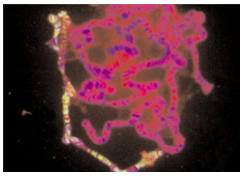
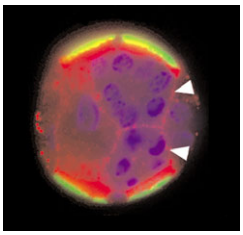


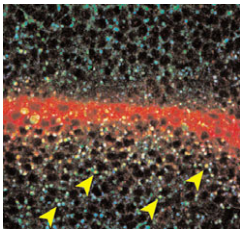
Subduing Su(var)3-9

The formation of heterochromatin – tightly packed, transcriptionally inactive chromosomal DNA – involves a complex arrangement of histone modifications, including histone H3K9 methylation, which, in flies, is catalysed by the methyltransferase Su(var)3-9. Having observed that hypomorphic mutations in *JIL-1* (a histone H3S10 kinase) cause heterochromatin to spread to ectopic chromosomal regions in *Drosophila*, Johansen and colleagues set out to explain why (see p. 229). To do so, they generated flies that carry both a null and a hypomorphic copy of *JIL-1*, which almost never survive to adulthood. But when these flies carry an additional copy of the *Su(var)3-9* gene that has reduced function, they mostly survive, indicating that Su(var)3-9 and JIL-1 function in the same pathway and are antagonistic. From their results, the authors propose that JIL-1 kinase marks transcriptionally active euchromatin – possibly by phosphorylating histone H3S10 – to prevent Su(var)3-9 from triggering the formation of heterochromatin at ectopic locations.



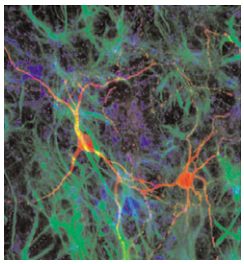
New COGs in the organogenesis wheel

Congenital disorder of glycosylation (CDG) causes multiple developmental abnormalities in humans. To investigate the role of glycosylation and the Golgi (the principle site of glycosylation) in organogenesis, Nishiwaki and co-workers turned to the worm gonad. On p. 263, they report the cloning of two genes that, when mutated, cause worms to phenotypically resemble *mig-17* mutants; *mig-17* codes for an ADAM protease that is implicated in gonadal development. The two identified genes – *cogc-1* and *cogc-3* – encode homologues of members of the conserved oligomeric Golgi (COG) complex, which is involved in CDG, and in vesicle trafficking to, from and within the Golgi. Mutant analysis shows that these genes are needed for proper MIG-17 glycosylation and gonad formation, possibly together with other COG components. Although the mechanisms linking the COG complex to CDG are still unclear, the worm gonad should be a useful model for studying the roles of glycosylation in organogenesis.



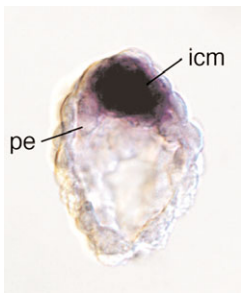
How flies spread their Wingless

Morphogen gradients are shaped by several dynamic processes, and on p. 307, Suzanne Eaton and colleagues determine the contribution of endocytosis to the maintenance of the Wingless (Wg) gradient, which is secreted at the dorsal-ventral boundary of the *Drosophila melanogaster* wing disc. Endocytosis requires the Rab GTPases, and specific endosomes are associated with specific Rab proteins. So the researchers used dominant-negative Rab proteins to disrupt particular branches of the endocytic pathway, and found that preventing Wg endocytosis increased its extracellular spread. Curiously, although overexpression of the glypican Dally-like (Dlp) – which is required for long-range Wg movement – caused the accumulation of extracellular Wg, it was not required for the spread of Wg when endocytosis was blocked. The authors report that Wg is only internalized from the apical and basal surfaces of the disc, and propose that Dlp promotes the spread of Wg by directing it to lateral membranes, where it is endocytosed less efficiently.



Stem cell role for p53 puts theory to test

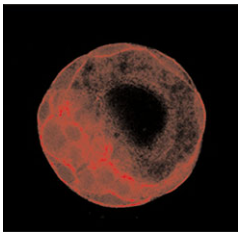
The 'cancer stem cell hypothesis' proposes that some cancer cells have properties of self-renewing stem cells. This prompted Jonas Frisén and colleagues (see p. 363) to investigate the role of a key tumour suppressor gene – p53 (which is mutated in most tumours, particularly those in the brain) – in the renewal of neural tissue stem cells. They discovered that cells of the brain's lateral ventricle stem-cell niche overproliferate in *p53*-null mice, and that p53 deficiency in 'neurospheres' (clonal aggregates of neural stem cells in vitro) results in increased renewal, owing to greater cell proliferation and less apoptosis. Analysis of the neural stem cell transcriptome identified several genes that are downregulated in *p53*-null neurospheres – most conspicuously, p21 and p27, which are known to negatively regulate proliferation in the lateral ventricle wall – leading the authors to speculate that several pathways with roles in stem-cell renewal might converge on p53.



GDF3: an early and conserved player in embryogenesis

Two papers in this issue focus on the role of growth differentiation factor 3 (GDF3) in early embryonic development. Mammalian GDF3 – which belongs to the bone morphogenetic protein (BMP) branch of the TGFβ superfamily – shares considerable amino acid similarity with *Xenopus* Vg1. By studying the role of GDF3 in early mouse patterning, Chen et al. (see p. 319) have found that Vg1 activity is remarkably well conserved. In *Xenopus*, Vg1 is essential for early patterning and signals through a Nodal-like pathway (see *Development* 133, 15-20). Here, the authors report that *Gdf3*-null mouse mutants resemble mice with absent or reduced Nodal signalling. Moreover, they report that GDF3 can interact with Nodal co-receptors and antagonists. Nodal signalling is crucial for the formation and positioning of the anterior visceral endoderm (AVE), which patterns the anteroposterior axis of the embryo. The researchers found that ~30% of *Gdf3* null mutants have an abnormally formed or positioned AVE, and they conclude that, like Vg1, GDF3 is required for Nodal pathway activity and for proper axial patterning in the early embryo.

In an accompanying paper (see p. 209), GDF3 and Nodal are reported to have even earlier roles in development than hitherto realised. By exploring the role of GDF3 in embryonic stem (ES) cells, Levine and Brivanlou have found that while higher GDF3 expression maintains pluripotency in human ES cells, it is lower GDF3 expression that maintains pluripotency in mouse ES cells. This apparent contradiction is consistent with their finding that GDF3 directly inhibits BMP4. BMPs, which are necessary for cell fate decisions in the blastocyst, promote human ES cell differentiation but maintain mouse ES cells in an undifferentiated state. The authors discuss several potential mechanisms – such as different sensitivities to BMP signalling – for these species-specific responses.



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