CDB SEMINAR

Hyung Don Ryoo

Department of Cell Biology, New York University School of Medicine

Thursday, December 9, 2010

11:00~12:00 A7F Seminar Room

Regulation of endoplasmic reticulum stress in *Drosophila*

Summary

Endoplasmic reticulum (ER) is a major site of protein synthesis and trafficking, and stress in this organelle can activate a number of signaling responses that helps the cells return to their normal physiological state. However, a chronic exposure to ER stress can trigger apoptosis of vital cells and manifest into disease. Over the past few years, we have been employing *Drosophila* genetics to better understand how cells cope with stress in the ER and succumb to apoptosis. To this end, we have developed a number of molecular sensors of ER stress and used these to determine that ER-stress underlies retinal degeneration caused by mutations in the *Drosophila* rhodopsin-1 gene, similar to the human condition known as Autosomal Dominant Retinitis Pigmentosa (ADRP). In addition, we have developed a *Drosophila* eye based assay where excessive ER-stress is inflicted during development, leading to abnormal adult structures. This system has allowed us to perform genetic interaction screens, through which we have discovered ER quality control genes as well as apoptosis regulators. Through one particular screen using the in vivo RNAi approach, we identified a previously unrecognized pro-apoptotic pathway that links distressed ER to the apoptotic machinery. This pathway, consisting of cdk5, mekk1 or JNK, inhibits ER-stress-induced apoptosis, while not affecting other branches of the ER stress-response signaling. Such conditions also delay the course of age-related retinal degeneration in the *Drosophila* model of ADRP. These finding reveal a novel pro-death signaling pathway relevant to disease caused by ER-stress-induced apoptosis.

This seminar is cosponsored by Kobe University Global COE.

Host:
Shigeo Hayashi
Morphogenetic Signaling, CDB
shayashi@cdb.riken.jp
Tel:078-306-3185 (ext:1523)