DUKE NUS
GRADUATE MEDICAL SCHOOL SINGAPORE

Title:

"Molecular Mechanisms Underlying Male Predominance of Hepatocellular Carcinoma: Linking the Viral-host Interaction and Cancer Epigenome by Androgen Receptor Signaling"

Abstract:

Hepatocellular carcinoma (HCC) is one of the commonest and deadliest cancers worldwide. A striking epidemiological characteristic of HCC regardless of localities and etiologies is prominent male predominance, which is even more pronounced in hepatitis B virus (HBV)-endemic areas. Androgen receptor (AR) is a ligand-activated nuclear receptor that regulates the development of male sexual phenotype. Aberrant AR signaling, however, has detrimental consequences in the development of male-predominant cancers. Using genome-wide location and functional analysis, we have uncovered *cell cycle-related kinase* (*CCRK*) as an AR direct transcriptional target that drives aberrant hepatocellular proliferation and tumorigenicity through β-catenin/T cell factor signaling (Feng *et al*. J Clin Invest 2011). Our recent findings demonstrate that CCRK mediates the interaction between AR signaling and the HBV X protein to form a viral-host oncogenic circuitry, thus highlighting the critical role of CCRK in HBV-associated hepatocarcinogenesis. The Polycomb protein Enhancer of zeste homolog 2 (EZH2) causes epigenetic silencing of tumor-suppressor genes by catalyzing histone H3 lysine 27 trimethylation. We have previously shown that EZH2 promotes β-catenin-dependent hepatocarcinogenesis (Cheng *et al*. Cancer Res 2011), but the mechanistic basis for its own regulation is not clearly defined. More recently, we have revealed a new role for AR signaling in the regulation of EZH2 expression and phosphorylation in HCC through CCRK activation. These studies have not only advanced our fundamental understanding of the gender disparity in HCC, but may also provide a new paradigm for nuclear receptor regulation of cancer epigenome. Elucidating the detailed signaling network of AR/CCRK/EZH2 will lead to the discovery and development of novel targeted therapies for HCC and other male-predominant cancers.

Date:

23 December (Monday)

Time:

12:00 PM to 1:00 PM

Venue:

Amphitheatre, Level 2
Duke-NUS Grad Med Sch
8 College Road, S169857

(Opposite Singapore General Hospital, Block 6/7)

Host:

Bin Tean TEH, Ph.D.
Professor
Program in Cancer & Stem Cell Biology
Duke-NUS Graduate medical School Singapore
National Cancer Centre Singapore

"No registration is required."
Any enquiry, pls contact:
Nellie Chai (Tel: 6601 1366)

Speaker:

Dr Alfred Sze-Lok Cheng, Ph.D

Associate Professor, School of Biomedical Sciences at Chinese University of Hong Kong

Biography:

Dr. Cheng is an Associate Professor in the School of Biomedical Sciences at the Chinese University of Hong Kong (CUHK). He completed his PhD under the supervision of Prof. Joseph Sung in the Department of Medicine and Therapeutics at CUHK in 2002 and went on postdoctoral training characterizing the roles of cyclooxygenase-2 in hepatitis B-induced hepatocarcinogenesis. From 2004-2007, he was trained as a postdoctoral researcher in Prof. Tim Huang's lab in the Ohio State University, USA, where he developed an integrated genome-wide and bioinformatics approach to interrogate gene regulatory network in cancer. His research interests are transcriptional and epigenetic mechanisms of carcinogenesis. He has received several scientific awards including the American Association of Cancer Research (AACR) Scholar-in-Training Awards for 3 consecutive years (2004-2006) and Travel Grants/Oral Free Paper Prize from the United European Gastroenterology for the past 3 years (2011-2013). Dr. Alfred Cheng published in international journals including *Molecular Cell*, *Nature Genetics*, *Journal of Clinical Investigation*, *Cancer Cell*, *Cancer Research* and *Gastroenterology*. He has presided as PI capacity in 8 competitive local (RGC-GRF, RFCID, HMRF) and national (NSFC) research projects.