CANCER SCIENCE
INSTITUTE OF SINGAPORE

RESEARCH MEETINGS

24 November 2017, Friday | 3pm – 4pm

LT35, Level 1, Centre for Translational Medicine (MD6)
14 Medical Drive, Singapore 117599

Zhang Mengyi | PhD Student, Prof Goh Boon Cher's Group (L11)

The Oncogenic Role of Trefoil Factor 3 (TFF3) in Non-Small Cell Lung Cancer

Trefoil factor 3(TFF3), is an oncogene which is found to be overexpressed in malignant tissues, and has been reported to promote tumor growth and metastasis. It has been showed that 93.7% of lung adenocarcinomas were TFF3-positive, whereas no expression of TFF3 was observed in squamous cell carcinomas, indicating that TFF3 could act as a novel biomarker to distinguish between lung adenocarcinoma (ADC) and lung squamous-cell carcinoma (SCC). The purpose of this project is to investigate the function of TFF3 in lung ADC, and subsequently determine its paracrine effect on SCC. The biological roles of TFF3 in ADC are investigated by analyzing the behavior of cell lines through either forced or depleted expression of TFF3 *in vitro*. Forced expression of TFF3 has enhanced the proliferation and survival, increased cell anchorage-independent growth and 3D Matrigel growth, and promoted cell migration and invasion for lung adenocarcinoma cells. In addition, TFF3 may involve in the progression of non-small cell lung carcinoma (NSCLC) through activating MAPK/ERK pathway, as ARAF expression was increased by forced expression of TFF3. In conclusion, TFF3 may play an important role in pulmonary tumorigenesis, pulmonary tumor growth, and lung cancer metastasis. The discovery of TFF3 inhibition drugs could contribute to lung cancer therapies in the future.

Cao Fan | Research Assistant, Dr Melissa Fullwood's Group (L12)

Predicting Chromatin Interactions from DNA Sequence

Various computational methods have been developed to predict chromatin interactions in recent years. Most of the methods rely on large collections of ChIP-Seq/RNA-Seq/DNase-Seq datasets and predict only enhancer-promoter interactions. In addition, some of the 'state-of-art' methods have poor experimental designs, leading to over-exaggerated performances and misleading conclusions. We developed a computational method, Chromatin Interaction Neural Network (CHINN), to predict chromatin interactions between DNase I hypersensitivity regions by using only DNA sequences of the interacting regions. CHINN is able to accurately predict both CTCF and POL2 chromatin interactions identified from ChIA-PET data as well as chromatin loops identified from Hi-C data. CHINN also shows high across-sample performance and captures various sequence features that are predictive of chromatin interactions. We believe that CHINN provides a platform to study how genetic variations could affect chromatin interactions.

Chow Mun Juinn | Research Fellow, Prof Teh Bin Tean's Group (L13)

Application of Novel Synthetic Methodology and Mechanism-Informed Phenotypic Screening for the Identification of Drug Candidates Against Drug-Resistant Cancers

Multidrug resistance is a major impediment to chemotherapy and limits the efficacies of conventional anticancer drugs. A strategy to bypass multidrug resistance is to develop new drug candidates capable of inducing apoptosis-independent programmed cell death. However, cellular pathways implicated in alternative programmed cell death are not well-elucidated and multifactorial, making a target-based discovery approach a challenge. As a proof-of-concept, a coordination-directed three-component assembly and phenotypic screening strategy was developed and employed as a viable strategy for the identification of drug candidates able to overcome apoptosis-resistance. Through an on-plate synthesis and screening of 195 organoruthenium compounds against apoptosis-sensitive and -resistant cancers, two apoptosis-independent hits with caspase-independent activity and equal efficacy in both apoptosis-sensitive and -resistant colorectal cancers were identified. I further discuss the possible application of this screening methodology to the identification of drug candidates against drug-resistant Acute Promyelocytic Leukemia and Breast Phyllodes Tumors, both expressing mutant Retinoic Acid Receptor α (RARα).