

Alpha-synuclein and ER-mitochondria interactions in Parkinson's

<https://neurodegenerationresearch.eu/survey/alpha-synuclein-and-er-mitochondria-interactions-in-parkinsons/>

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Country

United Kingdom

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Alpha-synuclein and ER-mitochondria interactions in Parkinson's

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Parkinson's UK

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2.5

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Research Abstract

The endoplasmic reticulum (ER) and mitochondria form close associations and these facilitate a number of fundamental physiological processes including Ca^{2+} exchange between the two organelles. Electron microscopy (EM) studies reveal the presence of tethers that link ER with mitochondria but their biochemical nature is not properly known. We have recently identified the ER protein VAPB and the outer mitochondrial membrane protein PTPIP51 as interacting proteins that form at least some of these tethers. Alpha-synuclein and other Parkinson's insults have recently been shown to disrupt ER-mitochondria associations. Our identification of VAPB and PTPIP51 as ER-mitochondria scaffolding proteins thus facilitates investigations to dissect the mechanisms that underlie these effects. The aim of this project is to test the hypothesis that

alpha-synuclein, a protein intimately linked to both sporadic and familial forms of Parkinson's, perturbs ER-mitochondria interactions and that this is via an effect on the VAPB-PTPIP51 interaction. We have already obtained evidence that alpha-synuclein is present within the specialized region of the ER that is associated with mitochondria and that expression of alpha-synuclein disrupts the VAPB-PTPIP51 interaction. The specific objectives are:

- i) To properly quantify the effect of alpha-synuclein on ER-mitochondria interactions.
- ii) To determine how alpha-synuclein disrupts the VAPB-PTPIP51 interaction.
- iii) To establish high throughput assays to screen for agents that modulate the effect of alpha-synuclein on the VAPB-PTPIP51 interaction. Such agents might represent novel lead therapeutics for the treatment of Parkinson's.

Further information available at:

Types:

Investments < €500k

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United Kingdom

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N/A

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