IJAE Vol. 115, n. 1/2 (Supplement), 2010

Mouse models of epsins in endocytosis

Alessandra Zatti[1], Hong Chen[2], Giuseppina Di Giacomo[1], Simona Ferron[1], Genevieve Ko[3], Elisa Sala[1], Annunziata Venuto[1], Pietro De Camilli[3], Ottavio Cremona[1]

[1] Experimental Imaging Centre, Università Vita-Salute San Raffaele, Milano, Italy
[2] Cardiovascular Biology Program, Oklahoma Medical Research Foundation, Oklahoma City, USA
[3] HHMI Institute, Departments of Cell Biology, Neurobiology and Pathology, Kavli Institute for Neuroscience, Yale University, New Haven, USA

Endocytosis has been traditionally considered as a mechanism to maintain plasma membrane homeostasis and internalize extracellular molecules. In the last few years, this view has been considerably expanded due to the accumulating evidence that endocytosis may also serve as a platform for intracellular signaling and actin dynamics. The multiplicity of endocytic actions relies on an extensive network of molecular interactions that are actively investigated both in vitro and in vivo. This network is supported by a variety of adaptor proteins that act as hubs for different cellular functions. Epsins are prototypes of such class of endocytic adaptors, with multiple interaction surfaces for factors implicated in endocytosis, actin dynamics, nuclear and ubiquitin function. By a genetic approach in mice, we systematically inactivated the three epsin genes in mammal. While single epsin knockouts (KO) do not show major phenotypic defects, double knockout (DKO) mice of the ubiquitously expressed epsins, i.e. the epn1/2 DKOs, are embryonic lethal at the beginning of organogenesis. Morphological, biochemical and expression analyses show defects that correlate with a disruption of the Notch signaling pathway. Strikingly, no alterations are observed in housekeeping internalization pathways as a consequence of epsin absence, strongly supporting the notion that epsins belong to a new class of endocytic adaptors with a specific function in intracellular signaling.

Key words
Epsins, endocytosis, gene targeting, Notch signalling