

# The Alzheimer Disease Connection to Down Syndrome's Mechanisms and Possible Treatments

## December 4

Tuesday, 12:30 pm

Weekly Colloquium

Billings Building  
Rosedale Conference Room



**Speaker: William C. Mobley, M.D., Ph.D.**  
Distinguished Professor  
Department of Neurosciences  
Associate Dean for Neurosciences  
Initiatives  
University of California, San Diego

**Host: Rajiv R. Ratan, M.D., Ph.D.**

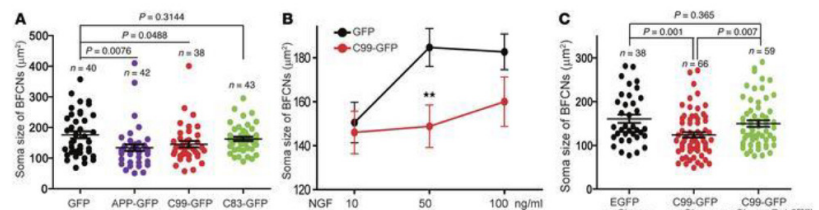
**For more information,  
please contact**  
Darlene White at  
[daw9085@med.cornell.edu](mailto:daw9085@med.cornell.edu)

**Burke Neurological Institute**  
Academic Affiliate of Weill Cornell Medicine  
785 Mamaroneck Avenue  
White Plains, NY 10605  
[burke.weill.cornell.edu](http://burke.weill.cornell.edu)

## Abstract

An important line of investigation focuses on the selective vulnerability of neuronal populations in degenerative disorders. Alzheimer disease is one such disorder and features early, consistent losses in a number of neuronal nuclei, including those harboring cholinergic neurons in the basal forebrain. We will review the evolution of ideas as to the cellular and molecular bases for loss of these neurons and review recent studies pointing to a critical role for endosomal dysfunction and compromised axonal transport of neurotrophic factor signaling. Our discussion will highlight insights from the genetics of Alzheimer disease and the contributions to be made by studies in adults with Down syndrome.

### Amyloid precursor protein-mediated endocytic pathway disruption induces axonal dysfunction and neurodegeneration



Xu W, Weissmiller AM, White JA 2nd, Fang F, Wang X, Wu Y, Pearn ML, Zhao X, Sawa M, Chen S, Gunawardena S, Ding J, Mobley WC, Wu C. Amyloid precursor protein-mediated endocytic pathway disruption induces axonal dysfunction and neurodegeneration. *J Clin Invest*. 2016 May 2;126(5):1815-33. doi: 10.1172/JCI82409

Wagner SL, Ryneason KD, Duddy SK, Zhang C, Nguyen PD, Becker A, Vo U, Masliah D, Monte L, Klee JB, ... Mobley WC, et al. Pharmacological and toxicological properties of the potent oral  $\gamma$ -secretase modulator BPN-15606. *J Pharmacol Exp Ther*. 2017 Jul;362(1):31-44. doi: 10.1124/jpet.117.240861

Chen XQ, Sawa M, Mobley WC. Dysregulation of neurotrophin signaling in the pathogenesis of Alzheimer disease and of Alzheimer disease in Down syndrome. *Free Radic Biol Med*. 2018 Jan;114:52-61. doi: 10.1016/j.freeradbiomed.2017.10.341.

Ballard C, Mobley W, Hardy J, Williams G, Corbett A. Dementia in Down's syndrome. *Lancet Neurol*. 2016 May;15(6):622-36. doi: 10.1016/S1474-4422(16)00063-6.



Burke  
Neurological  
Institute



Weill Cornell  
Medicine