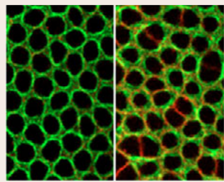
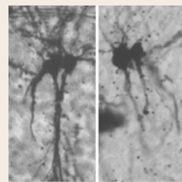
Journal of Cell Science

In this issue



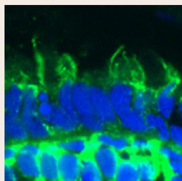
Actin' to form furrows

During the cellularisation step of *Drosophila* morphogenesis, numerous plasma-membrane furrows extend progressively into the syncytial embryo. Ingression is led by the furrow canal, a discrete F-actin- and Myosin-2-rich compartment that forms at the tip of each new furrow. The mechanisms that partition proteins into the furrow-canal compartment have been unclear, although the basal junctions that flank the compartment have been proposed to have a key role. On page 1815, however, Anna Marie Sokac and Eric Wieschaus show that furrow-canal compartmentalisation progresses normally in a *Drosophila* mutant that is deficient in Armadillo (a basal-junction component). By contrast, embryos treated with the F-actin-destabilising drug cytochalasin-D have defects in furrow-canal formation that echo the phenotype of the well-characterised *nulloX* cellularisation mutant: Myosin 2 is missing from some furrow canals (which leads to furrow regression) and markers of adjacent regions of the furrow are present in the furrow canal. The authors propose that actin polymerisation, regulated by Nullo, is central to furrow-canal formation and stabilisation, and therefore to cellularisation.



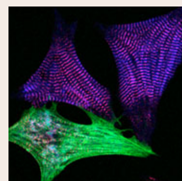
How to grow a dendrite with reelin

In addition to its role in neuronal positioning during development, the secreted protein reelin regulates hippocampal dendritogenesis. Reelin acts by binding to the cell-surface receptors ApoER2 and VLDLR; this binding promotes the tyrosine phosphorylation of the intracellular receptor-bound protein Dab1. In turn, several other proteins – such as Crk and CrkL – can bind to phosphorylated Dab1; however, the role of Dab1 and its binding partners in dendrite formation has been unclear. Now Brian Howell and colleagues (p. 1869) show that Dab1, Crk and CrkL are important in reelin-regulated dendritogenesis after birth. Using a mouse cell line that expresses a conditional *Dab1* allele, the authors inactivate *Dab1* postnatally and show that the dendrite complexity of hippocampal pyramidal neurons is reduced. The authors go on to show that, in primary hippocampal neurons in culture, reelin increases dendrite length by approximately twofold, but knocking down both Crk and CrkL prevents reelin-stimulated dendritogenesis. Notably, neither axon length nor BDNF-regulated dendritogenesis are affected by the absence of Crk and CrkL. Thus, reelin stimulates hippocampal dendrite formation via a signalling pathway that includes Dab1, Crk and CrkL.



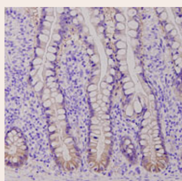
IFT proteins: not created equal

Vertebrate photoreceptor cells possess a modified cilium called the outer segment, which contains light-absorbing opsin proteins. Proteins are transported to the outer segment by intraflagellar transport (IFT) particles, which are complexes of IFT proteins that are translocated by axoneme-bound kinesin II. Mutations in IFT proteins perturb ciliogenesis; however, in many cases the roles of the individual IFT proteins in photoreceptor function are unknown. On page 1907, Bryan Krock and Brian Perkins compare the phenotypes of a zebrafish IFT57 loss-of-function mutant and a previously characterised IFT88 mutant. The authors demonstrate that IFT occurs inefficiently in photoreceptors of IFT57 mutant fish; consequently, the cells have short outer segments that contain reduced amounts of opsin. By contrast, outer segments are not visible in the photoreceptors of IFT88 mutants. Kinesin II co-immunoprecipitates with the IFT particle even in the absence of IFT57, but IFT20 (another IFT-particle component) does not. Notably, the ATP-dependent dissociation of kinesin II from the IFT particle is inhibited in the IFT57 mutant. These data indicate that individual IFT proteins have distinct roles in photoreceptor function.



Making sense of the M-band

To help maintain the highly ordered sarcomeric structure of myofibrils, the myosin-containing contractile filaments of striated muscle are crosslinked with other proteins at the M-band region of the sarcomere. The proteins titin and myomesin are known to interact with myosin filaments at the M-band, but the role of other M-band-localised proteins – such as the giant protein obscurin – is less well understood. On page 1841, Mathias Gautel and colleagues explore the interprotein interactions of obscurin and its newly discovered homologue obscurin-like 1 (Obsl1). Using a yeast two-hybrid system, the authors show that obscurin and Obsl1 both interact with myomesin and with the extreme C-terminal M10 domain of titin; moreover, obscurin can form a ternary complex with titin and myomesin. The M-band localisation of obscurin is disrupted when the titin- or myomesin-binding domains of obscurin (or the corresponding domains of myomesin and titin) are overexpressed, or when myomesin is knocked down. Importantly, muscle-disease-associated mutations in the titin M10 domain weaken the interaction between titin and obscurin or Obsl1. Based on their data, the authors propose a revised model of protein interactions at the M-band.



β-catenin: to the membrane and back

The canonical Wnt signalling pathway is a key regulator of cell proliferation. When an extracellular Wnt ligand is present, β-catenin – which is otherwise phosphorylated by the axin-containing destruction complex and subsequently degraded – accumulates in the nucleus and activates target genes. By contrast, axin redistributes to the plasma membrane, which has led to the suggestion that axin relocation is the key event that halts β-catenin destruction. Now, however, Maarten Fornerod and colleagues (p. 1793) describe a new step in the nuclear translocation of β-catenin. The authors show that, upon Wnt3a stimulation, unphosphorylated β-catenin is recruited to the plasma membrane (the protein can be detected at the membrane in E-cadherin$^{-/-}$ cells, indicating that it is distinct from E-cadherin-bound, junctional β-catenin). The redistribution of β-catenin to the membrane is an early event in the Wnt response and β-catenin colocalises with the Wnt co-receptor LRP6, and with axin and APC (another component of the destruction complex). Moreover, the association of β-catenin with LRP6 increases its transcriptional activity. These results imply that β-catenin is activated in a Wnt-receptor complex at the plasma membrane, before translocating to the nucleus.

Development in press

Shaping the Gurken gradient

In the *Drosophila* ovary, different levels of EGFR signalling establish the axis of the egg and the future embryo. A dorsoventral gradient of the morphogen Gurken, an EGFR ligand, is thought to control EGFR activation – but what is the precise shape of this gradient and how is it regulated? In a paper published in *Development*, Li-Mei Pai and colleagues report that the gradient of Gurken is directly regulated by Cbl, a protein that mediates the endocytosis of EGFR. They show that an HRP-Gurken fusion protein is internalised with EGFR into follicle cells and passes through the Rab5- and Rab7-associated endocytic pathway to the lysosome for degradation. Loss-of-function and overexpression studies show that Cbl facilitates this internalisation. Finally, the researchers show for the first time that the Gurken gradient extends from its source at the anterodorsal side of the egg to the ventral follicle cells, which suggests that Gurken is a long-range morphogen that directly determines the fate of these cells.

Chang, W.-L., Liou, W., Pen, H.-C., Chou, H.-Y., Chang, Y.-W., Li, W.-H., Chiang, W. and Pai, L.-M. (2008). The gradient of Gurken, a long-range morphogen, is directly regulated by Cbl-mediated endocytosis. *Development* **121**, 1923-1933.