Institute of Molecular and Cell Biology
A*STAR

SEMINAR ANNOUNCEMENT

DATE: 29 February 2012, Wednesday
TIME / VENUE: 11:00AM @ Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis
SPEAKER: Dr. Tan Nguan Soon Andrew
TITLE OF SEMINAR: **Angiopoietin-like 4 in cancer growth and metastasis**

Cancer is a leading cause of death worldwide. It is known that in response to the microenvironmental stress such as hypoxia and inflammation, tumor cells exploit various signaling molecules to promote their growth, invasion and metastasis. The loss-of-dependence on integrin-mediated extracellular matrix contacts for growth (or anoikis resistance), is an essential feature of tumor cells, yet how it is acquired is a central problem in cancer biology. Our study identifies tumor-derived angiopoietin-like 4 (ANGPTL4) as a novel player in redox cancer biology. We showed that ANGPTL4confer anoikis resistance and sustain tumor growth via an autocrine adhesion mimicry ANGPTL4 interacts with integrins beta1 and beta5. ANGPTL4-integrin ligation maintains a high O2-:H2O2 ratio for tumor survival as determined by a combination of electron paramagnetic resonance with spin trap measurements and fluorescence assays. The suppression of ANGPTL4, either by RNA interference technology or immunosuppression with a monoclonal antibody, modulated intracellular reactive oxygen species generation to attenuate tumor growth associated with enhanced apoptosis in vitro and in vivo. Theinhibition of ANGPTL4-mediated redox signaling induces tumor cells death highlights ANGPTL4 as a novel tumor biomarker. I will also present our preliminary data using novel small molecules to alter O2-:H2O2 ratio and to induce apoptosis in tumor.

Metastasis, during which cancer cells disseminate from primary tumors and establish secondary tumors in distant organs, is the most fatal stage of cancer progression. It entails establishing tumor-endothelium communication that consequently leads to the disruption of the vascular barrier. The degree of efficiency with which the tumor cells can break through the endothelial barrier will have significant consequences for the overall success of metastatic spread. ANGPTL4 is highly expressed in many metastatic tumors. We showed that ANGPTL4 weaken endothelial cell-cell contacts and increases paracellular vascular leakiness. Mice implanted with ANGPTL4-deficient tumor cells failed to develop metastasis in the axillary lymph nodes and lungs when compared to mice injected with ANGPTL4 control tumor cells. We identify ANGPTL4 as a novel upstream mediator of vascular permeability and provide a molecular basis for targeting ANGPTL4 in the treatment of cancer and other vascular-related pathologies.

Host: Prof. Wanjin Hong
