OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference on
Biomarkers & Clinical Research
July 15-17, 2013 Courtyard by Marriott Philadelphia Downtown, USA

A novel translational approach to Alzheimer disease using a peptide derived from neuronal cell cycle dependent like kinase5 (Cdk5) activator

Harish C. Pant
NIH, USA

During our studies on the compartment specific phosphorylation of cytoskeletal proteins in the neurons, we discovered a novel kinase, Cdk5, a Cell Cycle dependent like kinase in the brain. Though it binds with few cyclins, however, its activity is primarily restricted to neurons due to its binding and regulation by neuron specific molecules p35 and p39 (35 KDa and 39 KDa molecular weight respectively). By virtue of its tightly regulated, multifunctional role in neuronal development, migration, synaptic activity, synaptogenesis and survival, has emerged as a major player in neuronal function in health as well in disease. Over the 30 years now our studies continue to unravel the role of Cdk5 in neurogenesis and synaptic function but our most exciting recent findings have been related to its role in neurodegeneration.

Most of the therapeutic approaches targeting neurodegenerative disorders have focused primarily on drugs like roscovitine that inhibit kinase activities by interfering with the ATP binding domain of the kinases. All of these drugs, however, lack sufficient specificity, since all kinases including cell cycle Cdks, are vulnerable at the ATP binding site targeted by roscovitine and other drug molecules, analogs of ATP. We identified a 24 amino acid residue truncated fragment, P5 peptide, derived from the p35 activator (Cdk5 activator), and specifically inhibited hyperactive Cdk5/p25 activity involved in neurodegenerative diseases. In our recent studies we have demonstrated that P5 rescued cortical cells *in vitro* from abnormal AD-like phenotypes. It did this without affecting the function of the normal Cdk5/p35. This raised the exciting possibility that P5 might be a therapeutic candidate for the treatment of AD and other neurodegenerative disorders in which hyperactive Cdk5 is implicated. P5 was modified so that it can cross the blood brain barrier. P5 modified peptide crosses the BBB and is most effective in preventing the Alzheimer's disease like phenotypes *in vitro* and *in vivo* (AD model mice).

PantH@ninds.nih.gov