

# The role of mitochondrial DNA variation in Parkinson's

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

## **Name of Fellow**

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## **Institution**

## **Funder**

Parkinson's UK

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## **Country**

United Kingdom

## **Title of project/programme**

The role of mitochondrial DNA variation in Parkinson's

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Parkinson's UK

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## **The project/programme is most relevant to:**

Parkinson's disease & PD-related disorders

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## **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.

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