Mitochondrial DNA and Ape1 in Huntingtons Disease

https://www.neurodegenerationresearch.eu/survey/mitochondrial-dna-and-ape1-in-huntingtons-disease/

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Contact information of lead PI
Country

USA

Title of project or programme

Mitochondrial DNA and Ape1 in Huntingtons Disease

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,188,596.33

Start date of award

01/07/2015

Total duration of award in years

3

The project/programme is most relevant to:

Huntington's disease

Keywords

Huntington gene, Mitochondrial DNA, Huntington Disease, mitochondrial dysfunction, endonuclease

Research Abstract

? DESCRIPTION (provided by applicant): Substantial evidence suggests that oxidative stress and mitochondrial dysfunction may play a role in neurodegeneration associated with HD.

However, the precise mechanism(s) by which mutant huntingtin (htt) causes mitochondrial dysfunction remain largely unknown. We recently demonstrated a regulatory role of Ape1, the major mammalian apurinic/apyrimidinic (AP) endonuclease that participates in the base excision repair (BER) pathway, on mitochondrial function. Thus, our main objective is to determine the mechanisms of Ape1-mediated mitochondrial dysfunction in the context of mutant htt. This proposal will test the hypothesis that mutant htt, in combination with age-related effects, mediates mitochondrial dysfunction and neurodegeneration by targeting Ape1, which in turn results in deficient repair of mtDNA. We propose to test our hypothesis using a combination of in vivo and in vitro models of HD and directly test our hypothesis by determining if: 1) age-related changes in Ape1 synaptic nerve terminals contribute to mtDNA damage, mitochondrial dysfunction and neurodegeneration in HD and 2) what mechanism(s) might trigger Ape1-associated mitochondrial dysfunction in the context of the htt mutation. This study is likely to provide insight into a possible regulatory mechanism of Ape1 in mutant htt-induced mt dysfunction and neurodegeneration.

Lay Summary
PUBLIC HEALTH RELEVANCE: Narrative Oxidative damage to the mitochondrial DNA (mtDNA) is associated with Huntington’s disease (HD). The proposed studies will determine the role of mtDNA repair in mitochondrial dysfunction and the neuropathogenesis of HD. Completion of the proposed research will allow the identification of novel targets for the development of pharmacological interventions to treat HD patients.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Huntington's disease

Years:
2016

Database Categories:
N/A

Database Tags:
N/A