TEMS

Temasek External Monthly Seminar

TEMASEK LIFESCIENCES LABORATORY

ALL ARE WELCOME

19 December 2019 (Thursday), 3pm

The Auditorium (Level 1)

Hosted by: Dr Ong Chin Tong

Enzymatic DNA Oxidation in the Control of Mammalian Development

Dr XU Guoliang
Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, China

Dr. Xu is a principal investigator at the Institute of Biochemistry and Cell Biology (IBCB), Chinese Academy of Sciences, and a professor at Fudan University, Shanghai. He was trained for PhD at the Max Planck Institute for Molecular Genetics, Berlin and conducted his postdoctoral training at Columbia University, New York. Dr. Xu established the DNA metabolism research group in 2001 under the auspices of Max Planck research group at Shanghai IBCB, where his team investigates the function of DNA methylation (5-methylcytosine) in stem cells and development. In 2011 his team described a role for Tet DNA dioxygenases in oxidation of 5-methylcytosine to 5-carboxylcytosine and the involvement of a DNA glycosylase –TDG in active demethylation, a critical step for the epigenetic reprogramming of early embryos and throughout development.

Mammalian development begins with a zygote resulted from the fertilization of a sperm and an oocyte. The zygotic genome undergoes profound epigenetic reprogramming to prepare for development. The biological significance and mechanisms of reprogramming are poorly understood. We and others found that 5-methylcytosine (5mC), a prominent base modification present in genomic DNA, is selectively oxidized and demethylated in mouse zygotes by the Ten-Eleven-Translocation (Tet) family of dioxygenases. Deficiency in oocyte Tet3 impedes demethylation and reactivation of developmental genes such as Oct4 and Nanog in the early embryo, leading to embryonic lethality. Oocytes lacking Tet3 appear to be unable to reprogram injected somatic cell nuclei. Tet-mediated demethylation is thus required for embryonic development as well as for cell reprogramming. Recent advances in the understanding of DNA modifications in mouse development will be discussed. Findings from research with Tet homologs in other eukaryotes will also be presented.

Recent Publications:

1. Jian-Huang Xue, Guo-Dong Chen, Fuhua Hao, Hui Chen, et al. Kaiyao Huang, Huiru Tang & **Guo-Liang Xu** (2019) A vitamin C-derived DNA modification catalyzed by an algal TET homolog. ***Nature*** 569, 581–585.

Hai-Qiang Dai, Bang-An Wang, Lu Yang, Jia-Jia Chen et al., Xin Sun & **Guo-Liang Xu** (2016) DNA demethylation by TET dioxygenases controls gastrula patterning by regulating Lefty-Nodal signaling. ***Nature*** 538, 528–532.

Yu-Fei He, Bin-Zhong Li, et al., **Guo-Liang Xu** (2011) Tet-mediated formation of 5-carboxylcytosine and its excision by TDG in mammalian DNA. ***Science*** 333, 1303–1307.