Disgorging the MVB

The multivesicular body (MVB), a cluster of vesicles surrounded by a limiting membrane, is a ubiquitous but poorly understood structure in eukaryotic cells. On page 53, Kleijmeer et al. present the first evidence that the MVB can be used as a temporary storage depot for membranes and membrane proteins, which can then be deployed rapidly to the surface of the cell. The work also helps to explain how certain antigens are presented to initiate a primary T cell response. Previous work on this problem had left a basic topological question unresolved: how does antigen-presenting MHC II move from the internal vesicles of the MVB to the exterior surface of the plasma membrane? The authors found that in immature cultured dendritic cells, MHC II is concentrated in the internal vesicles of MVBs, while the peptide-loading accessory molecule DM is found mostly in the MVB limiting membrane. When the cells are activated, the internal vesicles fuse with the limiting membrane, presumably allowing DM to load antigen onto the MHC. The MVB then elongates into a tubular structure that extends toward the plasma membrane. Vesicles containing both MHC II and DM bud from the tip of this structure, possibly ending up at the cell surface where antigens are displayed.

Knock twice before invading

Neisseria meningitidis, also known as meningococcus, is a pathogen with a nasty habit of forcing normally nonphagocytic endothelial cells to engulf it, allowing the bacterium to penetrate cellular barriers. Hoffmann et al. now demonstrate on page 133 that N. meningitidis activates two distinct signaling pathways in host cells to cause actin cytoskeleton reorganization and engulfment of the bacterium. Adherence of the bacteria to endothelial cells causes massive and specific aggregation of the receptor tyrosine kinase ErbB2, which normally transduces signals by heterodimerization with other ErbB-like receptors. However, during N. meningitidis invasion, ErbB2 forms homodimers that, once autophosphorylated, can activate the src kinase. Inhibiting this process prevents internalization of the pathogen, but does not block the characteristic actin rearrangements induced by the bacterium. Blocking both ErbB2/src signaling and actin polymerization completely prevents bacterial engulfment, indicating that the two pathways are independent, but that both are required for invasion. While it is possible that ErbB2 is a receptor for the bacterial pilus, the data are also consistent with the recruitment of ErbB2 as part of a multiprotein complex that includes an unknown receptor.

In separate work, Bierne et al. (page 101) characterized phagocytosis induced by the pathogen Listeria monocytogenes, and observed actin cytoskeleton remodeling that is apparently mediated by the activation and deactivation of cofilin.

Apical transport gets motorized

To maintain distinct populations of proteins at their apical and basolateral membranes, polarized cells package and sort membrane proteins into vesicles, which then dock specifically at one membrane or the other. But is there also a selective transport system to carry the vesicles to their destinations, and, if so, how does it work? Noda et al. report on page 77 that a new kinesin family member, KIFC3, can act as a microtubule motor associated with apically targeted transport vesicles, apparently independently of cytoplasmic dynein–dynactin-dependent transport.

As microtubules in polarized cells extend their minus ends apically, the authors cloned and characterized KIFC3, a putative minus-end–directed microtubule motor protein uncovered in an earlier search for novel kinesins. KIFC3 is concentrated on membrane organelles near the apical plasma membrane of polarized epithelial cells, colocalizing with annexin XIIIb, a membrane protein found in apically targeted transport vesicles. Overexpressing a dominant-negative form of KIFC3 partially inhibits apically targeted transport. Interestingly, the KIFC3-associated vesicles lack cytoplasmic dynein, and electron microscopy confirms that the two motor proteins do not colocalize, suggesting that they drive independent transport pathways. Because KIFC3 expression levels vary significantly between tissues, the authors propose that cytoplasmic dynein may drive constitutive apical transport, which could be supplemented by KIFC3-mediated transport in some cell types.