Prion-like transmission of ?-synuclein in Parkinson’s disease

https://neurodegenerationresearch.eu/survey/prion-like-transmission-of-synuclein-in-parkinsons-disease/

Principal Investigators
Institution
Contact information of lead PI
Country

European Commission

Title of project or programme

Prion-like transmission of ?-synuclein in Parkinson's disease

Source of funding information

European Commission FP7-Seventh Framework Programme

Total sum awarded (Euro)

€ 2,499,998

Start date of award

01/06/2011

Total duration of award in years

5.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords
Research Abstract

Protein misfolding is implicated as a pathogenetic mechanism in several neurodegenerative disorders, including Parkinson¿s disease (PD). In prion disease, the misfolded protein spreads between cells and acts as a ¿permissive template¿, causing protein in the recipient cell to misfold. In 2008 we reported that classical neuropathological changes gradually propagate from a PD patient¿s brain to a graft of healthy neurons, over one decade after surgery. These groundbreaking findings suggest that the protein ¿-synuclei may transfer between cells and propagate protein aggregation in a ¿prion-like¿ fashion in PD. This molecular disease mechanism might explain how protein aggregates gradually spread throughout the nervous system and promote progression of disease symptoms. This highly novel concept represents a hitherto poorly explored route of intercellular communication and might have far-reaching implications well beyond PD. Little is known about how various forms of ¿-synuclein are taken

up; if they seed aggregation in the recipient cell; how they affect proteostasis in the recipient cells; if they are transported axonally; and, finally, whether they can cause spreading of PD-like pathology in the nervous system.
In a multidisciplinary project will now examine the molecular mechanisms underlying translocation of ¿-synuclein across a lipid membrane, from the outside to the inside of a cell; what the molecular and functional consequences are of importing ¿-synuclein; what the dynamics of ¿-synuclein transfer are in vivo; whether aggregates of misfolded ¿-synuclein can spread from one region of the nervous system to another; what genes influence the likelihood for ¿-synuclein transfer to take place; and, finally if small molecules that inhibit ¿-synuclein can be identified. Our studies will shed light on what appears to be a new principle for pathogenesis of neurodegenerative disorders and can open up avenues for new therapeutic strategies.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
European Commission

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
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