香港浸會大學
HONG KONG BAPTIST UNIVERSITY

School of 中醫藥學院
Chinese Medicine

Lysosomal calcium signaling regulates autophagy via calcineurin and TFEB

Dr. Diego Luis MEDINA

Head, High Content Screening Laboratory,
Telethon Institute of Genetics and Medicine (TIGEM), Napoli-Italy

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Facilitator	**:**	**Prof. Li Min**

Abstract

The view of the lysosome as the terminal end of cellular catabolic pathways has been challenged by recent studies showing a central role of this organelle in the control of cell function. Here we show that a lysosomal Ca^{2+} signaling mechanism controls the activities of the phosphatase calcineurin and of its substrate TFEB, a master transcriptional regulator of lysosomal biogenesis and autophagy. LysosomalCa^{2+} release via mucolipin 1 (MCOLN1) activates calcineurin, which binds and de-phosphorylates TFEB, thus promoting its nuclear translocation. Genetic and pharmacological inhibition of calcineurin suppressed TFEB activity during starvation and physical exercise, while calcineurin overexpression and constitutive activation had the opposite effect. Induction of autophagy and lysosomal biogenesis via TFEB required MCOLN1-mediated calcineurin activation, linking lysosomal calcium signaling to both calcineurinregulation and autophagy induction. Thus, the lysosome reveals itself as a hub for the signaling pathways that regulate cellular homeostasis.

*** All are welcome ***