Delineating protein-protein interaction network of hyperphosphorylated tau in tauopathies

https://www.neurodegenerationresearch.eu/survey/delineating-protein-protein-interaction-network-of-hyperphosphorylated-tau-in-tauopathies/

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1

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Research Abstract

Alzheimer’s disease (AD) currently attacks more than five million patients in the US. Without an effective treatment or preventative regime, AD patients in this country will be close to 14 million by 2050, with annual medical expenses topping 1.2 trillion US dollars. A major pathological

hallmark for AD and other neurodegenerative disorders collectively called tauopathies is the neurofibrillary tangles (NFTs) composed of hyperphosphorylated tau protein (p-tau). Pathological hyperphosphorylation of tau interferes with the normal, axonal transport-related function of tau. Multiple lines of evidence also reveal a gain-of-function cytotoxicity of p-tau. The identification of the molecular targets of p-tau that underlie neurodegeneration will likely provide novel targets for the development of early diagnostic tools and therapeutics. In this project, we propose to use complementary approaches to perform the first systematic identification of proteins that interact preferentially with p-tau. In the biochemical approach, we will use recombinant p-tau produced by the PIMAX-Cat technology to isolate p-tau binding proteins from neuroblastoma cell extracts. In the genetic approach, we will use the tethered catalysis/yeast two-hybrid (TC/Y2H) system, which is designed to identify protein-protein interactions induced by a post-translational modification including phosphorylation, to screen for p-tau binding proteins from a human brain cDNA library. All candidate hits discovered from these two methods will be verified and characterized in neural cell-based co-purification experiments. Database mining and data integration will reveal the protein-protein interaction network centering upon p-tau, and lead to models for p-tau inflicted neurodegeneration.

Further information available at:

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Investments < €500k

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United States of America

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