**Title of the talk:** Small molecule Activator of Master Epigenetic Enzyme, p300/CPB: Implications in Neural Disorders and Therapeutics

**Abstract:** Eukaryotic genome is organized into a highly dynamic nucleoprotein structure referred to as chromatin. The fundamental unit of chromatin is a nucleosome, comprising of around 200 base pairs of DNA and four different core histones. The epigenetic modification of DNA and core histones fine-tune the genome function, thereby serving as a fundamental regulator of cellular homeostasis, in physiological as well as pathophysiological conditions. Reversible acetylation of histone and non-histone proteins is one of the most well studied epigenetic modifications in the context of disease. In the brain, histone acetylation is associated with activity-regulated transcriptional changes that are required for synaptic plasticity and memory. These processes are dismantled in neurodegenerative diseases and depression. Our laboratory has discovered a natural compound derived small molecule TTK21, specific activator of the acetyltransferase KAT3 family (p300/CBP). We have shown that this activator can induce neurogenesis in the mouse brain and thereby enhance the formation of long term memory. We have demonstrated that synaptic plasticity and memory deficiencies can be restored in a mouse model of tauopathy following treatment with TTK21 conjugated to glucose derived carbon nanosphere (CSP). The CSP-TTK21 induces the H2B acetylation levels in several genes, including a series of super-enhancer –regulated genes, associated with plasticity and neuronal function in resting tauopathic mice. Thus by employing the CSP-TTK21, we could selectively reverse epigenetic, transcriptional, synaptic plasticity, and behavioral deficits associated with an Alzheimer's disease-related disorder. The effectiveness of the CSP-TTK21 is currently being studied in the other neurological disorders and depression.