Histone Deacetylase-3: Friend and Foe of the Brain

March 3

Tuesday, 12:30 pm

Weekly Colloquium

Billings Building
Rosedale Conference Room

Speaker: Santosh R. D'Mello, Ph.D.
Professor and Chair
Department of Biological Sciences
Southern Methodist University
Dallas, TX

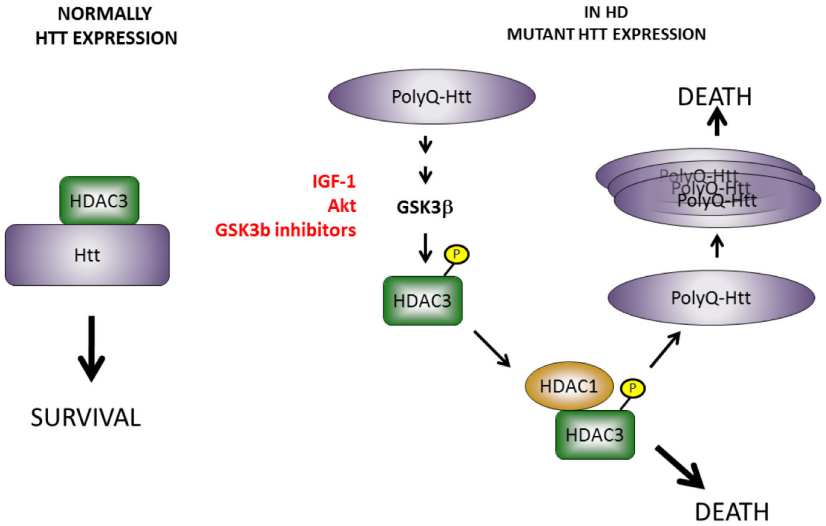
Hosts: Rajiv R. Ratan, M.D., Ph.D.

For more information, please contact
Lindsey Echevarria
lechevarria@med.cornell.edu

Burke Neurological Institute
Academic Affiliate of Weill Cornell Medicine
785 Mamaroneck Avenue
White Plains, NY 10605
burke.weill.cornell.edu

Abstract

Histone deacetylases (HDACs) are a group of enzymes that deacetylate lysine residues on histones and many other proteins in the nucleus, cytoplasm and mitochondria. Structurally distinct pharmacological inhibitors of HDACs inhibit neuronal death in cell culture and in vivo models of a variety neurodegenerative diseases. However, the identity of the HDAC(s) that are abnormally activated in neurodegenerative diseases and targeted by the inhibitors to affort protection has been unclear because of the non-selectivity of the inhibitors with regard to the different HDAC isoforms. In my presentation I will present evidence indicating that HDAC3 is a central player in the promotion of neuronal death. Neurotoxicity by HDAC3 depends on its phosphorylation and interaction with HDAC1. While promoting death of mature neurons, HDAC3 is required for normal brain development acting as a key regulator of distinct neurodevelopmental events. Evidence demonstrating the requirement for HDAC3 in brain development will be presented.



1. Bardai FH, D'Mello SR. (2011) Selective toxicity by HDAC3 in neurons: Regulation by Akt and GSK3β. J. Neurosci. 31:1746-51.
2. Bardai FH, Verma P, Smith C, Rawat V, Wang L, D'Mello SR. (2013) Disassociation of HDAC3 from normal huntingtin underlies mutant huntingtin neurotoxicity. J. Neurosci. 33:11833-11838.
3. Louis Sam Titus ACS, Sharma D, D'Mello SR. (2020) The BDNF and Npas4 genes are targets of HDAC3-mediated transcriptional repression. BMC Neuroscience 28;20(1):65.

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