CELL POLARITY

Coordinated positioning

Many epithelial cell types are polarized along two axes — the apical–basal (A–B) axis and a perpendicular axis, which establishes planar cell polarity (PCP). The coordination between these polarities determines the positioning of structural features on the cells and is essential for tissue development. A report in *Cell* now sheds light on the molecular connection between the A–B axis and PCP in the *Drosophila melanogaster* eye.

Factors that determine PCP are localized apically in fly imaginal-disc cells. Among them, Frizzled (Fz1) partially colocalizes with several determinants of A–B polarity, including the PALS-1-associated tight junction protein (Patj)-containing complex and a complex that comprises Bazooka (Baz), Par6 and atypical protein kinase C (aPKC). Marek Mlodzik and colleagues showed that one of these apical factors, aPKC, phosphorylates the C terminus of Fz1. Overexpression of wild-type Fz1 or a phosphorylation-defective mutant caused a gain-of-function PCP phenotype, whereas a mutant that mimics phosphorylated Fz1 had a reduced gain-of-function phenotype. So, aPKC phosphorylation seems to inhibit Fz1 activity.

Next, the authors asked how aPKC is recruited to the C terminus of Fz1. As it turned out, it was through another apical determinant of A–B polarity, Patj. Overexpression of a Fz1 mutant that lacked the Patj-binding site caused a stronger gain-of-function PCP phenotype compared with overexpression of wild-type Fz1, which indicates that aPKC and Patj are required for the inhibition of Fz1-mediated PCP.

It followed that Patj and aPKC should be absent, or at least downregulated, in R3 and R4 photoreceptor precursor cells that undergo active PCP establishment. Indeed, immunofluorescence studies showed the reduced presence of Patj and aPKC, and an increased signal for apically localized Fz1, in these cells. The opposite pattern was found in the neighbouring cells that lack PCP activity. Interestingly, Baz also showed a complementary immunofluorescence pattern compared with Patj and aPKC, implying it might antagonize the negative regulation of Fz1 by aPKC and Patj. Support for this model came from the finding that the removal of one copy of Baz suppressed the gain-of-function PCP phenotype of overexpressed Fz1.

The authors showed that aPKC phosphorylation did not affect the localization of Fz1 or the recruitment of another PCP factor, Dishevelled (Dsh). So, how does aPKC regulate Fz1 activity? The answer remains unknown for now, but Mlodzik and colleagues suggest that Fz1 phosphorylation might inhibit PCP-specific signalling to Dsh or, alternatively, promote the destabilization or turnover of Fz1.

Arianne Heinrichs

References and links

ORIGINAL RESEARCH PAPER Djiane, A. *et al.* The apical determinants aPKC and dPatj regulate Frizzled-dependent planar cell polarity in the *Drosophila* eye. *Cell* **121**, 621–631 (2005)

IN BRIEF

CELL FATE

Blimp1 is a critical determinant of the germ cell lineage in mice.

Ohinata, Y. *et al. Nature* 5 June 2005 (doi:10.1038/nature03813)

Primordial germ cells (PGCs), the precursors of germ cells, are formed by inductive signals from extra-embryonic tissues, and must then segregate from their somatic neighbours. Ohinata *et al.* showed that proximal posterior epiblast cells expressing the transcriptional repressor Blimp1 are lineage-restricted so that they only produce PGCs. Without Blimp1, fewer PGCs — which do not migrate, proliferate or undergo homeobox gene repression (as normally occurs) — were formed.

TRANSLATION

A newly discovered function for RNase L in regulating translation termination.

Le Roy, F. *et al. Nature Struct. Mol. Biol.* **12**, 505–512 (2005)

The endoribonuclease RNase L participates in inhibiting protein synthesis during interferon-mediated anti-viral and anti-proliferative effects. Le Roy *et al.* report a new function for RNase L — it regulates translation termination. The authors characterized RNA-binding protein (RNABP), a known partner of RNase L, and showed that it was human eRF3/GSPT1, a component of the translation termination complex. The RNase-L–eRF3/GSPT1 interaction increased ribosomal readthrough and increased the +1 frameshift efficiency.

SIGNALLING

Mechanism of divergent growth factor effects in mesenchymal stem cell differentiation.

Kratchmarova, I. *et al. Science* **308**, 1472–1477 (2005)

Why can epidermal growth factor (EGF), but not platelet-derived growth factor (PDGF), induce human mesenchymal stem cells (MSCs) to differentiate into osteoblasts? Both growth factors induce the phosphorylation of common protein subsets, but these authors used a mass-spectrometry-based proteomics approach to identify some differences in the response to EGF and PDGF. The accumulation of phosphorylated components of the phosphatidylinositol 3-kinase pathway in response to PDGF, but not EGF, accounts for the divergence of the differentiation response of MSCs.

CYTOSKELETON

Microtubule-induced focal adhesion disassembly is mediated by dynamin and focal adhesion kinase.

Ezratty, E. J., Partridge, M. A. & Gunderson, G. G. *Nature Cell Biol.* 15 May 2005 (doi:10.1038/ncb1262)

Rho-family GTPases are involved in focal adhesion assembly, but what mediates disassembly? These authors developed an assay in which they observed microtubule-regrowth-induced focal adhesion dissassembly after nocodazole washout (nocodazole depolymerizes microtubules). They showed that Rho or Rac weren't required for disassembly, but that focal adhesion kinase (FAK) and dynamin were — FAK localizes dynamin around focal adhesions, where it might endocytose focal adhesion components.