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Review Article

Planar cell polarity of the kidney

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Planar cell polarity (PCP) or tissue polarity refers to the polarization of tissues perpendicular to the apical-basal axis. Most epithelia, including the vertebrate kidney, show signs of planar polarity. In the kidney, defects in planar polarity are attributed to several disease states including multiple forms of cystic kidney disease. Indeed, planar cell polarity has been shown to be essential for several cellular processes that appear to be necessary for establishing and maintaining tubule diameter. However, uncovering the genetic mechanisms underlying PCP in the kidney has been complicated as the roles of many of the main players are not conserved in flies and vice versa. Here, we review a number of cellular and molecular processes that can affect PCP of the kidney with a particular emphasis on the mechanisms that do not appear to be conserved in flies or that are not part of canonical determinants.

Contents

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What is planar cell polarity?

Planar cell polarity (PCP), also known as tissue polarity, describes the coordinated polarization of cells within the plane of a tissue/epithelium, which is perpendicular to the apical-basal cell polarity axis. Although PCP is particularly apparent in tissues that give rise to oriented external structures, such as *Drosophila* wing hairs (Fig. 1) and cuticular bristles, mammalian body hair or the stereocilia in the inner ear (Fig. 2), most tissues show some aspect of PCP during their development or in their differentiated state. Examples are directional cell movement and oriented cell divisions during morphogenesis or the uniform orientation of asymmetrically shaped cells observed in many epithelial tissues.

PCP is important in a broad array of developmental and physiological processes in vertebrates, and defects in PCP signaling have been associated with many developmental anomalies and diseases [1]. Although roles for orthologs of the *Drosophila* PCP genes in PCP-like processes have been uncovered in vertebrates, in some cases the phenotypes are extremely mild and great effort must be made to find any sort of defect, suggesting that PCP in vertebrates may be much more complex than in flies. In agreement with this idea, a number of vertebrate-specific PCP components have been identified [2], some of which appear to have a more significant role in PCP than members of any of the *Drosophila* cassettes.

Several excellent reviews have recently been written on the topic of PCP, usually focused on one particular process, organism or tissue type. In this review, we will provide a brief overview of the conserved regulators of PCP as well as some vertebrate-specific PCP regulators. Further, we will discuss PCP in the kidney with a particular emphasis on data that we feel indicate novel regulation in this organ.

How is PCP established?

Genetic and molecular studies performed primarily in *Drosophila* have identified three signaling modules: one or more global directional modules that establish polarity with regard to the axes of the entire tissue, a core module that establishes local polarity, and a variety of tissue-specific effector modules downstream of the core and global modules that regulate polarity at the level of individual cells.

The role of the core and upstream groups appears to be largely conserved amongst different species although their precise mechanism may vary. However, it has been suggested that vertebrates also possess a number of regulators not found in flies. Although some of these may play indirect roles, others appear to be bona-fide PCP regulators. In this review, we will discuss the "universal" and "vertebrate specific" regulators as well as the role of morphogenesis in this process. As the tissue specific effectors

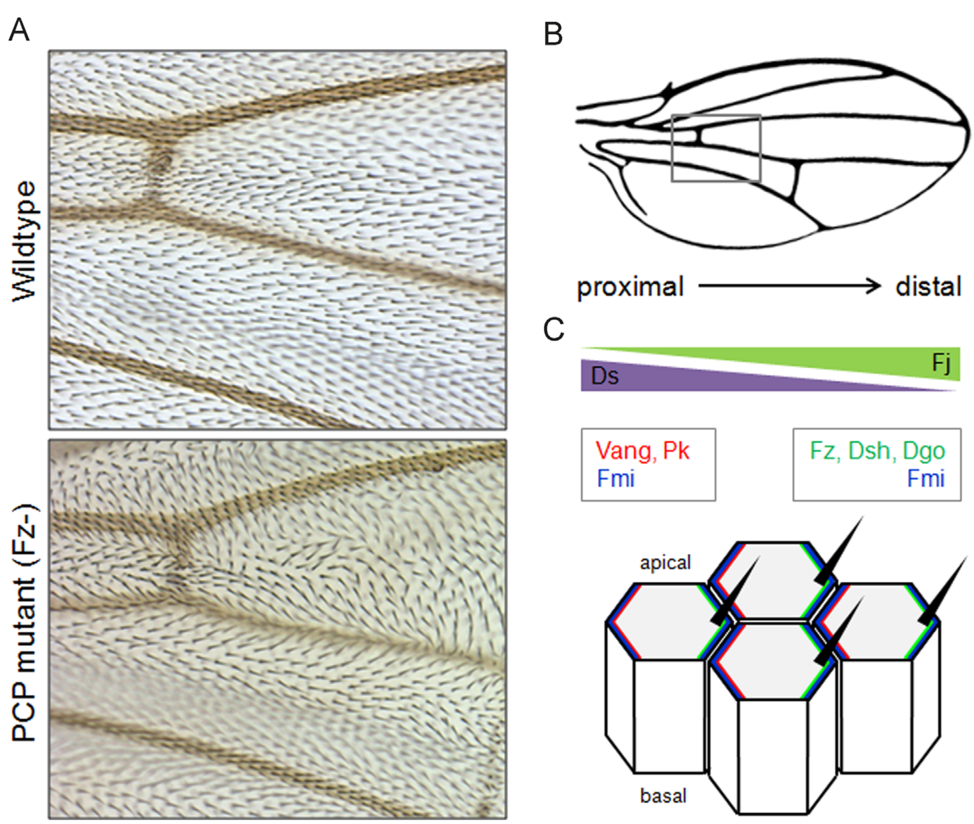

Fig. 1 – PCP signaling in the *Drosophila* wing. A) Epithelial cells in the wing blade generate an actin hair pointing distally in wildtype flies, while mutants lacking Fz show disturbed hair polarization with swirls and waves. The original images were kindly provided by Marek Mlodzik and Jun Wu. B) Schematic illustration of a wing. The grey box indicates the region shown in A. C) Global PCP components Ds and Fj are expressed in opposing gradients across the wing, while the core PCP proteins are asymmetrically localized at the cell junctions between neighboring cells. The asymmetries of global and core proteins generate tissue polarity.