Metabolic dysregulation in astrocytes derived from Parkin-mutant patients

https://neurodegenerationresearch.eu/survey/metabolic-dysregulation-in-astrocytes-derived-from-parkin-mutant-patients/

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Country

United Kingdom

Title of project or programme

Metabolic dysregulation in astrocytes derived from Parkin-mutant patients

Source of funding information

Parkinson's UK

Total sum awarded (Euro)

€ 67,790

Start date of award

01/01/2016

Total duration of award in years

1.5

Keywords
Research Abstract
Mounting evidence indicates that astrocytes might be involved in neurodegeneration in Parkinson’s disease (PD). Although the mechanisms involved in astrocyte neurotoxicity are largely unknown, astrocytes are responsible for supporting the metabolic status of neurons. Mitochondrial dysfunction is well established in both familial and sporadic forms of PD. Hypothesis: (i) Metabolic dysfunction in astrocytes derived from Parkin-mutant PD patients affects the viability of dopaminergic neurons. Patient-derived in vitro models (ii) will uncover metabolic defects in PD astrocytes and neurons and (iii) generate powerful tools for drug screening.

Objectives:
1.Generate and characterize astrocytes from Parkin-mutant PD patients
2.Define Parkin-mutant astrocytes metabolic profile
3.Setup co-cultures of astrocytes and neurons from patients and unaffected individuals to determine neuron growth and survival
4.Screen drugs previously identified to be protective in patient fibroblasts and neurons to determine their effect on astrocyte monocultures and co-cultures
Methods:
Aim 1&3: Reprogram fibroblasts from patients and controls to induced neural progenitors (iNPC) and differentiate them into astrocytes and dopaminergic neurons. Successful differentiation will be verified by PCR, Western and immunostaining.
Aim 2&4: In depth measurement of mitochondrial function using spectrophotometric and oxygen consumption methods. Investigate expression levels of the mitochondrial fission/fusion machinery.
Aim 4: Test drugs on astrocyte monocultures and co-cultures with dopaminergic neurons. Assess astrocytes and neuronal mitochondrial function and neuronal growth and survival
Expected outcome: Astrocytes from PD patients are metabolically dysfunctional and this contributes to neuronal degeneration. The in vitro models generated during this grant will likely enable identification of drugs with beneficial effects to patients.

Further information available at:

Types:
Investments < €500k

Member States:
United Kingdom

Diseases:
N/A

Years:
2016

Database Categories:
N/A

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