

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

<https://www.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 α -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 α -synuclein 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 α -synuclein may transfer between cells and propagate protein aggregation in a α -synuclein-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 α -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 α -synuclein across a lipid membrane, from the outside to the inside of a cell; what the molecular and functional consequences are of importing α -synuclein; what the dynamics of α -synuclein transfer are in vivo; whether aggregates of misfolded α -synuclein can spread from one region of the nervous system to another; what genes influence the likelihood for α -synuclein transfer to take place; and, finally if small molecules that inhibit α -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:

N/A

Database Tags:

N/A