Cancer Science Institute of Singapore

Research Meeting

Date: Friday, 5 June 2015
Time: 12pm – 1pm
Venue: LT36, Level 3 Auditorium, MD6
14 Medical Drive, Singapore 117599

Kwok Hui Si

PhD Student, Prof. Daniel Tenen's Group

The role of Sharp1 in MLL-AF6 acute myeloid leukemia

MLL-AF6-rearranged acute myeloid leukemia (AML) is a result of t(6;11)(q27;q23) chromosomal rearrangement and is generally associated with poor prognostic outcomes. Gene expression profiles of AMLs from more than 500 patients reveal specific upregulation of Sharp-1 in only patients harboring t(6;11) translocations. Sharp-1 is a basic helix-loop-helix transcription factor that is reported to act as a tumor suppressor in various cancers. Contrary to the reported suppressive roles of Sharp-1 in tumor development and progression in various cancers, we demonstrate that Sharp-1 contributes to leukemogenesis in MLL-AF6-specific leukemias. In this talk, I will discuss on Sharp-1 involvement in MLL-AF6 driven leukemias and how MLL-AF6 regulates Sharp-1 expression.

Vaidehi Krishnan

Senior Research Scientist, Prof. Yoshiaki Ito's Group

To make it or 'break' it: DNA damage during Epithelial to mesenchymal transition (EMT)

The epithelial mesenchymal transition (EMT) is a biological program associated with loss of cell-cell contact, increased cancer cell migration and chemoresistance. EMT is accompanied by wide-spread transcriptional and epigenetic changes. It is currently unknown if any EMT-specific molecular events generate genomic instability or modulate DNA repair. A clearer understanding of DNA repair in cells undergoing EMT may provide novel approaches to target mesenchymal cancers. To study the role of DNA damage repair during EMT, non-small cell lung cancer (NSCLC) cells were treated with TGF-β, a physiological inducer of EMT. When a panel of DNA repair genes/transcription factors were depleted in cells undergoing EMT, the depletion of transcriptional regulators RUNX3 or HMGA2 resulted in the dramatic accumulation of endogenous DNA damage. EMT-associated DNA damage was characterized by the presence of repair foci containing phosphorylated H2AX, 53BP1, pATM and pDNA-PK, indicating irreparable double strand breaks. Interestingly, cells bearing irreparable DNA breaks could not complete their EMT program. Instead, they underwent cellular senescence as evident by reduced S phase entry, replicative slowdown and positivity for senescence-associated β-galactosidase. The above results indicate that when cells going through EMT accumulate DNA breaks, they veer away from an EMT cell fate into cellular senescence. In this talk, the mechanistic aspects of EMT-associated DNA damage will be discussed and on how cancer therapy of mesenchymal tumors can be made more efficient by exploiting their intrinsic genomic instability.