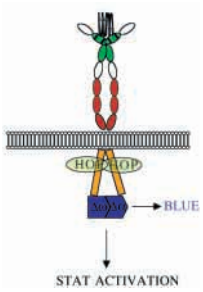
In this issue

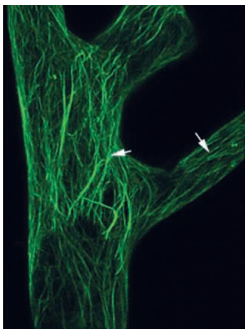
Novel mode of JAK-STAT pathway regulation

By adapting a technique that assays receptor dimerization in vitro for use in whole *Drosophila* embryos, Brown et al., on p. 3077, have discovered a novel level of JAK/STAT signalling regulation. The authors tackled the question of whether the JAK/STAT pathway is activated by ligand-induced receptor dimerization by studying DOME, the ubiquitously expressed fly receptor of the JAK/STAT pathway. They report that in developing fly embryos, DOME homo-dimerization is developmentally regulated and is not ligand induced. Moreover, ligand expression can only activate the pathway or affect embryonic development in cells with dimerized receptors. Thus, the ability to induce JAK/STAT signalling can be regulated by controlling receptor dimerization prior to ligand binding. As this pathway in flies is functionally identical to that in vertebrates, this regulatory mechanism could be conserved across phyla.



F-actin: shaping plant and animal cells

Specific cell types are generated partly by differential growth (when certain cell regions rapidly expand). In animal cells, this requires the actin cytoskeleton. Mathur et al. now report, on p. 3137, that an actin-based mechanism might also regulate differential growth in plants, with their discovery that a mutation in the plant orthologue of *ARPC5* causes random cell expansion and aberrant cell shape in *Arabidopsis CROOKED* mutants. ARPC5 is a subunit of the ARP2/3 complex – an actin polymerization modulator in many organisms that generates fine F-actin arrays. By studying polarized cells in mutant and normal plants, the authors found that localized cell expansion occurs only where fine F-actin is maintained, implicating F-actin density as a likely determinant of cell shape. Importantly, the rescue of *CROOKED* cells with human ARPC5 provides the first evidence that this complex is functionally conserved in higher plants.

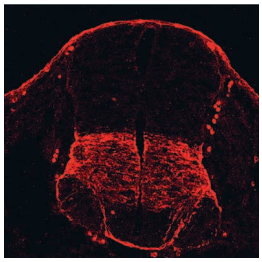


New insights into dauer development

The dauer stage of *C. elegans* development has been well studied to uncover how environmental signals regulate developmental fates. Dauer formation is regulated by three signalling pathways, which the nuclear hormone receptor DAF-12 integrates. On p. 3237, Ohkura et al. report a new dauer-like mutant, *sdf-9*, that resembles the *daf-12* and *daf-9* dauer mutants. By mosaic analysis, the authors show that s*df-9*, which encodes a tyrosine phosphatase-like molecule, is expressed in two mysterious cells in the head, XXXL/R, which also express *daf-9* and *npc-1*. (DAF-9 is involved in synthesizing the ligand of DAF-12 and NPC-1 functions in intracellular sterol transport.) Because ablating these cells reproduces the phenotype of the *sdf-9* mutant, the authors propose that they might play a key role in metabolizing a steroid hormone ligand for DAF-12 through the functions of DAF-9 and SDF-9.

Coordinating patterning and neurogenesis

Regulatory interactions between patterning genes and proneural genes are believed to coordinate the genetic programmes that regionalize the developing spinal cord and brain. Such an interaction, between Pax6 and the proneural gene *Ngn2*, is now shown to exist on p. 3269 by Scardigli et al. In developing mouse spinal cord and brain, the activity of the *Ngn2* enhancer E1 is highest where *Pax6* is most highly expressed. This enhancer contains a low-affinity binding site for Pax6, and its activity is disrupted in *Pax6* null mice and in mice carrying mutated binding-site sequences. Thus Pax6 is required for the activation of E1. However, this only occurs in vivo, as the authors show, at high Pax6 concentrations – increasing *Pax6* dosage in mouse embryos, for example, extends the domains of E1 activity. Together, these comprehensive findings highlight how *Pax6* expression gradients might establish specific gene-expression domains in the CNS and brain.



Floor-plate induction: where and when

The floor plate (FP) is a specialized ventral midline structure of the vertebrate neural tube that is required for CNS patterning, but how it is induced remains unresolved. One model proposes that it is formed by notochordal signals that induce overlying neural tube; another that the organizer generates midline precursor cells that produce the FP. Tian et al. now provide evidence for this latter model, on p. 3331, from a new temperature-sensitive (TS) zebrafish mutant. Cyclops is a zebrafish Nodal-related signalling factor, which in the TS mutant fails to function at 28°C, at which temperature FP development fails in mutant embryos. By shifting mutants between permissive and restrictive temperatures during development, the authors show that FP induction occurs during gastrulation and requires Cyc/Nodal signalling. Moreover, continuous Cyc signalling is required throughout gastrulation for complete ventral neural tube specification.

In *Journal of Cell Science*

Calcium signalling and cell polarity

Cells achieve complex spatiotemporal Ca^{2+} signals by localizing Ca^{2+} pumps and channels to specific subcellular regions. Inositol 1,4,5-trisphosphate receptors [Ins(1,4,5)P_3Rs] that release Ca^{2+} from the ER, for example, are often concentrated at one pole. Colosetti et al. have used immunofluorescence confocal microscopy and immunogold EM analysis to probe the relationship between Ins(1,4,5)P_3Rs and polarity in MDCK cells. In non-polarized cells, Ins(1,4,5)P_3Rs are present throughout the ER but become concentrated around tight junctions at the apical region of the lateral membrane as cells polarize. Culturing cells in Ca^{2+}-depleted medium disrupts polarity and rapidly abolishes this pattern of Ins(1,4,5)P_3R localization, which returns following Ca^{2+} restoration. The authors conclude that receptor localization is linked to cell polarization, and that forming tight junctions recruit Ins(1,4,5)P_3Rs to bring about local Ca^{2+} release.

Colosetti, P. et al. (2003). The type 3 inositol 1,4,5-trisphosphate receptor is concentrated at the tight junction level in polarized MDCK cells. *J. Cell Sci.* **116**, 2791-2803.