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Review

Asymmetric localisation of planar polarity proteins: Mechanisms and consequences

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ABSTRACT

Planar polarisation of tissues is essential for many aspects of developmental patterning. It is regulated by a conserved group of core planar polarity proteins, which localise asymmetrically within cells prior to morphological signs of polarisation. A subset of these core proteins also interact across cell boundaries, mediating intercellular communication that co-ordinates polarity between neighbouring cells. Core protein localisation subsequently mediates changes in the actin cytoskeleton which lead to overt polarisation. In this review we discuss the mechanisms by which the core planar polarity proteins become asymmetrically localised, and the significance of this subcellular localisation for both intercellular communication and downstream effects on the cytoskeleton.

Contents

1. Introduction

The polarisation of cells in the plane of an epithelium is widespread in the animal kingdom. For example it is evident in the polarised growth of feathers and hair, in ciliated epithelia where the cilia beat in the same direction, and the co-ordinated polarisation of sensory cells in the inner ear [reviewed in 1,2]. The processes leading to planar polarisation have been best studied in *Drosophila*, where polarity is evident in most adult tissues. These include the wing, in which trichomes point from proximal to distal (Fig. 1A), and the adult eye, in which ommatidia point away from the dorsal–ventral midline in a co-ordinated manner (Fig. 1C). A group of "core planar polarity genes" has long been known to control polarisation of diverse adult tissues, and one of the most notable findings in the last few years has been that the protein products of these genes localise asymmetrically in cells of the developing tissue shortly prior to any morphological manifestations of polarity. Another intriguing observation is that clones of cells mutant for some of the core planar polarity genes induce non-autonomous polarity defects in neighbouring wildtype cells, suggesting that they participate in intercellular signalling [reviewed in 3,4].

In this review, we will examine how the asymmetric localisation of core planar polarity proteins is related to the propagation of polarity information across the axes of the tissue. Next, we will discuss recent progress in understanding the mechanisms by which the core proteins become asymmetrically localised. Finally, we will consider how asymmetric localisation of core proteins leads to morphological changes in the actin cytoskeleton. We will focus our discussion on the *Drosophila* wing, as this is the system in which these processes have best been studied; however, it is expected that similar cellular mechanisms operate in other tissues.

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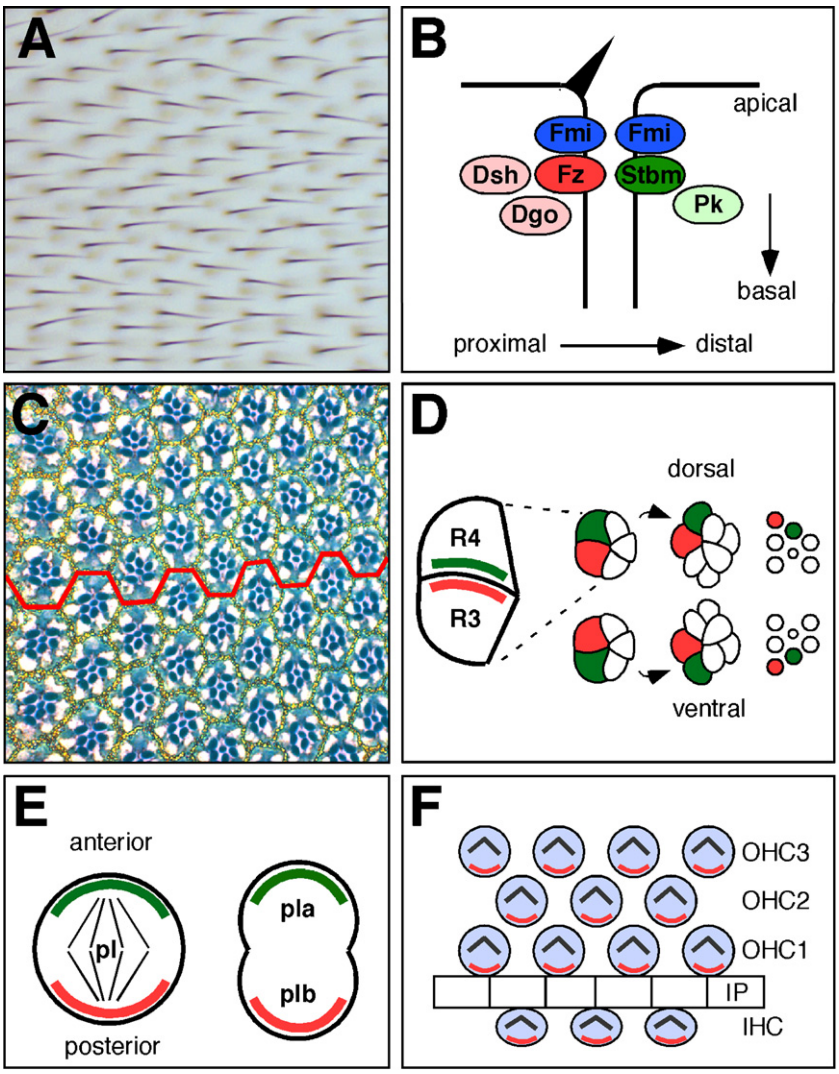

Fig. 1. Asymmetric localisation of core planar polarity proteins. (A) Wildtype adult wing, in which each cell produces a distally pointing trichome. (B) Prior to trichome emergence, core planar polarity proteins localise to the apicolateral junctional region, forming an asymmetric complex as illustrated. (C) Ommatidia in the adult eye point in opposite directions on either side of the dorsoventral midline (red line). (D) Fz (red) and Stbm (green) localise on either side of the R3-R4 photoreceptor cell boundary, with Fz localising on the side of the boundary closest to the dorsoventral midline. Ommatidia then rotate such that the cell localising Fz moves away from the midline. (E) In the sensory organ precursor cell pI, Stbm (green) localises at the anterior cortex and Fz (red) localises to the posterior cortex. This orients the axis of cell division and determines the correct segregation into daughter cells of anterior and posteriorly localised cell fate determinants. (F) Inner hair cells (IHCs) and outer hairs cells (OHCs) in the vertebrate Organ of Corti contain a chevron-shaped arrangement of stereocilia with a kinocilium at its apex. Core planar polarity protein homologues localise asymmetrically, for example Fz (red) localises to the cell cortex opposite the kinocilium.

2. Asymmetric localisation of planar polarity proteins

At the time of trichome formation, the pupal wing consists of an epithelium with apical–basal polarity, containing hundreds of approximately hexagonal cells. At the distal-most vertex of each cell, a single actin-rich trichome emerges from the apical surface (Fig. 1A). Mutations in a group of "core planar polarity genes" cause a delay in trichome initiation, and the trichome forms in the centre of the cell rather than at the distal edge [5]. Ultimately the trichomes form "swirling" patterns in the wing, rather than pointing distally.

One of the first characterised core planar polarity genes was *frizzled* (*fz*) which encodes a seven-pass transmembrane receptor protein [6], and belongs to a family of proteins best known for their roles as receptors for Wnt ligands in canonical Wnt signalling [7]. There is, however, no evidence that Wnt ligands are involved in planar polarity signalling in *Drosophila* (e.g. [8–10]). Frizzled localises to the apicolateral junctional region of pupal wing cells, and shortly prior to trichome emergence it adopts an asymmetric distribution at distal cell edges [11]. The cytoplasmic protein Dishevelled (Dsh) and the ankyrin repeat protein Diego (Dgo) are also localised distally with Fz [12–15]. Conversely, the four pass transmembrane protein Strabismus (Stbm, also known as Van Gogh) and the cytoplasmic protein Prickle (Pk) localise to proximal cell edges [16,17]. Finally, a seven-pass transmembrane cadherin protein Flamingo (Fmi, also known as Starry Night), localises to both proximal and distal cell edges (Fig. 1B) [8,18,19].

Although best studied in the pupal wing, there is increasing evidence that asymmetric localisation of core planar polarity proteins is common to many polarised tissues. In the *Drosophila* eye, the core proteins localise on either side of the R3/R4 photoreceptor cell boundary, and this localisation prefigures the rotation of the ommatidium either clockwise or anticlockwise (Fig. 1D) [20–23]. In sense organ precursor cells the planar polarity genes are essential for determining the axis of cell division and thus the correct partitioning of cell fate determinants [24]: again Fz is localised asymmetrically, at the posterior of these cells, whilst Stbm and Pk are anteriorly localised (Fig. 1E) [25]. More recently, asymmetric localisation of core planar polarity protein homologues has