# Can we protect neurons against mitochondrial dysfunction?

https://neurodegenerationresearch.eu/survey/can-we-protect-neurons-against-mitochondrial-dysfunction/

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**Funder**

Parkinson's UK

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**Country**

United Kingdom

**Title of project/programme**

Can we protect neurons against mitochondrial dysfunction?

**Source of funding information**

Parkinson's UK

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€ 338,893

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3.0

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

Parkinson's disease & PD-related disorders

**Keywords**

Neuroprotection | Molecular biology | Cell biology

**Research Abstract**

Mitochondrial dysfunction plays an integral role in the pathogenesis of Parkinson’s disease (PD), highlighted by the identification of mitochondrial gene mutations in familial PD. Despite

evidence showing that the neurons of the substantia nigra (SN) are particularly sensitive to mitochondrial dysfunction, the impact of this dysfunction on cellular survival remains unclear. My previous work has shown that SN neurons can tolerate mitochondrial defects occurring early in life, whereas defects in later life cause neuronal loss. This application will build on this success to define the mechanisms by which SN neurons adapt to mitochondrial dysfunction early in life and identify drugs which would allow similar adaptation to mitochondrial defects later in life. Using a library of compounds known to affect mitochondria, I will search for candidates which facilitate adaptation in dopaminergic neurons, with a view to finding new drugs to protect SN neurons from loss. I will use three complementary systems to investigate the response of SN neurons to mitochondrial dysfunction. (1) In human tissue I will investigate the modulation of key pathways in SN neurons harbouring mitochondrial defects. (2) I will use human induced pluripotent stem cells in a phenotypic screen to identify compounds which elicit the same adaptation, protecting dopaminergic neurons against dysfunction. (3) An alpha-synuclein mouse model will be utilised to expand knowledge of the relationship between alpha-synuclein and mitochondria. This project will enable a better understanding of the mechanisms involved in the loss of SN neurons in PD and highlight new therapeutic targets to prevent this loss.

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