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, 10/1/15, 4 PM, coffee at 3:45 PM
A-950

"The role of synucleins and Munc18-1 in maintaining synaptic function"

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Abstract:

My lab is interested in how specific synaptic dysfunctions trigger neurological disorders. Synapses are relay stations, mediating neuronal communication via neurotransmitter release. This process requires intact functioning of the protein expression and trafficking machinery, of mitochondria to meet the synapse's energy needs, of degradation mechanisms to clear aged and misfolded proteins, and of the synaptic vesicle cycle to mediate neurotransmitter release. Synaptic defects are known to occur long before neuropathological symptoms in various diseases appear, yet the underlying mechanisms remain unknown. We are pursuing three lines of investigation into the synaptic origins of chronic diseases: (1) To understand how synaptic dysfunction of α-, β- and γ-synucleins contributes to Parkinson's disease and related synucleinopathies; (2) To determine how mutations in the synaptic protein Munc18-1 trigger the infantile seizure disorders Ohtahara syndrome, West syndrome, and Dravet syndrome; and (3) To determine early changes at the synapse that trigger pathology in Parkinson's and Alzheimer's disease, using tau, Aβ and synuclein mouse models. We envision that understanding the molecular causes of synaptic dysfunction is essential, because it will enable us to (1) detect diseases at an earlier stage, (2) intervene earlier and during treatable stages, and (3) improve patient outcomes with rational Interventions.

Recent relevant publications:

- Burré J, Sharma M, Tsetsenis T, Buchman V, Etherton MR, Südhof TC. α-Synuclein promotes SNARE-complex assembly in vivo and in vitro. Science 329: 1663-1667 (2010).
- Burré J, Sharma M, Südhof TC. Systematic mutagenesis of α-synuclein reveals distinct sequence requirements for physiological and pathological activities. The Journal of Neuroscience, 32: 15227-15242 (2012).
- Burré J, Sharma M, Südhof TC. Definition of a molecular pathway mediating α-synuclein neurotoxicity. The Journal of Neuroscience, 35: 5221-5232 (2015).

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