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

PSS Pharmacological Society (Singapore)

Medical Pharmacology Seminar

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Epigenetics and Chronic Diseases: Translational Insights for Pharmacological Intervention

Epigenetics is gene function beyond the DNA sequence, operated by DNA modifications, DNA-associated protein modifications, and noncoding RNA. It is reversible and metabolically regulated, thus directly related to habit and lifestyle. Reversible histone modifications are one of the most investigated epigenetic modifications shown to be involved in diverse physiological as well as pathological phenomena. Several studies by us and others have demonstrated that the master Lysine acetyltransferases CBP/p300 catalytic activity could be critical for long-term memory formation. We have discovered a small molecule (TTK21) activator of CBP/p300, which, after conjugating to the glucose-derived carbon nanospheres (CSP), crosses the blood-brain barrier and reaches different parts of the brain without apparent toxicity. It induces adult neurogenesis and long-term memory. By administering this activator to the Alzheimer's Disease (AD) model, we could significantly reverse the memory loss in young and older mice. Recently, we have found that in Syngap1+/-, a mouse model of intellectual disability (ID) and autism spectrum disorder (ASD), the p300 KAT activity is dramatically reduced. Our results demonstrate that the oral administration of CSP-TTK21 in adult *Syngap1*$^{+/-}$mice rescued physiological and cognitive/emotional functions, presumably through restoring p300/CBP-mediated histone acetylation and adult neurogenesis. p300 plays an important role in regulating the expression of genes involved in lipid homeostasis. Our studies revealed that p300-mediated butyrylation is involved in adipogenesis and selectively inhibiting it with a semisynthetic compound LTK-14A can effectively curb Obesity in multiple mouse models. It was found that histones are hyperacetylated and arginine methylated in oral cancer patient samples, indicating the possible epigenetic language of tobacco habit-related cancer. Inhibition of the acetylation substantially reduces the tumor burden.

Date: 23 Sept 2025 Time: 10.30 - 11.30 am

Venue: MD3-02-01 – MD3, Tiered room, level 2

Chaired by: A/Prof Gautam Sethi