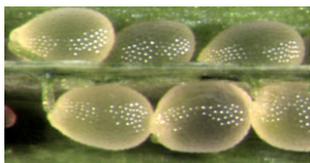




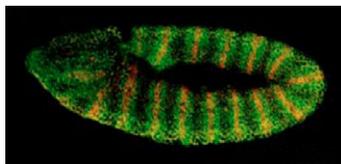
Hox function through collaboration

Hox proteins potentially regulate many targets within individual developing tissues, but how they selectively regulate diverse target genes and activate or repress target gene expression is poorly understood. To address these questions, Walsh and Carroll investigated the repression of the *spalt* (*sal*) gene by the Hox protein Ubx in the developing *Drosophila* hindwing (halter) (see p. 3585). Using both genetic and biochemical approaches, they found that two Smad proteins (Mad and Med), which are required for *sal* activation in the wing, collaborate with Ubx to directly repress *sal* in the haltere. This repression occurs via a *sal* cis-regulatory element that contains closely spaced Smad and Ubx binding sites and is perfectly conserved among four *Drosophila* species. Because Smad and Ubx proteins appear not to interact directly, the authors argue that they might instead 'collaborate' to co-regulate *sal*, and that collaboration might be a widespread requirement for Hox function in which two or more regulatory proteins bind to the same site but not to each other.



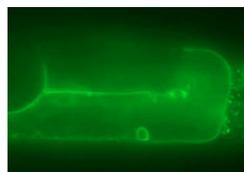
FIS Polycomb protein functions take seed

The Polycomb group (PcG) chromatin remodelling proteins have conserved roles in the stable maintenance of gene expression patterns. In *Arabidopsis*, mutations in the genes of the FERTILIZATION INDEPENDENT SEED (FIS) PcG complex cause seed abortion when maternally inherited. In the case of two FIS-class gene mutations, seed abortion occurs because these genes (*MEA* and *FIS2*) are paternally imprinted in the endosperm. On p. 3639, Leroy and colleagues now report that the *FIS* gene *MSI1* is not similarly imprinted; *MSI1* is bi-allelically expressed in the embryo and endosperm, and its early paternal expression does not rescue *msi1* mutant seeds. By contrast, its expression in *msi1* mutant female gametophytes (which enclose the female gamete) does restore seed development. From their findings, the authors conclude that an intact FIS complex is required in the female gametophyte to maintain normal gene expression patterns in the central cell (from which the endosperm develops). In its absence, endosperm defects occur that cause both embryo arrest and seed abortion.



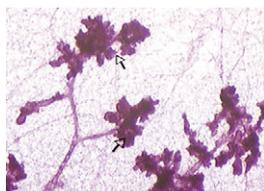
Hh signals break up

In *Drosophila*, when Hh binds to its receptor Ptc, Ptc releases its inhibition of Smo, resulting in Smo's phosphorylation and stabilization at the plasma membrane. Smo then transmits a signal to a multi-protein complex that contains the kinase Fu, the kinesin-like Cos2 and the Gli-like transcription factor Ci. In their investigation of Cos2's role in Hh signalling in *Drosophila* on p. 3677, Pascal Théron's lab report that the phosphorylation of Cos2 by Fu induces it to undergo a conformational change that leads to this complex's disassembly, probably to free Ci to translocate to the nucleus to activate target genes. Their findings show that the Cos2 residue Ser572 is necessary for Hh signal transduction and is phosphorylated by Fu, either directly or indirectly. By using an antibody that specifically recognizes phosphorylated Ser572, the authors show that upon its phosphorylation, Cos2's association with Smo and Ci strongly decreases in vivo and in vitro. This study's results provide new mechanistic insights into Hh signal transduction, about which much remains unknown.



Differing routes to apoptosis by RB

The well-known tumour suppressor functions of Retinoblastoma (RB) protein are mainly attributed to its cell-cycle blocking activities. But now on p. 3691, Schertel and Conradt report that RB and its associated proteins also function by promoting apoptosis in differing ways. Their studies of *lin-35* RB loss-of-function *C. elegans* mutants, in which the constitutive germ cell apoptosis that normally occurs in adult hermaphrodites is decreased, show that *lin-35* promotes germ cell apoptosis by repressing *ced-9* – an anti-apoptotic gene and *BCL2* orthologue. The genes *dpl-1* DP, *efl-1* E2F and *efl-2* E2F, which encode proteins that complex with RB, also promote germ cell apoptosis, but they do so by inducing the expression of the pro-apoptotic genes *ced-4* and *ced-3*. Finally, the authors show that *lin-35*, *dpl-1* DP and *efl-2* E2F also promote DNA-damage-induced apoptosis but by controlling the expression of different target genes and not via *ced-9*, *ced-4* and *ced-3*. Together, these important findings provide new avenues of research for investigating the differing tumour-suppressor functions of RB, particularly in mammals.



Progesterone and β -catenin: priming mammary development

The mammary gland undergoes significant postnatal development that is temporally regulated by hormonal signalling. During pregnancy, side branches form from the mammary ductal tree and alveoli develop at their tips; both are lost in progesterone receptor (*Pgr*)-null mice. To investigate how hormonal and β -catenin signalling (which also acts in pregnancy-induced mammary differentiation) intersect during postnatal mammary development, Hiremath et al. tested whether a non-degradable form of β -catenin (MMTV- Δ N89 β -catenin) could rescue the phenotype of *Pgr*-null mice (see p. 3703). They found that although stabilized β -catenin rescues alveogenesis at ductal tips, it cannot stimulate alveolar development along the lateral borders of mammary ducts. This, the authors propose, is due to the existence of two β -catenin-responsive cell populations: one at ductal tips that is intrinsically β -catenin responsive; the other, a progenitor population, at the lateral ductal borders of virgin glands that requires *Pgr* signalling to become primed for alveogenesis in response to β -catenin. These findings advance mammary development research, not least by identifying this novel progenitor population.

IN JOURNAL OF CELL SCIENCE Endocytosis and JAK/STAT signalling

JAK/STAT signalling controls many aspects of the immune system and several developmental pathways. In *J. Cell Sci.*, Stéphane Noselli and colleagues investigate the role of receptor endocytosis in this pathway in *Drosophila* follicle cells. Using endocytic markers, they identify the receptor Dome in early and late endosomes and show that it is mislocalised in cells with a mutated clathrin heavy chain, indicating that clathrin-mediated internalization controls the amount of Dome available for ligand interactions. By monitoring the activity of STAT transcription factors, they also demonstrate that mutations in several endocytic pathway components block signalling, showing that both internalization and trafficking are required for JAK/STAT signalling. However, mutations in Rab11 – a protein required for recycling from endosomes – do not affect STAT activity. Consequently, they conclude that ligand-bound Dome is targeted to the lysosome for both signalling and degradation, suggesting that endocytosis, but not recycling, regulates JAK-STAT signalling.

Devergne, O., Ghiglione, C. and Noselli, S. (2007). The endocytic control of JAK/STAT signalling in *Drosophila*. *J. Cell Sci.* 120, 3457–3464.