Differentiation of GMP-grade human embryonic stem cells to midbrain dopaminergic neurons for transplantation

https://neurodegenerationresearch.eu/survey/differentiation-of-gmp-grade-human-embryonic-stem-cells-to-midbrain-dopaminergic-neurons-for-transplantation/

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Country

United Kingdom

Title of project or programme

Differentiation of GMP-grade human embryonic stem cells to midbrain dopaminergic neurons for transplantation

Source of funding information

MRC

Total sum awarded (Euro)

€ 644,995

Start date of award

02/05/2013

Total duration of award in years

3.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords
Research Abstract
Transplantation of fetal midbrain tissue to treat Parkinson’s disease (PD) has demonstrated proof-of-concept that some patients can benefit from such grafts. An international multi-centre

Framework 7 European clinical trial, TRANSEURO, is underway to re-visit fetal midbrain transplants and systematically address all protocol and procedural issues with the earlier clinical trials. There is a pressing need to resolve the critical questions of scaleable supply and quality of appropriate Good Manufacturing Practice (GMP) grade dopaminergic cells for any future widespread use in the treatment of PD. Replacing fetal midbrain tissue with midbrain dopaminergic (mDA) neurons differentiated from human embryonic stem cells (hESCs) is the most realistic solution to the cell source problem. We will modify and optimise a novel method to differentiate hESCs to mDA neurons, which relies on a developmental protocol based on floor plate specification. GMP-grade hESCs from multiple sources throughout the UK will be quantitatively assessed for efficiency of mDA differentiation. The best performing hESC line will be used to establish procedures to produce GMP-capable mDA preparations for transplantation. All experiments will be performed with research-grade reagents that have a suitable GMP-grade equivalent available. The mDA neuronal populations will be transplanted into two nude rat models of PD (i) a 6-hydroxydopamine lesion model and (ii) an adeno-associated virus-alpha-synuclein model. Graft survival, behavioural improvements, and absence of tumour formation will be assessed. This collaborative proposal will bring together expertise in pluripotent stem cell differentiation, pre-clinical models of PD, and the UK ‘s clinical-grade hESCs, with the ultimate aim of moving to first-in-human clinical trials.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A