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Epsins function in Notch signaling activation

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In mechanistic terms, endocytosis is the process by which plasma membrane (PM) components, together with extracellular solutes, macromolecules and particles, are internalized in the cell. Once the endocytic vesicle (or vacuole) is formed by fission of the PM, it is generally delivered to a specialized membrane compartment – the endosome – for recycling, degradation or re-routing.

In cell-physiological terms, endocytosis exerts multiple functions, which are only partially known and characterized. At a minimum, it maintains PM homeostasis by counterbalancing the apposition of new membrane (due to exocytosis) and by renewing PM components. More extensively, endocytosis constantly modulates PM composition and takes an active part in a variety of normal and pathological cell processes, including cell nutrition, cell motility, mitosis, neurotransmission, immune response, and microorganism entry. In recent years, much of the effort to investigate this extensive endocytic activity has been focused upon unveiling the reciprocal interplay between endocytosis and cell signaling.

Our laboratory, in collaboration with the laboratory of Pietro De Camilli (Yale University, USA) has pioneered the use of genetic models in mice to study several aspects of the endocytic function, mostly at the synapse. Recently, we generated mice models for a highly conserved gene family of multidomain adaptors – the epsin family - whose function was linked to endocytosis. By characterizing the phenotypic defects of the epsin1/2 double knockout mice, we found that epsins are essential components of the machinery required for Notch signaling activation during embryogenesis in mammals [1].

More recently, we characterized that epsins molecular action is exerted in a ubiquitin-dependent endocytic reaction that triggers the internalization of the Notch ligand, a process necessary for the activation of the Notch receptor. Our preliminary data extend epsin function to Notch signaling activation in primary keratinocytes and to VEGF signaling modulation in angiogenesis.

References

[1] Chen H, Ko G, Zatti A, Di Giacomo G, Liu L, Raiteri E, Perucco E, Collesi C, Min W, Zeiss C, De Camilli P, Cremona O (2009) Embryonic arrest at midgestation and disruption of Notch signaling produced by the absence of both epsin 1 and epsin 2 in mice. Proc. Natl. Acad. Sci. U. S. A. 106: 13838-13843.

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