CANCER SCIENCE INSTITUTE OF SINGAPORE

SEMINAR ANNOUNCEMENT

Masanobu Oshima

Professor, Cancer Research Institute
Kanazawa University



Inflammatory microenvironment that accelerates gastrointestinal tumorigenesis

Date: Wednesday, 24 February 2016
Time: 3.30pm - 4.30pm
Venue: LT36, Level 3 Auditorium, CeTM (14 Medical Drive, Singapore 117599)
Host: Prof Yoshiaki Ito

Abstract:

Helicobacter pylori infection is closely associated with gastric cancer, and infection-associated chronic inflammation is one of the important tumor-promoting mechanisms. COX-2/PGE_2 pathway is induced by *H. pylori* infection, and is important for tumor promotion through generation of inflammatory microenvironment. We have constructed gastric tumor model, Gan mice, that develop inflammation-associated gastric tumors by simultaneous activation of "COX-2/PGE_2 pathway" and "Wnt signaling" in gastric mucosa. IPA analyses using TCGA database indicate that these two pathways are also activated in human tubular-type and papillary-type gastric cancers. Using Gan mouse model, we found that innate immune signaling through TLR/MyD88 in BMDCs is required for induction of inflammatory responses in tumor tissues, which further induces expression of TLR2 in tumor epithelial cells. It has been shown that cell-intrinsic TLR2 signaling through NF-κB plays a role in maintenance of stemness. Accordingly, such interplay of COX-2/PGE_2 and TLR/MyD88 pathways will be a possible target for gastric cancer prevention. We also examined the role of inflammatory microenvironment in malignant progression of intestinal tumors using *Apc* and *Tgfbr2* mutant mice. Notably, we found that chronic inflammation promotes invasive cancer development in TGF-β signaling-suppressed colonic mucosa, even if Wnt signaling is not activated. These results suggest that targeting inflammatory microenvironment will be an effective strategy also for malignant progression stage of colon carcinogenesis.

Biography:

Dr. Oshima graduated Hokkaido Univ. School of Veterinary Medicine, Japan and worked in Chugai Pharmaceutical Co. Ltd, Japan, and Merck Research Laboratories, USA as research staff. Then, he moved to Kyoto Univ. School of Medicine as Associate Professor at 2000 and Cancer Research Institute of Kanazawa Univ. as a Professor at 2005. Now Dr. Oshima is a Director of Cancer Research Institute, Kanazawa University. His research group has been studying mechanisms of gastrointestinal tumorigenesis by construction of inflammation-associated gastric tumor development model (Gan mice), and found novel mechanisms of inflammatory responses in gastric tumorigenesis including the role of COX-2/PGE2 pathway and innate immunity. Currently, he is also interested in the mechanism of malignant progression step of gastric and colon cancer, including roles of host inflammatory responses that contribute to TGF-β signaling-suppressed invasion and p53 mutation-related metastasis.