Sorting and Surface Delivery of Planar Cell Polarity Proteins: Molecular Mechanisms and Physiological Implication

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Planar cell polarity (PCP), a phenomenon in which epithelial tissue is polarized within the plane of the epithelium, plays a crucial role in development and organ function. The establishment of PCP is controlled by a group of conserved signaling proteins that are localized asymmetrically on opposing cellular boundaries. Although fundamentally important, how newly synthesized PCP proteins are delivered to their specific destination to perform their physiological functions remains largely elusive. Here, we isolated TGN-derived vesicles enriched with a PCP protein, Frizzled6 (Fzd6). Quantitative mass spectrometry analyses revealed several transmembrane proteins that are specifically packaged in Fzd6 vesicles. Among them, a SNARE protein, VTI1B, enhances the interaction between Fzd6 and its cargo adaptor, epsinR, and promotes TGN-to-cell surface delivery of Fzd6. Another protein, SCAMP2, was demonstrated to regulate transport of Fzd6 to lysosomes for degradation. Knockdown of the *Drosophila* homologue of VTI1B or SCAMP2 causes defects in wing hair orientation. These analyses indicate that VTI1B and SCAMP2 are co-packaged with Fzd6 in TGN-derived vesicles, and mediate post-Golgi trafficking of Fzd6 for the propagation of PCP. In addition, our study establishes a robust approach to reveal protein profiling of vesicles enriched with a specific cargo protein, providing a powerful tool to identify novel factors regulating vesicular trafficking.