



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, 5/29/14, 4 PM, coffee at 3:45 PM
Weill Auditorium

Disorder to Order Transitions in Neuro-transmission and -degeneration

David Eliezer, Ph.D.

Associate Professor of Biochemistry and Neuroscience, WCMC

Abstract:



This talk will focus on the role of three different disordered proteins in processes linked to neurodegeneration and neurotransmission and will seek to illustrate a role for structural biology in formulating models for the function and dysfunction of such proteins. The protein alpha-synuclein is genetically and histopathologically associated with familial and sporadic Parkinson's disease. Functionally, alpha-synuclein is thought to modulate synaptic vesicle exocytosis via either direct or indirect interactions with SNARE proteins and complexes. Structurally, alpha-synuclein undergoes a coil-to-helix transition upon binding to membranes, where it can adopt different helical conformations, which are proposed to mediate both its normal function and its membrane-induced aggregation into amyloid fibrils. Interestingly, one of the few proteins that responds to changes in synuclein levels in cells is the protein complexin, which also regulates SNARE-mediated vesicle fusion. Like synuclein, the C-terminal domain of complexin is intrinsically disordered, yet can be demonstrated to interact with membranes in a manner that is required for proper complexin function. Tau is a microtubule-binding protein that forms filamentous aggregates linked to Alzheimer's disease and other dementias but little is known about its microtubule bound state. Tau also interacts with anionic lipids and detergents in ways that may recapitulate important aspects of both its microtubule interactions and its pathological aggregation.

Recent relevant publications:

Characterization of semisynthetic and naturally N α -acetylated α -synuclein in vitro and in intact cells: implications for aggregation and cellular properties of α -synuclein. JBC 2012 287:28243

Synaptic vesicles position complexin to block spontaneous fusion. NEURON 2013 77:323

Structural transitions in tau k18 upon micelle binding suggest a hierarchy in the efficacy of individual microtubule-binding repeats in filament nucleation. PROTEIN SCIENCE 2013 In Press



Weill Cornell Medical College

