香港浸會大學
HONG KONG BAPTIST UNIVERSITY

School of 中醫藥學院
Chinese Medicine

SCM Seminar

The double-edged Sword of Autophagy and Nrf2 in Cancer

Prof. Ding Wenxing

Department of Pharmacology, Toxicology and Therapeutics,
University of Kansas Medical Center, USA

Date: 28 July 2014 (Monday)
Time: 4:30-6:00 P.M.
Venue: SCM 809
Language: English / Putonghua
Facilitator：Dr. Li Min

Abstract

Autophagy is a genetically programmed, evolutionarily conserved intracellular degradation pathway involved in the trafficking of long-lived proteins and cellular organelles to the lysosome for degradation to maintain cellular homeostasis. It has been generally thought that autophagy serves as a tumor suppressor mechanism against tumorigenesis. In contrast, cancer cells can also use autophagy as a cell survival mechanism against traditional chemotherapy resulting in drug resistance. However, the exact mechanisms by which autophagy works as a double-edged sword in cancer are largely unknown. We found that hepatocyte-specific Atg5 knockout mice had hepatomegaly, increased cell death followed by inflammation, hepatic fibrosis and spontaneous liver tumor formation. Interestingly, we found that these mice are resistant to further drug or TNFa induced hepatocyte cell death due to the compensatory activation of Nrf2, a transcriptional facto that regulates expression of antioxidant genes. Intriguingly, further deletion of Nrf2 in Atg5 liver-specific knockout mice markedly abolished these pathological changes indicating a key role for this transcription factor in the mechanism of hepatic injury and tumorigenesis. In contrast, cancer cells that have higher Nrf2 activation are resistant to chemotherapy. The physiological significance and mechanisms of autophagy and Nrf2 in regulating tumorigenesis and cancer cell survival will be discussed.

**** All are welcome ****