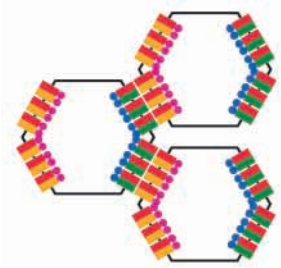
In this issue

Evolutionary insights into skeletal development

In sea urchin embryogenesis, large blastomeres, called micromeres, and their progeny act as an important signalling centre and give rise to mesenchymal skeleton-forming cells. Ettensohn et al. have now identified a new and essential component of the gene network that controls micromere specification – Alx1, the first known invertebrate member of the Cart1/Alx3/Alx4 family of vertebrate paired-class homeodomain proteins that function in limb and craniofacial skeletal development. Morpholino knockdown and gene expression experiments show that Alx1 controls genes required for epithelial-mesenchymal transition and biomineralization. Importantly, these findings, on p. 2917, hint at an evolutionary link between certain features of skeletal development in vertebrates and sea urchins, and indicate that the ancestral deuterostome from which they derive might have had a mesenchymal cell lineage that engaged in biomineralization, in which an Alx1-like protein functioned.

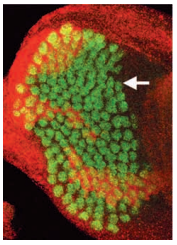
Strabismus functions in planar polarity

Planar cell polarity (PCP) studies in the fly have identified several key proteins, such as Strabismus (Stbm), that are required for planar polarity decisions and act by forming asymmetrically localized complexes. In a study of how Stbm functions in this process, Bastock et al. now show, on p. 3007, that Stbm localizes preferentially to the proximal edge of wing cells in the adherens junction zone where other PCP proteins, such as Dishevelled (Dsh) and Prickle (Pk), also localize. Here, Stbm binds directly to Dsh and Pk to recruit them to cell membranes – in its absence, both proteins become mislocalized. In a two-step model, the authors propose that Stbm acts with Frizzled and Flamingo to apicolaterally localize other PCP proteins, including Dsh and Pk. Dsh and Pk then mediate the asymmetric localization of these proteins to the proximal-distal axis.



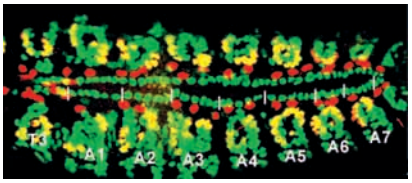
New Hh targets in the eye

In the *Drosophila* eye, loss of Hh signalling blocks the initiation of photoreceptor morphogenesis, but how this comes about is poorly understood. Using loss- and gain-of-function genetics, Graeme Mardon and colleagues have now discovered that the principal role of Hh signalling in *Drosophila* eye development is to alleviate the repression of two key genes that function in a retinal determination network – *dpp* and *eya*. Hh signalling does this, they propose on p. 3053, by blocking the cleavage of the active form of Cubitus interruptus, a Hh pathway component, into its repressive form, which represses *dpp*. Once *dpp* expression is established, it acts with another gene, *ey*, to initiate *eya* expression, in a vital step towards establishing the retinal determination network. Importantly, Hh acts here not as a classical morphogen but as a binary switch that initiates photoreceptor differentiation.



Flying to the heart of heart development

Striking molecular and developmental similarities in heart development exist between flies and vertebrates. For example, both develop from bilaterally symmetrical rows of mesodermal cells that fuse to form a heart tube, which in flies consists of outer pericardial and inner myocardial (cardioblast) cells. The factors that regulate heart development are also conserved between flies and vertebrates, including *tinman* (vertebrate NKX2.5), *dpp* (BMP2/4) and *pannier* (*pnr*, GATA transcription factor homologue). Now three *Development* papers shed new light on heart cell lineages and on the transcriptional mechanisms that control *Drosophila* heart development – findings that will inform studies of vertebrate cardiogenesis. When Alvarez et al. investigated the cardiogenic function of *pnr* and *pointed* (*pnt*), they found that they act sequentially: *pnr* acts early in mesoderm development to bring about cardiac mesoderm (CM) formation, and *pnt* regulates CM cell fate choice. In its absence, cardioblasts form at the expense of pericardial cells, but only in the posterior domain of the heart. Importantly, their findings on p. 3015 indicate that a developmental and genetic distinction exists between the anterior and posterior regions of the heart, with potential functional consequences. Klinedinst and Bodmer, on p. 3027, also investigated *pnr* function and that of its binding partner *u-shaped* (*ush*) in loss-of-function and germ-layer-specific rescue experiments. They report that *pnr* and *ush* are required to initiate and maintain cardiogenesis, respectively, and for myocardial and pericardial cell fates to form. Pnr is also required in the ectoderm, where it might mediate and maintain cardiogenic *dpp* signalling. In a different approach, Han and Bodmer explored heart cell lineages by arresting cardiac cell divisions at various developmental stages. They found, on p. 3039, that the non-dividing progenitors of symmetric cell lineages adopt myocardial- or pericardial-only fates, whereas those of asymmetric divisions adopt a myocardial fate through the inhibition of Notch signalling.



In *Journal of Cell Science*

Rethinking Wnt antagonists?

Wnts regulate cell fate and cell behaviour by binding to Frizzled (Fz) receptors to activate a canonical signalling pathway that stabilizes the transcription factor β-catenin, and by non-canonical mechanisms, such as in planar cell polarity. Secreted Fz-related proteins (SFRPs) antagonize Wnt signalling and act as putative competitive inhibitors by preventing Wnts from interacting with Fz receptors. Esteve et al., however, now report that SFRP function might actually be more complex. They demonstrate that, during chick retinal development, SFRP1 promotes retinal ganglion and cone photoreceptor cell generation, while inhibiting that of amacrine cells. Interestingly, SFRP1 appears to promote retinal cell differentiation without affecting β-catenin-dependent transcription; in fact, canonical Wnt signalling seemingly does not operate in these cells under normal conditions. The authors implicate GSK3β inhibition (usually caused by Wnt activation rather than antagonism) in the SFRP1 effect, and suggest that Wnt-independent mechanisms of SRFP1 action exist, perhaps involving its binding to Fz receptors.

Esteve, P. *et al.* (2003). SFRP1 modulates retinal cell differentiation through a β-catenin-independent mechanism. *J. Cell Sci.* **116**, 2471-2481.