furthermore, we have developed vectors that can be regulated by oral drug delivery based on protein stability rather that transcriptional activity (Tai et al, 2012, Quintino et al, 2013). At this point we will make use of the technology we have developed, further refine it and utilize it as a base for therapeutic approaches in models of Parkinson's disease (PD).
Our main objective in this project is to develop cell-specific lentiviral vectors that can be regulated and used to treat the hallmarks features of PD, as well as be instrumental as research tools for the further understanding of the molecular mechanisms that govern the development of these hallmarks.
Towards this purpose we will investigate the differential expression miRNAs in subpopulations of neurons in the striatum in different states of dopamine signaling status and use this data to develop vectors specific for subpopulations of striatal neurons. Furthermore, using new, innovative retrogradely transported vectors we will test the hypothesis that selective inhibition of signaling molecules in D1-neurons in the striatum will be more effective to ameliorate L-DOPA induced dyskinesia symptoms. Using our recently developed system for transgene regulation we will attempt to reinstate the GDNF response in nigral neurons, that is lost due dysexpression of alpha-synuclein. Moreover, this system will also be used to analyze the longlivety of the neurotrophic outcomes of GDNF expression in a model of Parkinson's disease, thus testing the feasibility of the therapy over long treatment periods in a controlled pre-clinical setting.

Further information available at:

Types:
Investments < €500k

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Sweden

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