A Fast Clathrin-independent Endocytic Mechanism

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Abstract

Cell shape is adapted to function. Organelle shape and local membrane architectures are likewise optimised for the processes that take place on and within these microenvironments. We focus on the dynamic regulation of membrane shape, which can occur by the interplay between the transient and regulated insertion of membrane bending motifs and the detection and stabilisation of membrane shape. This approach has allowed us not only to describe the biophysics of membrane shape changes but also to take a fresh look at membrane dynamics in physiological processes like exocytosis and endocytosis. In doing so we have noted that proteins with amphipathic helices or hydrophobic membrane-inserting loops are likely to effect or respond to curvature and that the membrane interaction surfaces of proteins can sense shape (like proteins of the BAR Superfamily). This molecular view has allowed us to ascribe novel cell-biological functions to proteins (e.g. the mechanistic affect of synaptotagmin in membrane fusion) and to give a more insightful view of how these processes work. Thus we can now go from the biophysics of a molecule, to better understanding of known pathways and to the molecular characterisation of novel cellular trafficking pathways both of endocytosis and exocytosis. I will present one such novel pathway that we are in the midst of characterising. It is a ubiquitous pathway operating especially in synapses but also in all cell types we have tested. It is clathrin-independent and dynamin dependent and operates at a much faster timescale that clathrin vesicle formation. We believe that a molecular understanding of this pathway will lead to fresh insights into fast membrane trafficking responses, like synaptic vesicle retrieval. For further details of our approaches see: http://www.endocytosis.org/