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THE HONG KONG UNIVERSITY OF SCIENCE & TECHNOLOGY
Division of Life Science
Center of Systems Biology and Human Health

LIFS Seminar Series

EPG5: tethering autophagosome maturation to Vici syndrome

by

Prof. Hong ZHANG
State Key Laboratory of Biomacromolecules,
Institute of Biophysics, Chinese Academy of Sciences, Beijing

Abstract:

Autophagy involves the sequestration of a portion of the cytosolic contents in an enclosed double-membrane autophagosomal structure and its subsequent delivery to lysosomes for degradation. The molecular understanding of autophagy has originated almost exclusively from yeast genetic studies. The autophagy process exhibits fundamental differences between yeast and higher eukaryotes, including the presence of steps unique to higher eukaryotes (e.g. autophagosomes maturation). My lab established *C. elegans* as one of the premier genetic models to study autophagy. Using this model, we carried out the first systematic genetic screens in multicellular organisms and identified a set of metazoan specific autophagy genes, known as *epg* genes.

Among the identified *epg* genes, we demonstrated that EPG-5 acts a tethering factor that determines the fusion specificity of autophagosomes with late endosomes/lysosomes. EPG5 is recruited to late endosomes/lysosomes by direct interaction with Rab7. EPG5 also binds to LC3/LGG-1 (mammalian and *C. elegans* Atg8 homolog, respectively) on autophagosomes. EPG5 stabilizes and facilitates the assembly of STX17-SNAP29-VAMP7/8 *trans*-SNARE complexes for fusion of autophagosomes with late endosomes/lysosomes. By performing genetic suppressor screens, we revealed that a block in *O*-GlcNAc-modification of SNAP29 facilitates formation of the trans-SNARE complex and suppresses the accumulation of autophagic vacuoles caused by *EPG5* deficiency. To investigate the physiological function of *Epg5* in mammals, we generated *Epg5/epg-5* knockout mice and found that *Epg5* deficiency causes selective damage of certain neuronal populations. Recent studies revealed that *EPG5* mutations are causatively linked with the multisystem disorder Vici syndrome. *Epg5* knockout mice recapitulate key features of Vici syndrome. Our study reveals that EPG5 is a Rab7 effector involved in autophagosome maturation, providing insight into the molecular mechanism underlying Vici syndrome.

Date : 26 May 2017 (Friday)

Time : 4:00 p.m.

Venue : Lecture Theatre G
The Hong Kong University of Science & Technology
Clear Water Bay, Kowloon

(Host faculty: Prof. Zilong Wen)

All are Welcome!!