Biochemical analysis of the PINK1-Parkin signalling pathway in Parkinson’s disease.

https://www.neurodegenerationresearch.eu/survey/biochemical-analysis-of-the-pink1-parkin-signalling-pathway-in-parkinsons-disease/

Name of Fellow

Dr Miratul Muqit

Institution
Funder

Wellcome Trust

Contact information of fellow
Country

United Kingdom

Title of project/programme

Biochemical analysis of the PINK1-Parkin signalling pathway in Parkinson's disease.

Source of funding information

Wellcome Trust

Total sum awarded (Euro)

€ 2,867,329

Start date of award

01/07/13

Total duration of award in years

5.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Neurodegen | Parkinson

Research Abstract

Mutations in PTEN-induced kinase 1 (PINK1) cause hereditary Parkinson’s disease (PD).

Understanding how PINK1 mutations lead to PD remains a major question in the PD field. During the last 4 years, my laboratory has made a series of significant advances that have shed light on the regulation and function of the PINK1 kinase. I have found that PINK1 is activated following mitochondrial membrane potential depolarization and that it phosphorylates another PD-linked protein, the RING E3 ligase Parki n, at Serine 65. This leads to activation of Parkin E3 ligase activity. This proposal is aimed at addressing key questions that arise from these findings. I will investigate the mechanism by which PINK1 becomes activated by mitochondrial depolarization. I will utilize highly sensitive monoclonal phospho-specific antibodies to determine whether the PINK1-Parkin pathway is disrupted in patients with sporadic PD. I will investigate the physiological role of the PINK1-Parkin pathway in vivo by ch aracterizing a Parkin Ser65Ala knock-in mouse and determine whether this leads to neurodegeneration or mitochondrial defects. I will employ state-of-the-art mass spectrometry technologies to search for physiological substrate(s) of Parkin whose ubiquitylation is dependent on Parkin phosphorylation at Serine 65 in these mice. I will investigate the function of newly discovered PINK1 substrates, Rab 8a/b and Rab 13. I will elucidate the crystal structure of PINK1. Greater understanding of the role of the PINK1-Parkin pathway in PD may lead to new insights to diagnose, monitor and treat the underlying disease process.

Types:
Fellowships

Member States:
United Kingdom

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A