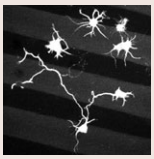
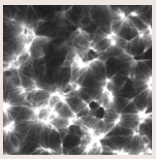
In this issue



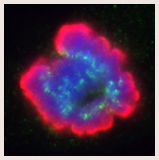
Galectin-3 branches out

Glycoproteins have a central role in directing axon growth and branching in the central nervous system. For example, the glycoprotein and neural-cell-adhesion molecule L1 localises to axons and promotes branching by recruiting ezrin-radixin-moesin (ERM) proteins, which link actin and membranes. The branched glycan chains of proteins such as L1 act as sugar-encoded signals that are bound and translated by sugar-binding proteins. The galectins are one such family of proteins and, on page 671, José Abad-Rodríguez and colleagues define a role for galectin-3 (Gal-3) in axon branching. They show that post-translational modification of this protein is important for its function: phosphorylated Gal-3 (Gal-3-*P*) complexed with the ECM component heparan sulphate proteoglycan (Gal-3-*P*–HS) promotes axonal branching in vitro, whereas soluble Gal-3-*P* and Gal-3 do not. Gal-3-*P* interacts with L1 and promotes redistribution of L1 to lipid-raft-rich regions of the plasma membrane and, subsequently, the recruitment of ERM proteins. Accordingly, cells grown on Gal-3-*P*–HS have more F-actin-containing branches than cells grown on HS alone. The authors propose that Gal-3's role in axon branching is regulated by its phosphorylation state, and by its distribution in and presentation by the ECM. Whether Gal-3 phosphorylation can act as a signal for nerve regeneration is an issue for future study.



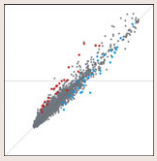
Importin-β: fine-tuning APC function

Mutations in the gene encoding the tumour suppressor adenomatous polyposis coli (Apc) are frequent in colorectal cancers. Cancer-causing mutations impair interactions between Apc and its many interaction partners and disrupt its normal cellular functions, including control of Wnt-regulated β-catenin turnover and regulation of microtubule (MT) dynamics. On page 736, Dina Dikovskaya and colleagues uncover a new regulatory binding partner for Apc that influences its ability to assemble MTs: they show that importin-β, a nuclear transport factor with a role in mitotic-spindle formation, binds directly to Apc in a manner that depends on the small GTPase Ran. They also identify three importin-β-binding sites and two MT-binding sites (one of which is novel) in Apc. Although importin-β does not affect the ability of Apc to bind to MTs or to the plus-end-directed MT-binding protein EB1, it inhibits Apc-mediated MT assembly and bundling. Furthermore, in *Xenopus* egg extracts (an in vitro model of spindle assembly), a Ran-insensitive mutant of importin-β prevents the spindle-promoting activity of Apc. Therefore, the authors conclude, Ran-mediated release of Apc from importin-β is necessary for Apc to assemble and bundle MTs, thereby promoting spindle stabilisation. The mechanisms by which Apc bundles MTs await elucidation.



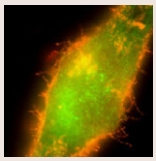
Coordinating chromosome cohesion

Bub1 was one of the first protein kinases identified as a component of the spindle-assembly checkpoint (SAC), but evidence that its kinase activity is essential for regulating the SAC in mammalian cells is conflicting. On page 653, David Perera and Stephen Taylor now shed light on this issue by carrying out complementation studies in *Bub1*-null mouse embryonic fibroblasts (MEFs), which exhibit a nonfunctional SAC, abnormal chromosome alignment and defective localisation of Sgo1 (which protects sister-chromatid cohesion at centromeres). They find that adenoviral-mediated expression of Bub1 lacking the kinase domain, or containing a point mutation in the kinase domain, restores SAC function and chromosome alignment in *Bub1*-null MEFs to the same extent as does wild-type Bub1. By contrast, neither mutant restores the defective localisation of Sgo1 at centromeres in prometaphase *Bub1*-null MEFs. But why does Sgo1 mislocalisation not cause defective centromeric cohesion in this context? The authors go on to show that the pattern of Sgo1 localisation has three distinct stages during the late cell cycle: it localises at centromeric heterochromatin in early to mid G2, is diffuse in late G2 and early prophase, and returns to centromeres at the onset of mitosis. The authors conclude that the kinase activity of Bub1 is only required for Sgo1 localisation in the latter phase, which is not essential for centromeric cohesion.



DHH1 takes post-transcriptional control

Gene expression in trypanosomes is predominantly regulated post-transcriptionally, making these parasites an ideal system for studying the molecular mechanisms involved. On page 699, Mark Carrington and colleagues investigate mRNA turnover and translational repression in the insect-stage form of *Trypanosoma brucei*, focussing on the role of the DEAD-box RNA helicase DHH1. This protein, which localises to P-bodies (cytoplasmic ribonucleoprotein-processing bodies), was previously identified in a screen for factors that regulate the expression of developmental-stage-specific mRNAs. Here, the authors report that expressing mutant forms of DHH1 decreases parasite growth. The most marked phenotype is observed with a DHH1 mutant lacking ATPase activity: as well as blocking proliferation, it induces a decrease in the number of polysomes and an increase in P-body size, suggesting that the mutant causes the release of mRNAs from polysomes. Microarray experiments reveal that DHH1 activity is selective: through effects on stability, it increases the amount of a distinct subset mRNAs while decreasing others. Notably, these effects are mainly specific for developmentally regulated mRNAs. Overall, these data shed light on regulatory mechanisms of gene expression in trypanosomes and identify a new DHH1-dependent pathway by which developmental gene expression is selectively controlled.



Insight into EGFR endocytosis

EGFR on the cell surface is dynamic, undergoing continuous exo- and endocytosis. These processes are tightly controlled by many regulatory molecules; for example, SNAREs mediate membrane-fusion events during exocytosis, whereas adaptors such as AP-2 take part in endocytosis. Lydia Danglot, Thierry Galli and colleagues (p. 723) now uncover a new mechanism by which EGFR cell-surface expression and signalling are regulated. They show that knocking down of the v-SNARE TI-VAMP (also known as VAMP7) accelerates EGF-induced clathrin-mediated endocytosis of EGFR, thereby decreasing its cell-surface diffusion and impairing early EGFR signalling events. Rather than affecting EGFR endocytosis directly, TI-VAMP depletion disrupts the trafficking of cargo-containing vesicles from the Golgi to the cell surface. Notably, the trafficking of CD82 (a tetraspanin that regulates EGFR endocytosis) is impaired, leading to reduced cell-surface expression of CD82 when TI-VAMP is depleted. Finally, decreased cell-surface expression of CD82 correlates with increased recruitment of AP-2 clusters specifically following EGF stimulation, suggesting that enhanced recruitment of the endocytic machinery underlies accelerated EGFR endocytosis in TI-VAMP-depleted cells.

Development in press

Slowdown in muscle integrity

During development, adhesion between distinct cell types is crucial for tissue assembly. In a paper published in *Development*, Eliezer Gilsohn and Talila Volk now show that the novel tendon-derived protein Slowdown (Slow) promotes muscle integrity in *Drosophila* embryos by ensuring that myotendinous junctions (MTJs) form correctly between muscle and tendon cells to 'glue' them together. MTJs, a type of hemi-adherens junction, consist mainly of muscle-specific integrin receptors and their tendon-derived extracellular-matrix ligand thrombospondin. The authors identified Slow in a microarray screen for target genes of the tendon-specific transcription factor Stripe. They show that muscle and/or tendons rupture upon muscle contraction in *slow* mutant larvae and that *slow* mutant flies are unable to fly. These defects, they report, are the result of improper assembly of the embryonic MTJs. Other experiments indicate that Slow normally forms a complex with thrombospondin that can alter the morphology and directionality of muscle ends. Therefore, the authors conclude, Slow promotes muscle integrity by modulating integrin-mediated adhesion at MTJs.

Gilsohn, E. and Volk, T. (2010). Slowdown promotes muscle integrity by modulating integrin-mediated adhesion at the myotendinous junction. *Development* **137**, 785-794.