Editorial

Editorial Overview: Membrane Traffic and Cell Polarity

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The marriage between cell polarization and membrane traffic has been long appreciated, but until recently has been poorly understood. To build a polarized cell with asymmetrically organized cell surfaces, such as an apical-basal polarized epithelium, cells must deliver and maintain proteins, lipids, and secreted components to a common cell cortex (1). Accompanying any cell surface polarity rearrangement is an equally complex intracellular organelle reorganization (2). This simple idea can be used by neighbouring cells to give rise to very complex tissues; organize apical-basal polarization in the same orientation between neighbours and a monolayer can be made. Do the same radially around an intercellular space and a lumen may form. Two key events in such polarization are the generation of cadherin-based cell-cell adhesion, and the formation of the apical surface (3). This set of reviews walks the aisle of this polarity and trafficking marriage to focus on how trafficking of cadherins and apical domain-generating proteins is regulated and how it contributes to apical-basal polarization and tissue morphogenesis.

The first review by West and Harris (4) summarises the regulators and consequence of cadherin trafficking, with a focus on tissue morphogenesis. Studies in *D. melanogaster* and *C. elegans* have illuminated the consequence of altering cadherin trafficking, and the morphogenetic processes that require cadherin endocytosis and recycling in order to remodel tissues. Although how cadherin trafficking is utilised may differ between model systems, a key concept has arisen: endocytosis of cadherin, and possible transit through Rab11-positive recycling endosomes, is essential to regulating cadherin cell surface levels (5-7). Given the fundamental roles for cadherins in controlling cell adhesion and the actin cytoskeleton (8), altering surface cadherin levels can provide an instructive mechanism for how mechanotransduction is transmitted across a tissue.

The review from Román-Fernández and Bryant (9) examines the function and regulation of apical domain-promoting proteins in the formation of epithelial polarity. The review summarizes the trafficking itineraries and their regulators, for three apical proteins that have emerged as core regulators of apical domain formation: the Crumbs family of proteins, the light-sensor molecule Rhodopsin, and the CD34-family sialomucin protein Podocalyxin (3, 10). More than just being static transport routes that merely transport polarity-inducing cargo, intracellular organelle asymmetry itself has emerged as key to forming apical-basal polarization (2, 11). These studies underscore the notion that trafficking and polarity are not two independent processes, but are part of the same morphogenetic process to deliver and maintain distinct proteins and lipids to distinct cell surface domains.

The final review from Cadwell and colleagues [reference needs to be updated] delves deep into the trafficking pathways, machineries, and sorting mechanisms that control cadherin endocytosis and recycling. Membrane trafficking as a mechanism to remodel cell-cell interfaces has become increasingly appreciated since the first demonstration of E-cadherin recycling as a mechanism to control surface levels (6), the sorting motifs that contribute cadherin surface targeting (12), and the mechanisms that induce its endocytosis (13). At the heart of all of these processes is the factotum p120-catenin, which through binding and potentially masking various

sorting motifs in the cadherin tail modulates the spatial regulation of cadherin endocytosis (14). The list of cadherin modifications and the machineries that recognise and route endocytic cadherin molecules continues to grow. These studies paint a picture of a complex relationship between cadherin trafficking and cell morphogenesis, which highlights the central importance of controlling just the right amount of cadherin on the cell surface at any one time.

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