Analysis of mitochondrial homeostasis in ageing and neurodegeneration

https://neurodegenerationresearch.eu/survey/analysis-of-mitochondrial-homeostasis-in-ageing-and-neurodegeneration/

Principal Investigators

Dr AJ Whitworth

Institution

MRC Centre Cambridge

Contact information of lead PI
Country

United Kingdom

Title of project or programme

Analysis of mitochondrial homeostasis in ageing and neurodegeneration

Source of funding information

MRC

Total sum awarded (Euro)

€ 1,736,780

Start date of award

01/09/2015

Total duration of award in years

5.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders|Motor neurone diseases|Neurodegenerative disease in general

Keywords
Research Abstract

The survival of our most active tissues, such as the brain and heart, throughout decades of a human lifespan presents an extraordinary biological challenge. Mitochondria are central to the life and death of these tissues. They provide the cellular energy required by these cells and protect them by buffering potentially lethal levels of cytoplasmic calcium, while at the same time

mitochondria produce many of the molecules that cause cellular damage and contain a lethal arsenal of apoptotic cell death machinery. Thus, these organelles require exquisite maintenance processes to keep them intact and prevent potentially catastrophic disruption. Failure in mitochondrial homeostasis is strongly linked to age-related conditions such as neurodegeneration. To perform the myriad essential cellular roles in such morphologically elaborate cells as neurons mitochondria must be extremely dynamic organelles. Individual mitochondria must be transported over large distances to respond to changing spatiotemporal demands for energy and calcium buffering. Locally, interaction with multiple other organelles and the mitochondrial network undergoes frequent fission and homotypic fusion events. These dynamic events are known to be important in the regulation of cellular and mitochondrial homeostasis, and been linked to several neurodegenerative disorders. The long-lived, post-mitotic nature of adult neurons permits the accumulation of oxidatively damaged macromolecules. When cellular defence mechanisms become compromised, especially with age, mitochondria are particularly susceptible to accumulated damage. One key mechanism that mediates the destruction of terminally damaged organelles is through the selective degradation by autophagy, known as mitophagy. The identification that two genes linked to Parkinson’s disease, PINK1 and parkin, regulate mitophagy has emphasized the importance of this process to neuronal survival. However, much of our current understanding comes from in vitro studies, so we still have a poor understanding of this process in a physiological context. Our group’s aim is to understand the influence of mitochondrial dynamics on maintaining normal neuronal function and survival, and its impact on neurodegenerative diseases such as Parkinson’s disease and motor neuron disease. We use a combination of the powerful genetic techniques of Drosophila and molecular, cell biology and biochemical approaches in mammalian cells. Insights into these mechanisms will deliver a greater understanding of the role of mitochondrial dynamics in the health and dysfunction of the nervous system in a physiological context and will help guide therapeutic development to combat neurodegenerative diseases.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Motor neurone diseases, Neurodegenerative disease in general, Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A