PrPC&PDK1: The PrPC / PDK1 / TACE signaling axis at the cross-road of several aggregate-prone protein-associated neurodegenerative diseases

https://neurodegenerationresearch.eu/survey/prpcpdk1-the-prpc-pdk1-tace-signaling-axis-at-the-cross-road-of-several-aggregate-prone-protein-associated-neurodegenerative-diseases/

Principal Investigators

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Multiple

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Country

France|Belgium|Canada|Norway|Germany

Title of project or programme

PrPC&PDK1: The PrPC / PDK1 / TACE signaling axis at the cross-road of several aggregate-prone protein-associated neurodegenerative diseases

Source of funding information

JPND-Cross Disease

Total sum awarded (Euro)

€ 1,461,047

Start date of award

01/01/2015

Total duration of award in years

3.0

The project/programme is most relevant to:

Prion disease|Alzheimer's disease & other dementias

Keywords
Research Abstract

Neurodegenerative diseases such as Alzheimer’s, Prion, Parkinson’s diseases, Amyotrophic Lateral Sclerosis, Spino- cerebellar Ataxia and Fronto-temporal Dementia make up a group of pathologies with distinct etiologies and pathophysiological features characterized by the accumulation in the nervous system of abnormal proteins that are toxic for neurons. Although each disease displays specific clinical manifestations, the abnormal proteins may exert their toxicity through common pathways.
This project is based on our previous identification of neurodegenerative mechanisms common to both Prion and Alzheimer’s diseases. In diseased neurons, an enzyme, PDK1, is over-activated and blocks the protective action of another enzyme, TACE, which not only amplifies the production of pathogenic prions (prion diseases) or neurotoxic Abeta peptides (Alzheimer’s disease) but also renders diseased neurons highly sensitive to inflammatory factors.
Inhibiting PDK1 in mouse models with prion or Alzheimer’s diseases counteracts the toxicity of prions and Abeta and mitigates these pathologies.
Combining in vitro and in vivo approaches as well as the analyses of human cells and tissues, this project will probe the implication of the PDK1/TACE pathway in the above-mentioned neurodegenerative diseases. Currently, there are no efficient therapies to delay or stop these fatal diseases. Our work will determine if PDK1 is a therapeutic target for these disorders

Lay Summary
Further information available at:

Types:
Investments > €500k, JPND Projects

Member States:
Belgium, Canada, France, Germany, JPND, Norway

Diseases:
Alzheimer's disease & other dementias, Prion disease

Years:
2016

Database Categories:
N/A

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