NUS National University of Singapore | Department of Anatomy
Yong Loo Lin School of Medicine

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EPIGENETIC REGULATION OF MICROGLIAL ACTIVATION VIA MODULATION OF HISTONE 3-LYSINE 9-ACETYLATION IN A RODENT MODEL OF ISCHEMIC STROKE

FRIDAY
3rd FEBRUARY 2017

3:00PM – 4:00PM

ANATOMY SEMINAR ROOM, L2, MD10, DEPARTMENT OF ANATOMY, NUS.

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Abstract:

Cerebral Ischemia leads to microglial activation which can resolve post-ischemic pathology. However, chronic activation of microglia, as seen during reperfusion, worsens disease progression. A better understanding of epigenetic mechanisms regulating microglial activation will aid in mitigating microglia-mediated neurotoxicity in ischemia. In this study, we investigated histone modification Histone 3-Lysine 9-acetylation (H3K9ac) and its regulation *via* Histone deacetylase (HDAC) inhibitors in an experimental mouse model of middle cerebral artery occlusion (MCAO). HDAC inhibitor mediates neuroprotection by epigenetically regulating the microglial inflammatory response. Following MCAO, HDAC inhibition by sodium butyrate (SB) downregulated expression of pro-inflammatory mediators TNF-α and NOS2 in activated microglia, upregulated their anti-inflammatory IL10 expression, and improved neuronal survival. SB altered H3K9ac enrichment and transcription at pro- and anti-inflammatory gene promoters *in vitro,* while inducing the IL10/STAT3 anti-inflammatory pathway. Altogether, these results provide evidence of HDAC inhibition being a promising molecular switch to epigenetically modify microglial behavior to alleviate microglia-mediated neurotoxicity.

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