



The Singapore Bioimaging Consortium (SBIC)
presents a seminar

on

“Coupling of the Keap1-Nrf2 system to Autophagy”

Speaker: Dr Masaaki Komatsu
Senior investigator
Tokyo Metropolitan Insutitute of Medical Science
Tokyo Metropolitan Organization for Medical Research

Date : Tuesday, 9 April 2013
Time : 11.00am – 12.00pm
Venue : SBIC Seminar Room, 11 Biopolis Way
Level 2, Helios Building
Singapore 138667
(Please use Level 1 entrance)

Abstract

Autophagy and the Keap1-Nrf2 system are both involved in the oxidative-stress response, metabolic pathways, and innate immunity, and dysregulation of these processes is associated with pathogenic processes. However, the interplay between these two pathways remains largely unknown. Dr Komatsu will show that phosphorylation of the autophagy-adaptor protein p62 markedly increases p62's binding affinity for Keap1, an adaptor of the Cul3-ubiquitin E3 ligase complex responsible for degrading Nrf2. Thus, p62 phosphorylation induces expression of cytoprotective Nrf2 target genes. p62 is assembled and subsequently phosphorylated on selective autophagic cargos such as ubiquitinated organelles, implying that the Keap1-Nrf2 and selective-autophagy systems are coupled. Furthermore, persistent activation of Nrf2 through significant accumulation of phosphorylated p62 contributes to growth of human hepatocellular carcinomas (HCC). These results demonstrate that selective autophagy and the Keap1-Nrf2 pathway are mutually dependent, and that inhibitors of the interaction between phosphorylated p62 and Keap1 have potential as therapeutic agents against human HCC.

About the Speaker

After PhD training in biochemistry at Juntendo University School of Medicine and postdoc work in mouse genetic study of autophagy, Dr Komatsu became an independent investigator at Tokyo Met. Inst. Med. Sci (TMIMS). Dr Komatsu has been a pioneer in autophagy research with mouse genetics. The long-term goal of the Komatsu Laboratory is to understand cellular and molecular mechanisms of autophagy regulation in physiology and pathology.

--- Admission is free and all are welcome ---