

Deficient Wnt signalling in synapse degeneration and its contribution to Parkinson's Disease

<https://www.neurodegenerationresearch.eu/survey/deficient-wnt-signalling-in-synapse-degeneration-and-its-contribution-to-parkinsons-disease/>

Principal Investigators

Professor PC Salinas

Institution

University College London

Contact information of lead PI Country

United Kingdom

Title of project or programme

Deficient Wnt signalling in synapse degeneration and its contribution to Parkinson's Disease

Source of funding information

MRC

Total sum awarded (Euro)

€ 843,189

Start date of award

01/02/2015

Total duration of award in years

3.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Research Abstract

Mounting evidence suggests that synapse loss and dysfunction are early events in Parkinson's disease. Importantly, synapse vulnerability might contribute to the subsequent degeneration of dopamine neurons. However, little is known about how synapses degenerate. Several studies

support a role for deficient canonical Wnt signalling in PD. To test the contribution of this signalling pathway in neuronal and synaptic degeneration, we generated inducible transgenic mice that express the secreted Wnt antagonist Dickkopf-1 (Dkk1) in the adult striatum. These mice exhibit degeneration of cortico-striatal and dopaminergic synapses accompanied by motor defects without neuronal loss. Thus, these mice provide an ideal model to unravel the mechanisms that contribute to synapse vulnerability. Our main objectives are: 1) What are the mechanisms that trigger synapse degeneration in the adult striatum? Through our high through put analyses we have identified key molecules that are affected during synapse degeneration in Dkk1 mice. We will examine the functional contribution using in vivo gain and loss of function experiments to test their function in synapse vulnerability, neuronal death and motor behaviour. 2) What is the impact of deficiency in Wnt signalling on synaptic transmission and plasticity in the adult striatum? Here we will use electrophysiological approaches to determine the impact of deficient Wnt signalling on striatal circuits using specific transgenic lines that label striatal neurons of the direct and indirect pathways. 3) Does deficient Wnt signalling increase synapse and cell vulnerability in ageing? Although ageing is a major risk factor in PD, little is known about how synapses change and become vulnerable during ageing. We will examine how deficiency in Wnt signalling in the striatum affects synapses in ageing animals.

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