Department of Biomedical Sciences

presents a seminar

"Understanding the roles of the stemness factors LIN28A/B in the conversion to pluripotent states and tumorigenesis"

Dr. Sutheera Ratanasirintrawoot
Chualalongkorn University

Date : 28 July 2017
Time: 10:30am to 11:30am
Venue: Meeting Room 2-130, 1/F, Block 2, To Yuen Building

Abstract

The advent of somatic cell reprogramming is ground-breaking, as it allows for conversion of somatic cell types to pluripotent cell type called induced pluripotent stem (iPS) cells. This reprogramming process holds great promise for biomedical applications as scientists can now generate patient-specific iPS cells, which can be used for disease modeling, drug testing, and cell therapy. Through enforced expression of transcription factors, we traced the kinetics of reprogramming using live imaging and were able to isolated distinct colony types. With battery of molecular and functional assays, we determined markers and assays which can distinguish partially and completely reprogrammed cells. Comparing gene expression profile of partially reprogrammed intermediates and completely reprogrammed pluripotent stem cells, we identified a differentially expressed gene, LIN28A, as one of the key regulators of reprogramming process. LIN28A is an RNA binding protein which has one paralog, LIN28B. Both proteins function through two modes of actions, repressing pro-differentiation let-7 microRNAs and regulating the translation of target mRNAs. Studying LIN28A and LIN28B in the context of reprogramming, we found that both promoted efficient reprogramming, repressed mitochondrial oxidative metabolism and modulated histone methylation. Such effects occurred through both let-7-dependent and less well-understood let-7-independent mechanisms. In addition to reprogramming, LIN28 is involved in malignant transformation of multiple cancer types. Recent report showed that Lin28b could initiate and maintain liver cancer. As deletion of Lin28a/b showed reduced tumor burden, Lin28 may represent a therapeutic target. Cholangiocarcinoma (CCA) or bile duct cancer is a devastating disease with no reliable early markers and mostly results in a poor outcome. Since both cholangiocytes and hepatocytes are believed to emerge from the bipotent progenitors, we reasoned that factors and pathways which drive cholangiocytes to adopt a tumorigenic phenotype could be similar to that of hepatocytes. Using immunohistochemistry, we detected expression of LIN28B but not LIN28A in patient CCA samples. Through overexpression of LIN28A or LIN28B in an immortalized cholangiocyte cell line, we observed increased proliferative capacity, migratory phenotype, and colony formation. With further investigation, we hope to gain insights into mechanistic roles of LIN28 in CCA and to determine whether LIN28 pathway genes could potentially be markers and/or therapeutic targets for CCA.

About the Speaker

Sutheera Ratanasirintrawoot obtained her bachelor's degree in Biochemical Sciences from Harvard College in 2007. She then pursued her Ph.D. at Harvard Medical School under the direction of Dr. George Daley studying somatic cell reprogramming and stem cell pluripotency. Since coming back to Thailand in 2014, she has been a Lecturer at Faculty of Medicine, Chulalongkorn University, and a Principal Investigator at CU Stem Cell and Cell Therapy Research Center. Her current research focuses on the roles of stemness-related pathways in regulating cancer initiation and progression, particularly in the bile duct cancer Cholangiocarcinoma. Her work has been funded by Ratchadaphiseksomphot Endowment Fund Chulalongkorn University and Thailand's National Science and Technology Development Agency.

Enquiry:
Miss Janice Leung (3442-4902, janice.leung@cityu.edu.hk)

All are welcome!