Tau-mediated regulation of axonal transport

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Country

USA

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Tau-mediated regulation of axonal transport

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NIH (NIA)

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4

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Axonal Transport, tau Proteins, Kinesin, Microtubules, FTD with parkinsonism

Research Abstract
Tau is a microtubule associated protein (MAP) primarily expressed in neurons that has traditionally been thought to promote microtubule assembly and stability in the axon. However, recent in vitro motility experiments have also demonstrated that tau is a potent inhibitor of processive kinesin movement along microtubules. These results present an interesting paradox, namely – how can kinesin processively transport its cargo along microtubules in the presence of

tau, which is highly expressed in neurons and localized to the axon? The answer to this question has important implications for axonal transport, a critical process in neurons required for the efficient delivery of organelles, proteins, nucleic acids, and small molecules synthesized in the cell body to their site of function in distal regions of the axon. Defects in any one of the protein components in the axonal transport machinery, which includes microtubules, members of the kinesin superfamily of motor proteins, a variety of adapter molecules that link kinesin to its intracellular cargo, and MAPs such as tau, result in serious and often lethal neurodegenerative diseases, including Alzheimer's, Parkinson's, Huntington's, and ALS. This proposal will test the hypothesis that tau is a conformationally dynamic protein that can adopt multiple modes of interaction with different nucleotide states of the microtubule lattice. Furthermore, the mechanistic basis for isoform specific differences in tau's function will also be examined, with an emphasis its ability to modulate the processive motility of kinesin-1, the major molecular motor involved in axonal transport.

Lay Summary
Defects in any one of the protein components in the axonal transport machinery, such as the microtubule associated proteins tau, result in serious and often lethal neurodegenerative diseases, including Alzheimer's, Parkinson's, Huntington's, and ALS. Thus understanding tau's role in modulating kinesin-1 (a major molecular motor protein in the axon) function in the neuron is imperative to elucidating the molecular mechanisms of axonal transport in both normal and pathological states.

Further information available at:

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Investments > €500k

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United States of America

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