香港浸會大學
HONG KONG BAPTIST UNIVERSITY

School of 中醫藥學院
Chinese Medicine

ATP13A2 Regulates HDAC6 Activity to Control Autophagosome-Lysosome Fusion

Dr. Tan Jieqiong

Center of Medical Genetics
Central South University, Changsha, Hunan, China

Date	:	6 February 2018 (Tuesday)
Time	:	4:30 pm – 6:00 pm
Venue	:	SCM 809
Language	:	English
Facilitator	:	Prof. Li Min

Abstract

Loss of function mutations of ATP13A2, a lysosomal P5 type ATPase, cause Kufor-Rakeb syndrome (KRS), an autosomal recessive form of juvenile-onset atypical Parkinson disease (PD). The pathophysiological function of ATP13A2 is not fully understood. Our results indicate loss of ATP13A2 lead to lysosome accumulation and dysfunction, and the inhibitor of autophagic flux. In ATP13A2 deficient HEK293 cells, mouse liver and *Drosophila* neural tissues, HDAC6 activity was inhibited. Overexpression of HDAC6 WT in ATP13A2 null cells and ATP13A2 deficient *Drosophila* neural cells, both lysosomal abnormality and ubiquitinated protein were restored or degraded, while these abnormalities cannot be restored by HDAC6 deacetylase domain mutants. Through *in vitro* fusion assay, we identified loss of ATP13A2 further block lysosome sequencial engulfment of autophagosomes which could be the molecular basis of ATP13A2 function in autophagic flux. Our results also proved ATP13A2 needs cortactin to assemble actin filament on lysosome which is indispensable for lysosome association with autophagosome. Interestingly, loss of ATP13A2 leads to mouse liver hepatomegaly and injured organelles or autophagosomes accumulation which coordinated with autophagy related genes mouse phenotypes. This study identifies a novel function of ATP13A2 and a mechanism of autophagosome-lysosome fusion in autophagy with an essential role of ATP13A2, and opens a new avenue to design treatment strategies targeting HDAC6-mediated autophagy for both KRS and PD

~ All are welcome ~