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 afford 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.