

## PROGRESS IN NEUROSCIENCE PINS

Seminar Series of the Brain & Mind Research Institute Weill Cornell Medical College (WCMC) &



The Graduate Program in Neuroscience of WCMC and Sloan Kettering Institute

Thursday, 1/12/17, 4 PM, coffee at 3:45 PM Weill Auditorium

## "Transmission of Misfolded Proteins in Neurodegenerative Disorders: A Common Mechanism of Disease Progression"

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## Abstract



The deposition of  $\beta$ -sheet rich amyloid aggregates formed by disease-specific proteins is a common feature of many neurodegenerative diseases and are believed to cause neuronal dysfunction directly or indirectly. Recent studies have strongly implicated cell-to-cell transmission of misfolded proteins through templated recruitment as a common mechanism for the onset and progression of various neurodegenerative disorders. Emerging evidence also suggests the presence of conformationally diverse "strains" for each type of disease protein, which may be another shared feature of amyloid aggregates, accounting for the tremendous heterogeneity within each category of diseases. In Alzheimer's disease and other age-related tauopathies, the normally soluble tau protein accumulate as insoluble neurofibrillary tangles (NFTs) whereas in Parkinson's disease and other related synucleinopathies, the highly soluble α-synuclein protein are converted to aggregated Lewy bodies (LBs) in neuron and glia. We have developed non-transgenic mouse models of tauopathies and synucleinopathies and have used them to test the "transmission" hypothesis and the "strain" hypothesis in order to elucidate mechanisms of progressive spread of NFTs and LBs as well as to explore the molecular basis of strain heterogeneity.

## **Recent Relevant Publications:**

- Pathological α-synuclein transmission initiates Parkinson-like neurodegeneration in nontransgenic mice. Luk KC, Kehm V, Carroll J, Zhang B, O'Brien P, Trojanowski JQ, Lee VM.Science. 2012 Nov 16;338(6109):949-53. doi: 10.1126/science.1227157. PMID: 23161999
- Unique pathological tau conformers from Alzheimer's brains transmit tau pathology in nontransgenic mice. Guo JL, Narasimhan S, Changolkar L, He Z, Stieber A, Zhang B, Gathagan RJ, Iba M, McBride JD, Trojanowski JQ, Lee VM. J Exp Med. 2016 Nov 14;213(12):2635-2654. PMID: 27810929
- Distinct α-synuclein strains differentially promote tau inclusions in neurons. Guo JL, Covell DJ, Daniels JP, Iba M, Stieber A, Zhang B, Riddle DM, Kwong LK, Xu Y, Trojanowski JQ, Lee VM. Cell. 2013 Jul 3;154(1):103-17. doi: 10.1016/j.cell.2013.05.057. PMID: 23827677



