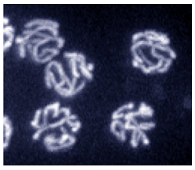
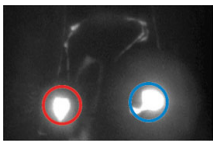


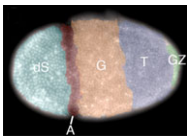
How FBFs time meiotic transition in GSCs

The transition from an undifferentiated, mitotically dividing germline stem cell to a differentiating germ cell that is ready for meiosis is a crucial step in germline development. In *C. elegans*, the Puf-domain RNA-binding proteins FBF-1 and FBF-2 (collectively FBF) stop this transition from occurring prematurely by inhibiting the expression of meiotic regulators. Now, Christopher Merritt and Geraldine Seydoux report that FBF also inhibits the premature expression of synaptonemal complex (SC) proteins in the *C. elegans* germline (see p. 1787). The SC normally forms between homologous chromosomes during meiotic prophase. The researchers show that FBF directly inhibits the expression of five SC proteins until shortly before meiotic entry via FBF binding sites in the 3′ UTRs of the SC protein mRNAs. In the absence of FBF, they report, SC proteins are expressed prematurely in germline stem cells and SC formation at meiotic entry fails. These studies underscore the importance of post-transcriptional mechanisms in the transition from germline stem cell to differentiating germ cell.



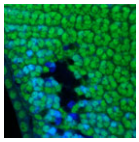
Don't grouch: short Grouchos don't just repress

The Groucho/TLE family of conserved WD40 domain-containing transcriptional co-repressors are important regulators of development in many species. Several short Groucho-like proteins that lack the C-terminal WD40 domains also exist and can act in vitro as antagonists or agonists of Groucho/TLE proteins. But what is their in-vivo function? On p. 1799, Oliver Hobert and co-workers report that, in *C. elegans*, the novel, short Groucho-like protein LSY-22 promotes the function of the Groucho orthologue UNC-37. In a screen for genes that control a left/right asymmetric cell fate decision in the *C. elegans* nervous system, the researchers isolated loss-of-function alleles in two distinct loci that cause identical changes in neuronal fate specification and in several other developmental processes. These loci encode UNC-37, the *C. elegans* orthologue of *Drosophila* Groucho, and a short Groucho-like protein, LSY-22, which, the researchers show, physically interact in vivo. These results suggest that, instead of antagonising Groucho functions as previously proposed, short Groucho-like proteins may instead promote Groucho functions.



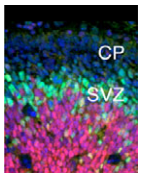
Orthodenticle heads *Tribolium* development sideways

In *Drosophila*, anteroposterior (AP) axis formation depends on a gradient of the maternal transcription factor Bicoid. But *bicoid* is unique to higher dipterans, so what patterns the AP axis in other insects? In the short-germ beetle *Tribolium castaneum*, one hypothesis is that the head gap gene *orthodenticle* (*Tc-otd*) substitutes for *bicoid*. However, on p. 1853, Michael Schoppmeier and colleagues unexpectedly report that the role of *Tc-otd* in AP blastoderm patterning depends on its impact on dorsoventral (DV) patterning. RNAi depletion of *Tc-otd* produces lateralised embryos, they report, by reducing the expression of *short gastrulation* (*Tc-sog*), which normally establishes the DV Decapentaplegic gradient. In addition, an anterior shift of the jaw segment primordia in *Tc-otd*-depleted embryos is largely due to reduced expression of *Tc-zen-1*, another DV patterning gene. Neither *Tc-sog* nor *Tc-zen-1* is likely to receive Tc-Otd gradient-mediated positional information, note the researchers. Instead, the blastoderm-patterning function of Tc-Otd probably depends on its initially ubiquitous maternal expression. Its early patterning role, therefore, has little in common with Bicoid.



Acid test for endosomal Notch activation

Cell-cell signalling via Notch regulates multiple cell behaviours during development, and inappropriate Notch activation is a hallmark of many cancers. Consequently, it is important to understand exactly how Notch signalling is regulated. Thomas Vaccari and co-workers bring this goal a step closer on p. 1825 by reporting that the vacuolar ATPase (V-ATPase) proton pump, which acidifies endosomal compartments, is required for physiological and pathological Notch receptor activation in *Drosophila*. Once it is ligand bound, Notch is activated by γ-secretase-mediated cleavage, but mounting evidence suggests that Notch's entry into endosomes promotes its signalling. In a search for factors that regulate Notch activation in endosomes, the researchers isolated mutants in the *Drosophila* genes that encode V-ATPase subunits. Their characterisation of these mutants indicates that V-ATPase, probably via the acidification of early endosomes, promotes not only the lysosomal degradation of Notch to prevent excess signalling, but also the endosomal activation of Notch signalling. Thus, it might be possible to curtail Notch overactivation in tumours using V-ATPase inhibitors.



Centrosome defects take the rap for microcephaly

Microcephaly (an abnormally small cerebral cortex) can be caused by mutations in the gene encoding CDK5RAP2 (cyclin-dependent kinase 5 related activator protein 2). But why do mutations in this centrosomal protein cause microcephaly? To find out, Mark Fleming, Christopher Walsh and colleagues have been studying a mouse model of human microcephaly and now reveal that Cdk5rap2 is essential for cortical progenitor proliferation and survival in mice (see p. 1907). They show that the Hertwig's anemia (*an*) mouse mutant carries a mutation in *Cdk5rap2* and exhibits microcephaly that arises from proliferative and survival defects in neuronal progenitors. *Cdk5rap2*$^{an/an}$ neuronal precursors exit the cell cycle prematurely, they report, and often undergo apoptosis. Finally, they show that these proliferative and survival defects are associated with impaired mitotic progression and with an abnormal mitotic spindle pole number and orientation. The researchers suggest, therefore, that defects in centrosome function and chromosome segregation might underlie the reduction in human brain size caused by mutations in *CDK5RAP2*.

Jane Bradbury

IN JOURNAL OF CELL SCIENCE

Quantifying mRNA in space and time

Gene expression regulation occurs at multiple levels and varies depending on the gene. For example, the subcellular expression of β-actin is controlled by the localisation of its mRNA to actin-rich peripheral regions of migrating cells. In *J. Cell Sci.*, Shav-Tal and colleagues report a novel system for quantifying β-actin expression at the single-cell level. They created a human cell line expressing a transcriptionally inducible form of chicken β-actin that enables transcribed mRNA and translated protein to be visualised in individual cells. Four-dimensional imaging experiments show that, in this inducible system, transcription gradually increases to a maximum rate after ~1 hour, then gradually decreases. β-actin mRNA elongates at a speed of 3.3 kb/minute and, once exported from the nucleus, it moves through the cytoplasm by diffusion. Notably, β-actin mRNA that localises to the cell periphery derives from a pre-existing mRNA pool and not from newly transcribed mRNA. So, the initial localisation of β-actin mRNA to the cell periphery is not coupled to the initiation of β-actin transcription. This is the first study to follow the complete cellular pathway of a protein-coding mammalian mRNA in live cells.

Ben-Ari, Y. et al. (2010). The life of an mRNA in space and time. J. Cell Sci. 123, 1761-1774.