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THE HONG KONG UNIVERSITY OF SCIENCE & TECHNOLOGY
Division of Life Science

Seminar

Role of Epigenetic Regulators in Cancer Stem Cell Biology and Cancer Development

by

Dr. Stephen Hon-Kit Wong
School of Medicine, Stanford University

Bulk tumor cells are a population of heterogeneous cells comprised of a small fraction of cancer stem cells (CSCs) bestowed with unlimited self-renewal capability to sustain cancer cells growth and malignancy. Studies in human leukemia (Bonnet & Dick, 1997) provided the first evidence of existence of leukemia stem cells (LSCs) that later served as the paradigm of CSCs model. Given the prospect as potential targets for efficacious therapy, CSCs model has since promoted more than a decade of active cancer stem cells research in many other cancer diseases. Using a mouse leukemia transplantation model with human MLL gene mutation, we have first defined the frequencies of LSCs, their potential hierarchical organization and their degree of maturation (Somervaille, et al., 2006, 2009). The elegant mouse leukemia model enabled us to isolate sufficient quantity of LSCs for large scale genomic and epigenomic studies which eventually led to the discovery of a critical epigenetic regulator KDM5B (an H3K4 demethylase) that regulates the LSCs self-renewal property (Wong, et al., 2015). We found that a diminished level of KDM5B in LSCs maintains them in an epigenomic state with global high H3K4 methylation level that prevents them from differentiation. Demonstrated by in-vitro and in-vivo, exogenous overexpression of KDM5B in LSCs enforces them to exit self-renewal compartment and enter into terminal differentiation. In addition, mice transplanted with leukemia cells overexpressed with KDM5B survive longer than control cells, indicating a strong tumor suppressive role of KDM5B in MLL-associated leukemia. In another research work (unpublished), we have found that the mRNA level of SETDB2, an H3K9me3 methyltransferase, is reduced in primary samples of multiple subtypes of human acute leukemia. Intervention of SETDB2 by depletion (shRNA) or deletion (CRISPR-Cas9) in human leukemia cells demonstrates a critical oncogenic role of SETDB2 in human acute leukemia. Taken together, epigenetic regulators play an important role in leukemia stem cells regulation as well as leukemia development and therefore serve as compelling therapeutic targets.

Date : **8 February 2017 (Wednesday)**
Time : **11:00 am**
Venue : **Room 5566 (Lift No. 27-28)**

All Are Welcome!