Mito-ND: Mitochondrial Neurodegeneration

https://neurodegenerationresearch.eu/survey/mito-nd-mitochondrial-neurodegeneration-2/

Principal Investigators

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Country

United Kingdom|Germany

Title of project or programme

Mito-ND: Mitochondrial Neurodegeneration

Source of funding information

CoEN

Total sum awarded (Euro)

€ 405,779

Start date of award

01/06/2018

Total duration of award in years

2

Keywords
Research Abstract

The brain is a major target in primary, genetically determined mitochondrial disease. Mitochondrial dysfunction is also a prominent feature in more prevalent neurodegenerative diseases including Alzheimer's dementia (AD). AD is characterized
by the accumulation of Amyloid beta (A-beta) in the neuropil. A fraction of A-beta is deemed to be present in the inner compartment of mitochondria, where it is quantitatively digested by the pitrilysin metallopeptidase 1 (PITRM1). PITRM1 is
also responsible for clearing mitochondria from toxic mitochondrial targeting sequences (MTS) derived from proteins imported within the organelle. We recently found a family carrying a missense mutation in PITRM1 associated with
progressive neurodegeneration. Investigation in a PITRM1 KO mouse model showed that whilst the Pitrm1-/- genotype is embryonic lethal, Pitrm1+/- mice develop progressive neurological

symptoms and accumulation of A-beta-immunoreactive
material in brain. This suggests that not only recessive variants, but also dominant or sporadic mutations in PITRM1 could cause adult-onset neurodegeneration, characterized by accumulation of A-beta deposits. Mito-ND will test whether PITRM1 variants are indeed associated with human amyloidotic neurodegeneration, including AD, and elucidate the long-debated, but still unresolved, involvement of altered mitochondrial proteostasis in neurodegenerative dementia.

Further information available at:

Types:
Investments < €500k

Member States:
Germany, United Kingdom

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A