Harish C. Pant, J Mol Biomark Diagn, 3:4
http://dx.doi.org/10.4172/2155-9929.S1.011

OMICS Group Conferences
Accelerating Scientific Discovery

3rd International Conference on
Biomarkers & Clinical Research

July 2-4, 2012 Embassy Suites Las Vegas, USA

A novel approach to prevent the deregulation of a neuronal kinase involved in neurodegenerative diseases

Harish C. Pant
NINDS, NIH, Bethesda, USA

The Biology of Neurodegeneration program evolved from our laboratory studying the basic biology of neuronal cytoskeletal protein phosphorylation during development and normal function in the adult. To understand the molecular basis of neurodegeneration our major focus has been to study the regulation of compartment-specific patterns of cytoskeletal protein phosphorylation in neuronal perikarya and axons. We have demonstrated that phosphorylation of the numerous acceptor sites on such proteins as Tau and neurofilament was tightly regulated topographically and generally confined to the axonal compartment. We identified cyclin dependent kinase5 (Cdk5); a neuron specific kinase is the major kinase involved in the phosphorylation of these cytoskeletal proteins in the nervous system. It was recognized that in neurodegenerative disorders such as Alzheimer's disease (AD) and Amyotrophic lateral sclerosis (ALS), the pathology was characterized by hyper activation of Cdk5 and accumulation of aberrantly hyper phosphorylated cytoskeletal proteins in cell bodies, suggesting that topographic regulation had been compromised. This led inevitably into studies of neurodegeneration in cell culture and model mice with emphasis on Cdk5, that targets numerous neuronal proteins including cytoskeletal protein regulation by phosphorylation, which when deregulated, is responsible for the pathology seen in neurodegenerative diseases. In cell systems, neuronal stress leads to deregulated kinases, for example, Cdk5, accompanied by abnormal cytoskeletal protein phosphorylation and cell death characteristic of neurodegeneration. Recently we have developed peptides derived from, p35, and a neuron specific activator of Cdk5, for deregulated Cdk5 activity which rescue cells in vitro from stress induced pathology. The questions currently being investigated are (1) How is cytoskeletal protein phosphorylation topographically regulated in neurons? (2) What factors are responsible for the deregulation of Cdk5 in neurons? (3) Can mouse models of AD and ALS be treated therapeutically with peptides that specifically inhibit deregulated Cdk5?

PantH@ninds.nih.gov