City University of Hong Kong
Department of Biomedical Sciences
presents a seminar

"AUTOPHAGY REGULATES HEPATOCELLULAR CARCINOMA TUMORIGENESIS THROUGH THE SELECTIVE DEGRADATION MACHINERY"

by

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Date: **1 March 2016 (Tuesday)**
Time: **10:30 am - 12:00 noon**
Venue: **Meeting room 2-130, 1/F, Block 2, To Yuen Building, CityU**

Abstract

Autophagy, microRNA (miRNA) and cell cycle regulator cyclin D1 are regulators during cancer cell tumorigenesis. Impaired autophagy and high expression of miR-224 and cyclin D1 are prevalent in hepatocellular carcinoma (HCC); however, the relationship among has not been explored. We demonstrated that in human HCC, low autophagic activity together with high expression of miR-224 and cyclin D1 is detected and correlated with poor overall survival rate. The former caused the decreased expression of miR-224 target gene Smad4, which negatively regulates cell migration and tumor formation. The latter is responsible for cell cycle arresting at G0/G1 phase and decreased cell proliferation. Selective recruitment of both miR-224 and ubiqutinated-cyclin D1 in the purified autophagosomes was confirmed by a) miRNA in situ hybridization under confocal microscopy, and b) immune-gold labeling of miR-224 and cyclin D1 under electron microscopy. We further found that an antiarrhythmic drug, amiodarone effectively suppressed HCC tumorigenesis through autophagy-mediated selective degradation of miR-224 and cyclin D1 both in vitro and in vivo. In summary, we are the first to demonstrate that autophagy may regulate two oncogenic factors simultaneously through the selective autophagic degradation machinery. Our findings strongly suggest that amiodarone, as an off-label drug, is a novel autophagy inducer with the potential for suppression of liver tumor formation. Further research on the clinical treatment of HCC patients showing aberrant autophagic activity is warranted.

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All are welcome