Mitochondrial function in sporadic Parkinson’s

https://neurodegenerationresearch.eu/survey/mitochondrial-function-in-sporadic-parkinsons/

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Country

United Kingdom

Title of project or programme

Mitochondrial function in sporadic Parkinson's

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Parkinson's UK

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4

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Research Abstract

There is strong evidence for mitochondrial dysfunction in at least some subtypes of familial Parkinson’s (f-PD). However, the prevalence and aetiology of mitochondrial dysfunction in the more common sporadic form of Parkinson’s (s-PD) is largely unknown. Pilot data: We have previously described mitochondrial dysfunction in fibroblasts of f-PD patients. We then showed that Rapamycin-mediated activation of 4E-BP rescues mitochondrial function and have identified novel compounds with a dramatic rescue effect on mitochondrial function in parkin-mutant fibroblasts.
Overall aim: To characterize mitochondrial dysfunction in s-PD, identify the underlying mechanisms and undertake rescue experiments in patient tissue.
Specific objectives (methods): 1. Assessment of mitochondrial function and morphology in fibroblasts of 100 s-PD patients (High-throughput biochemical and morphological analysis,

already established); 2. Exposure of all those s-PD fibroblast cultures with normal baseline mitochondrial function to toxins (rotenone or paraquat with subsequent assessment of mitochondrial function and morphology) to identify patients with increased susceptibility; 3. Quantification of PGC-1alpha mRNA (Q-PCR) and 4E-BP protein levels (Western blots of phosphorylated vs non-phosphorylated 4E-BP); 4. Rescue experiments with Rapamycin and ‘top hits’ from our own compound screen (pre-treatment for 24h at established doses) Patient recruitment: s-PD patients are already being recruited and skin biopsies already being taken as part of the Oxford Monument study.
Expected outcome: Our study will give a better understanding of the prevalence and underlying causes of mitochondrial impairment in s-PD, provide insight into mechanisms and determine whether mitochondrial rescue compounds efficient in parkin-mutant patient tissue are also effective in s-PD.

Further information available at:

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