

PHYSIOLOGY LECTURE SERIES

Daniel G. TENEN

Director, Cancer Science Institute of Singapore
Programme Leader & Senior Principal Investigator
Distinguished Professor in Medicine, NUS

Date: 10th November 2017 (Friday)
Time: 12:00pm – 1:00pm
Venue: MD9, Level 1, Workshop I & II

NEW THERAPEUTICS TARGETING THE CEBP PATHWAY IN ACUTE MYELOID LEUKEMIA

Abstract

An intact CEBPA pathway is required for myeloid differentiation, and this key transcription factor pathway is mutated, downregulated, or inactivated in many forms of Acute Myeloid Leukemia (AML). A number of therapeutics utilized in AML actually serve to restore CEBPA expression and/or function, including all trans retinoic acid (ATRA) in Acute Promyelocytic Leukemia; FLT3 tyrosine kinase inhibitors in FLT3-ITD positive AMLs; CDC2/CDK1 inhibitors; Histone Deacetylase (HDAC) inhibitors; CDDO; DOT1L inhibitors; and Imatinib in CML myeloid blast crisis. We and others have recently developed a number of novel therapeutics resulting in activation of CEBPA expression and/or function, including small molecules, long noncoding RNAs, and short activating RNAs. These result in more specific activation of CEBPA and subsequent differentiation of AML cells. In addition, similar approaches can be utilized to induce demethylation and activation of expression of other tumor suppressors, including p15 and p16, with potential applicability in both leukemias and solid tumors, such as liver cancer.

Biography

Over the past 32 years my laboratory has made seminal contributions to understanding the role of gene regulation in cell differentiation and the role of disruption of these pathways in leukemia, lung cancer, and liver cancer. I have been PI on many individual US NIH R01 grants and Program grants. Since 2008 I have been Director of the Cancer Science Institute of Singapore. My recent studies have focused on noncoding RNAs, and include published findings on antisense RNAs, RNA editing, and noncoding RNAs in gene regulation, methylation, and cancer. Our most recent studies demonstrated that RNA can regulate DNA methylation, and that RNA can be utilized to induce demethylation in a gene-specific manner. If successful, potential future clinical applications could include the ability to specifically reverse disease related DNA methylation, such as methylation and/or of tumor suppressor genes.

Convener: A/Prof Reshma Taneja

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

NUHS National University Health System