**Weekly Colloquium**

Tuesday, 1/10/2017, 12:30pm, Billings Building – Rosedale Conference Room

"Treating Alzheimer's disease by shifting balance from neurodegeneration to regeneration of the brain"

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**Research Summary:**

Alzheimer’s disease (AD) is a slow chronic progressive multifactorial disorder in which neurodegeneration is associated with neurofibrillary tangles of abnormally hyperphosphorylated tau, and Abeta core-neuritic (senile) plaques. Tangles and not plaques are required for clinical expression of the disease, the dementia. Hippocampus is most affected with tau pathology and neurodegeneration. AD brain attempts to repair itself by initiating neurogenesis and synaptogenesis, which, however, most likely because of a lack of sufficient neurotrophic support does not materialize into the formation of new mature functional neurons and enhancement of synaptic plasticity. We have found that a neurotrophic compound that enhances dentate gyrus neurogenesis by competitively inhibiting Leukemia inhibitory factor (LIF) and promotes synaptogenesis by increasing the transcription of brain derived growth factor (BDNF) can not only rescue neurogenesis and synaptic plasticity deficits but also reduce tau and Abeta pathologies and reverse cognitive impairment in 3xTg-AD transgenic mouse model of AD. These findings provide a novel therapeutic approach to AD and related neurodegenerative conditions. In an independent set of studies we have found that passive immunization with tau antibodies targeting the amino-terminal domain of tau can rescue not only tau but also Abeta pathology and cognitive impairment in 3xTg-AD mice. Collectively, these findings suggest a primary role of neuronal connectivity in the etiopathogenesis of AD and its potential as a therapeutic target.

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**Publications:**

