

Targeting Parkin and Mitochondrial Dynamics in Huntington's disease

<https://neurodegenerationresearch.eu/survey/targeting-parkin-and-mitochondrial-dynamics-in-huntingtons-disease/>

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Country

United Kingdom

Title of project or programme

Targeting Parkin and Mitochondrial Dynamics in Huntington's disease

Source of funding information

MRC

Total sum awarded (Euro)

€ 590,489

Start date of award

01/02/2015

Total duration of award in years

3.0

The project/programme is most relevant to:

Huntington's disease

Keywords

Research Abstract

Huntington's disease (HD) is an incurable, fatal neurodegenerative disorder caused by the expansion of a polyglutamine tract in the huntingtin (HTT) protein. This mutation causes HTT to misfold and aggregate, leading to widespread dysfunction and death of vulnerable neurons. As with several other neurodegenerative disorders, the pathogenesis of HD has been closely linked with mitochondrial dysfunction, which includes alterations in mitochondrial dynamics (e.g.

increased mitochondrial fragmentation). In preliminary studies we have recently found that the Parkinson's-linked protein parkin alleviates several disease phenotypes in HD flies when overexpressed. Parkin plays a role in clearance of damaged mitochondria (mitophagy), via modulation of mitochondrial dynamics. Here we propose to further investigate the mechanisms underlying parkin protection in HD fruit flies and a PC12 cell model, and also explore the role of mitochondrial dynamics and mitophagy in pathogenesis of this disorder. We will use genetic approaches to modulate parkin expression in HD models – as well as related proteins (e.g. PINK1, Mfn, Opa1, Drp1) – and ascertain the influence upon mitochondrial phenotypes (e.g. mitochondrial morphology, mitochondrial respiration). Relatedly, as parkin has been found to participate in protein degradation and autophagy of aggregated molecules and reduce proteotoxicity, we will also explore the relationship between parkin and HTT. In total, this work will explore the protective role of parkin in HD, and interrogate mitophagy and mitochondrial dynamics in this disorder. These studies may ultimately contribute to therapeutic strategies for HD.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

United Kingdom

Diseases:

Huntington's disease

Years:

2016

Database Categories:

N/A

Database Tags:

N/A