

CANCER SCIENCE INSTITUTE OF SINGAPORE

SEMINAR ANNOUNCEMENT

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Resistance to EGFR Tyrosine Kinase Inhibitors

Date: Thursday, 19 September 2019
Time: 11.00am – 12.00pm
Venue: L1 Auditorium, Clinical Research Centre (MD11)
 10 Medical Drive, Singapore 117597
Host: Dr Takaomi Sanda

Abstract:

The discovery of somatic mutations in *epidermal growth factor receptor (EGFR)* and development of EGFR tyrosine kinase inhibitors (TKIs) have revolutionized treatment for non-small cell lung cancer (NSCLC) with *EGFR* mutations. These oncogenic *EGFR* mutations trigger both pro-survival and anti-apoptotic signals, and inhibition of these aberrant signals causes massive apoptosis of tumor cells and tumor regression. Recently, it has been shown that osimertinib, a third-generation *EGFR* inhibitor that was originally developed to target the gatekeeper *EGFR*-T790M mutation, can be used as first-line therapy for advanced NSCLC with *EGFR* mutations. However, intrinsic and acquired resistance to osimertinib remains a serious problem in clinic. In this presentation, I will summarize the current knowledge about mechanisms of resistance to osimertinib and other preclinical *EGFR* TKIs. In addition, I will share our recent data demonstrating that β -catenin may contribute to the emergence of drug-tolerant cells in the presence of *EGFR* TKIs. Targeting these critical signaling pathways downstream of mutant *EGFR* may provide novel strategies to prevent lung cancer development or overcome resistance to *EGFR* TKIs.

Biosketch:

Dr. Susumu Kobayashi is Associate Professor of Medicine at Harvard Medical School in Boston, United States, and Chief of Division of Translational Genomics at National Cancer Center, Kashiwa Japan. He received his M.D. and Ph.D. degrees from Kyoto University in 1994 and 2003, respectively. He completed clinical training in Internal Medicine in Japan. In 2002, he moved to Boston and completed research training as a postdoctoral fellow in Dr. Daniel Tenen's laboratory at Bath Israel Deaconess Medical Center. He established his own independent laboratory at the same institution in 2009 and started his NCC laboratory in 2018. Currently, his research concentrates on three topics: 1) studying the mechanisms of resistance caused by *EGFR* tyrosine kinase inhibitors (TKIs); 2) studying the *bcl-2* family proteins, which are responsible for tyrosine kinase inhibitor-induced apoptosis; 3) screening and pharmacogenomics studies of compounds, which induce cell differentiation of lung cancer and leukemia. His team's goal is to provide novel therapeutic options to prevent/overcome resistance to current therapies leading to a better prognosis of cancer patients. In recognition of his work, Dr. Kobayashi received several awards, including Team Science Award from American Association of Cancer Research in 2010.