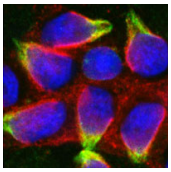
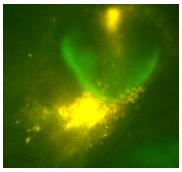


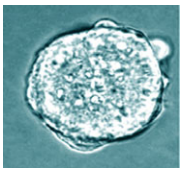
RIM-BP3 hooks up spermiogenesis

During spermiogenesis (the final stage of sperm production), elongation, nuclear reshaping and other morphological changes convert round spermatids into motile sperm. But what controls spermiogenesis? On p. 373, Zhou and colleagues report that the novel, conserved protein RIM-BP3 (a member of a family of multidomain proteins that probably function as adaptors during vesicle fusion and release) is essential for spermiogenesis in mice. The researchers show that RIM-BP3 is a testis-specific protein and that its expression is associated with the manchette, a transient microtubular structure that is required for spermatid morphogenesis. Targeted deletion of *RIM-BP3*, they report, causes the production of sperm with abnormal heads and male infertility. They also report that RIM-BP3 interacts with Hook1 (another manchette-associated protein involved in sperm head morphogenesis) and suggest that this interaction might correctly position the manchette. Because infertility in male mammals is often associated with the production of sperm with abnormal heads, these results suggest that dysfunctions in the pathways that involve RIM-BP3 might underlie some forms of human male infertility.



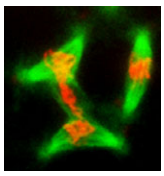
Dental mesenchyme shows its teeth

During tooth development, the dentition has the potential to generate extra teeth, and it is not clear what prevents this. Here, Pauliina Munne and colleagues show that in the mouse, the dental mesenchyme, which has the potential to induce teeth even from non-dental epithelium, is also involved in restricting tooth number and acts, at least partly, via the BMP and Wnt antagonist Sostdc1 (ectodin) (p. 393). By analysing *Sostdc1* mutant mice, which form an extra incisor, the authors establish that the extra tooth is attributable to the loss of *Sostdc1* in the dental mesenchyme. Surgically reducing the amount of dental mesenchyme produces extra incisors in wild-type tooth explant cultures; in *Sostdc1*-deficient explants, it also triggers de novo incisor formation from the epithelium, indicating the presence of additional restrictive mesenchymal factors. The negative regulation of both BMP and Wnt signalling also contributes to this restrictive mesenchymal activity. Thus, dental mesenchyme plays a pivotal dual role in regulating tooth development by both inducing teeth and restricting their number.



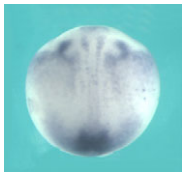
ES cells make an imprint

Genomic imprinting – parental-specific gene expression in which either the maternal or paternal copy of a gene is expressed – is important in early development and can contribute to disease. To date, imprinting has been mostly studied in mammalian embryos, which often entails long experimental time frames. Now, on p. 437, Denise Barlow and colleagues demonstrate that differentiating embryonic stem (ES) cells provide a much-needed in vitro system for studying this phenomenon. The authors show that imprinted expression of the *Igf2r* gene is established when ES cells differentiate, and that this coincides with the onset of the paternal-specific expression of *Airn*, a non-coding RNA that, in the mouse, silences the paternal allele of *Igf2r*. These events mimic aspects of imprinting that occur in the mouse embryo during and after implantation. Surprisingly, during ES cell differentiation, expression from the paternal *Igf2r* promoter remains constant instead of being silenced, while expression from the maternal *Igf2r* promoter increases up to tenfold, revealing a novel mechanism for *Airn*-mediated imprinting – through an expression bias rather than silencing.



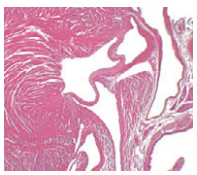
Cells cycle with *no poles*

In *Drosophila*, the nuclear divisions following fertilisation oscillate rapidly between S and M phases, with no growth phases or cytoplasmic cleavage. Metazoan development depends on correct cell-cycle control, but it remains unknown how DNA replication and mitosis are coordinated during such rapid divisions. On p. 449, Laura Lee and co-workers reveal that *no poles* (*nopo*), a gene encoding a putative ubiquitin ligase, is essential for the preservation of genomic integrity during these early stages of *Drosophila* development. The researchers find that *nopo* mutant flies have misshapen spindles and undergo mitotic arrest, and that a mutation in the gene encoding the DNA checkpoint kinase CHK2 partially rescues these defects. Thus, the *nopo* phenotype is probably due to CHK2-mediated centrosome inactivation, a protective mechanism in flies that prevents nuclear division after DNA damage or incomplete replication. In addition, the researchers demonstrate that NOPO interacts with BEN, a ubiquitin-conjugating enzyme, leading them to propose that NOPO and BEN form a ubiquitin ligase complex that is required to prevent DNA defects during *Drosophila* embryogenesis.



New biosynthetic code for retinoic acid gradient formation

Retinoic acid (RA) gradients regulate many developmental processes, including the specification of the embryonic body axes and pattern formation in the brain. RA synthesis from vitamin A is a two-step process, the second step of which – the conversion of retinal to RA by retinal dehydrogenases (RALDHs) – is crucial for tissue-specific RA production. Now, Strate and co-workers report that retinol dehydrogenase 10 (RDH10), which converts vitamin A to retinal, cooperates with RALDHs to establish RA signalling in *Xenopus* embryos (see p. 461). They show, for example, that *XRDH10* expression in early embryos partly overlaps with that of *XRALDH2*. Overexpression of *XRDH10* mimics RA responses, they report, and synergises with XRALDH2 to posteriorise the developing brain, whereas the knockdown of XRDH10 and XRALDH2 causes anteriorisation of the brain. These and other results lead the authors to propose a revised model for the generation and stabilisation of an RA gradient in early embryos that involves the combined expression and action of both XRDH10 and XRALDH2.



In close Prox1mity to a healthy heart

A properly formed heart that contains a rhythmically contracting meshwork of myofibrils is essential for a healthy life. However, little is known about the molecular regulation of the morphogenetic processes that are involved in heart muscle development. Now, Risebro and colleagues report that the homeobox transcription factor Prox1 maintains muscle structure and growth in developing hearts (see p. 495). Cardiac-specific inactivation of *Prox1* in mouse embryos, they show, disrupts the expression and localisation of several sarcomeric proteins (a sarcomere is the basic structural and functional unit of a myofibril) and results in abnormal myofibril organisation and growth-retarded hearts. Other experiments indicate that Prox1 directly regulates the expression of several sarcomeric structural proteins that help to coordinate heart contraction. Together, these results provide new insights into the molecular mechanisms that control the ultrastructure and growth of cardiac muscle during development. They also suggest that altered Prox1 expression might underlie some cardiomyopathies, diseases in which the heart muscle is weakened or structurally altered.