SynSpread: Role and mechanism of alpha-synuclein and ataxin-3 spreading in Parkinson and Machado-Joseph diseases

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Question
Principal Investigators

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Related
Institution

Multiple

Contact information of lead PI
Country

Portugal|Luxembourg|France

Title of project or programme

SynSpread: Role and mechanism of alpha-synuclein and ataxin-3 spreading in Parkinson and Machado-Joseph diseases

Source of funding information

JPND-Cross Disease

Total sum awarded (Euro)

€ 842,920

Start date of award

01/01/2015

Total duration of award in years

3.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders|Spinocerebellar ataxia (SCA)

Keywords
Research Abstract

Parkinson's disease (PD) and Machado Joseph disease (MJD) represent two incurable prototypical neuro- degenerative diseases associated with protein aggregation and progressive spread of disease in the brain. Preliminary evidence suggest that both disorders share a common mechanism where autophagosome trafficking and exosome secretion intersect. While autophagosomes are important intracellular vesicles for routing proteins and organelles for lysosomal degradation, extracellular microvesicles (exosomes) contain collections of proteins, RNA and lipids that are important cell-to-cell carriers for intercellular signaling-molecules. How this common mechanism causes PD and MJD will be investigated by the Synspread consortium in neurons and astrocytes derived from PD and MJD patients' inducible pluripotent stem cells (iPSC) cells, using state-of-the-art super-resolution imaging of autophagosome and exosome formation/secretion and whole- brain imaging of cleared tissue to trace the routes of synuclein and ataxin-3 protein spreading. The results will be plugged into a novel computational model of aggregate and exosome propagation in the mouse brain to predict disease progression and identify biochemical pathways underlying progression.This SynSpread project is expected to generate unique insights into the process of protein and aggregate spreading in PD, MJD and potentially other neurodegenerative disorders, and to lead to identification of new targets and modifiers for therapeutic intervention in a significant step towards treatment of patients.

Lay Summary
Further information available at:

Types:
Investments > €500k, JPND Projects

Member States:
France, JPND, Luxembourg, Portugal

Diseases:
Parkinson's disease & PD-related disorders, Spinocerebellar ataxia (SCA)

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Database Tags:
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