Biological and Pathological Interactions between Tau and LRRK2

https://www.neurodegenerationresearch.eu/survey/biological-and-pathological-interactions-between-tau-and-lrrk2/

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Country

USA

Title of project or programme

Biological and Pathological Interactions between Tau and LRRK2

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NIH (NIA)

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01/07/2013

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2

The project/programme is most relevant to:

Alzheimer's disease & other dementias|Parkinson's disease & PD-related disorders

Keywords

LRRK2 gene, tau Proteins, Tauopathies, tau phosphorylation, Parkinson Disease

Research Abstract

DESCRIPTION (provided by applicant): The tau protein plays a fundamental role in the cytoarchitecture of the brain and in axonal transport; however, its function and regulation can be disrupted as it becomes hyperphosphorylated and aggregated in a family of neurodegenerative

diseases termed tauopathies. Tau mutation is causative for the tauopathy frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17t) while tau polymorphisms are associated with an increased risk of other parkinsonisms including progressive supranuclear palsy (PSP), corticobasal degeneration (CBD) and Parkinson disease (PD). Interestingly, PD is not primarily classified as a tauopathy, although a significant subset of cases also develop aggregated, hyperphosphorylated tau pathology. The gene that encodes the tau protein has been repeated identified as a risk locus in genome wide-association studies for PD. Furthermore, the co-PI of this proposal and others have shown that the PD-linked protein alpha-synuclein and tau can interact to exacerbate PD-relevant pathologies. More recently, pathological studies of individuals carrying PD-linked mutations in the LRRK2 gene have shown tau pathology in a subset of mutation carriers. Additionally, transgenic mice expressing LRRK2 with PD-relevant mutations present with abnormally phosphorylated tau. Despite these lines of evidence, the link between PD and tau, specifically through the action of LRRK2, has been largely deemed circumstantial as even the role of LRRK2 in normal biology has been unclear. Our preliminary data suggests that LRRK2 plays a regulatory role in tau biology and that this role may have implications in neurodegenerative diseases. In the current proposal, we will directly assess using several complementary methods including in vitro, cell culture, and transgenic mouse studies if LRRK2 and tau interact in normal and disease biology, providing important insights for the development of novel therapeutic approaches.

Lay Summary
PUBLIC HEALTH RELEVANCE: Tau protein plays a critical role in both the normal brain and neurodegenerative diseases, most of which occur in the absence of tau mutation. Based on our preliminary data and a growing base of publications, this proposal will determine if the Parkinson’s disease-linked protein LRRK2 and tau can interact and how this contributes to normal and disease biology. Understanding the relationship between these disease-relevant proteins could eventually identify targets for therapeutic intervention.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias, Parkinson's disease & PD-related disorders

Years:
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