Investigating the role of Myosin VI in quality control of mitochondria linked to Parkinson’s disease pathology

https://neurodegenerationresearch.eu/survey/investigating-the-role-of-myosin-vi-in-quality-control-of-mitochondria-linked-to-parkinsons-disease-pathology/

Principal Investigators

Dr F Buss

Institution

University of Cambridge

Contact information of lead PI
Country

United Kingdom

Title of project or programme

Investigating the role of Myosin VI in quality control of mitochondria linked to Parkinson's disease pathology

Source of funding information

MRC

Total sum awarded (Euro)

€ 733,816

Start date of award

01/03/2016

Total duration of award in years

3.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords
Research Abstract
In this project we will investigate the molecular function of the actin-based motor protein myosin VI in mitochondrial quality control. Defects in mitochondrial turnover are closely linked to

Parkinson’s disease (PD), the second most common neurodegenerative disorder. A hereditary form of PD is caused by mutations in the E3 ubiquitin ligase Parkin; this protein has been shown to mediate selective autophagy of damaged mitochondria, called mitophagy. Several lines of evidence and data from published large-scale whole genome studies suggest a functional link between Parkin and myosin VI and its cargo adaptors. To test this hypothesis and analyse the link between myosin VI and Parkin in more detail we will use in situ proximity labeling and a combination of confocal fluorescence microscopy, live cell and super-resolution microscopy as well as electron microscopy. To determine the requirement of myosin VI and its adaptor proteins for Parkin-mediated mitophagy, we will use siRNA KD cells, KO cells created by CRISPR/Cas9 genome editing, primary fibroblasts and neurons from our myosin VI KO mouse as well as iPS cells generated from human PD patient fibroblasts. In addition we will employ multiple approaches to assess whether loss of myosin VI or its adaptor proteins affects mitophagy and thereby leads to an accumulation of damaged mitochondria with reduced function.

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