The role of mitochondrial DNA variation in Parkinson’s

https://neurodegenerationresearch.eu/survey/the-role-of-mitochondrial-dna-variation-in-parkinsons/

Name of Fellow

Dr Gavin Hudson

Institution
Funder

Parkinson's UK

Contact information of fellow
Country

United Kingdom

Title of project/programme

The role of mitochondrial DNA variation in Parkinson's

Source of funding information

Parkinson's UK

Total sum awarded (Euro)

€ 338,116

Start date of award

01/10/12

Total duration of award in years

4.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Molecular biology | Genetic studies | Biomarkers

Research Abstract

Mitochondria are intracellular organelles, whose function is critical to a number of metabolic processes. They are the site of oxidative phosphorylation; the protein components of which are

partly encoded by mitochondrial DNA (mtDNA). Variation in mtDNA can affect the efficiency of oxidative phosphorylation. Increasing evidence links mitochondrial dysfunction to Parkinson’s disease (PD). PD patients have reduced respiratory chain function, specifically in the substantia nigra (SN), and inhibition of respiratory chain components has been shown to cause dopaminergic neuron loss in humans. Studies linking inherited mtDNA variants to PD have been inconclusive, reporting conflicting associations with common mtDNA haplogroups or with rare pathogenic variants. These studies were often underpowered, dependent on poorly defined haplogroup structures, and failed to link mtDNA variation to the somatic mutations well-described in the post mortem SN of PD patients. My hypothesis is that inherited and somatic mtDNA variation is intrinsically linked, combining to make a significant contribution to the multi-factorial aetiology of PD. I will test this hypothesis in two ways: 1) by defining the inherited variants at the whole mitochondrial genome level, and 2) correlating these findings with somatic mutation load in post mortem PD brains. I will utilise a large sample cohort and NGS to address the first point, subsequently addressing the second point by correlating risk conferring variants to somatic mtDNA mutations in post-mortem PD brains. I anticipate that these findings will identify a key component of the disease mechanism of PD, whilst explaining part of the ‘missing heritability’ of PD.

Types:
Fellowships

Member States:
United Kingdom

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A