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

NUHS National University Health System

HYPOXIA-INDUCED HISTONE MODIFICATIONS IN ACTIVATED MICROGLIA *IN VITRO*

FRIDAY
21 APRIL 2017

3PM – 3.30PM

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

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Microglia are resident immune cells that act as the first form of active defence in the central nervous system (CNS). These cells constantly monitor the tissue microenvironment and react rapidly in response to hypoxia, infection and injuries in CNS. Hypoxia in the brain has been detected in several neuropathological conditions such as Alzheimer's disease, cerebral palsy and in response to adverse environmental conditions in the developing brain. Hypoxic conditions activate microglial cells resulting in the release of proinflammatory cytokines and chemokines in the brain. We hypothesize that hypoxic conditions activate microglia through epigenetic mechanisms such as changes in histone modifications. In this study, histone modifications were studied in BV2 microglia cells subjected to hypoxic conditions.

Using immunocytochemistry (ICC), we analyzed expressions of proinflammatory cytokines in microglia after exposure to hypoxic conditions. We observe an increase in TNFα after hypoxic exposure showing that microglia was activated in response to hypoxia. We further profiled the expressions of histone markers such as H3K9ac, H3K4me3 (activation mark) and H3K27me3 (repressor mark) in microglia after exposure to hypoxia. There was an increase in expressions in HeK4me3 and decrease in the expression in the H3K27me3 markers in microglia after 6 and 24 hrs of hypoxic point. It is suggested that, hypoxia causes histone modifications, thereby resulting in microglial activation. Future study would involve determination of altered expression of genes caused by the histone modifications in hypoxia-induced activated microglia.

ADVANCED MASS SPECTROMETRY-BASED STRATEGIES FOR TRACKING SMALL MOLECULE DRUG-TARGET ENGAGEMENT

FRIDAY
21 APRIL 2017

3.30PM – 4PM

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Drug discovery is a long-term and resource-extensive process. However, the success in drug discovery has been limited to 10 – 20% owing to many of drug candidates fail with serious safety and efficacy issues at clinical trial stages. It is being increasingly realized that high attrition rate is related to lack of detailed knowledge of the biological mode-of-action of drugs which is attributed to failure in identifying true drug-binding protein(s) in biological systems. This underscores the need for advancement in current drug-target identification approaches as currently available methods have great weaknesses. Among small molecule drug-target identification technologies, mass spectrometry-based quantitative proteomics has emerged as a powerful tool for tracking small molecule drug-target engagement. The main focus on this seminar will be on such proteomics methods, their capabilities as well as shortcomings. The preliminary results on protein target identification of a selected drug will be discussed.

Address enquiries Dr Hu Qidong at 66013730 or Ms Carolyne Ang at 65163200. All are welcome.