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

NUHS National University Health System

## RESEARCH SEMINAR

# COORDINATION OF EMBRYONIC CELL FATE BY THE 5-METHYLCYTOSINE DIOXYGENASE TET1

Global changes in gene expression and DNA methylation orchestrate pluripotency cell state transitions and lineage priming during early mammalian development and epigenetic reprogramming. The role of active DNA demethylation in these processes has been elusive until the discovery of Tet-Eleven-Translocation (TET) enzymes which catalyze oxidation of 5-methylcytosine. Among TET family genes, Tet1 expression is elevated specifically with pluripotency acquisition. We have generated Tet1 null mouse models to clarify how its catalytic and non-catalytic functions interplay to regulate both embryonic and extra-embryonic lineage genes in the pre-gastrula stage embryo. Surprisingly, TET1 suppresses primitive streak gene expression to prevent precocious differentiation and neural tube closure defects of post-gastrulation stages. Promoter demethylation by TET1 in the gastrulation-primed epiblast provides an epigenetic safeguard against late-onset diseases related to aging, neurodegeneration and cancer. During reprogramming somatic cells to induced pluripotent stem cells (iPSCs), TET1 is involved in two sequential waves of global DNA demethylation targeting distinct genomic regions, which are uncoupled with transcriptional activation. Absence of TET1 generates iPSCs with aberrant DNA methylation and chromosomal instability. Collectively, our studies suggest that regulation of DNA methylation by TET1 at pivotal stages of pluripotency and cell fate transitions is critical in the rejuvenation process of cellular reprogramming and in the balance between health and disease.

**Thursday**
**31 October 2019**
**10.00 am – 11.00 am**
**Seminar Room, MD10**
**Level 2, Anatomy Museum**

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