

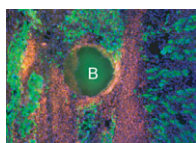
### Liver organogenesis: location matters

During embryogenesis, mesodermal signals induce the morphogenesis of endodermal organs. But what establishes the correct spatial relationship between the mesodermal signal-producing cells and the target endoderm? On p. 3209, Huang and colleagues report that, during zebrafish liver organogenesis, the expression of myosin phosphatase targeting subunit 1 (*Mypt1*, a protein that regulates myosin) in the lateral plate mesoderm (LPM) ensures that the liver primordium receives the mesodermal signals needed for its development by setting the relative positions of these two tissues. The authors identify a liverless mutant, *sq181*, that has an inactivating mutation in *mypt1*. Hepatoblasts form in this mutant but proliferate poorly and are lost by apoptosis. Other experiments indicate that the mutation alters the morphogenesis of the LPM, which leads to the mispositioning of *bmp2a*-expressing LPM cells relative to the liver primordium; this mispositioning of Bmp signals probably causes the *sq181* phenotype. Thus, *Mypt1* function (and myosin contractility) may establish the spatial interaction between mesoderm and endoderm that is essential for liver organogenesis in zebrafish.



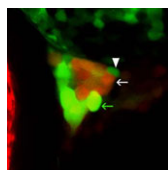
### Calcium asymmetry signals left from right

In mouse embryos, the establishment of left-right (LR) asymmetry, which initiates the proper positioning of the internal organs, requires intracellular calcium ( $\text{Ca}_i^{2+}$ ) enrichment along the left side of the node. But does this mechanism also establish laterality in other vertebrates? On p. 3271, Susan Smith and colleagues report that chick embryos also use a left-side enriched  $\text{Ca}_i^{2+}$  asymmetry to establish laterality. They show that  $\text{Ca}_i^{2+}$  is enriched along the front edge of Hensen's node (the chick's organizer) by the definitive primitive streak stage. Subsequent left-side enrichment of  $\text{Ca}_i^{2+}$  requires the activity of ryanodine receptors (intracellular calcium channels) and extracellular calcium, which suggests that calcium-induced calcium release supplies the  $\text{Ca}_i^{2+}$ . Furthermore, the manipulation of  $\text{Ca}_i^{2+}$  across the node randomizes heart laterality and disrupts asymmetric gene expression. Finally, other established laterality mediators regulate LR identity by directly affecting node  $\text{Ca}_i^{2+}$  concentrations, the authors report. Thus, they suggest,  $\text{Ca}_i^{2+}$  asymmetry across the node may be a conserved mechanism for establishing laterality among vertebrates, despite differences in node architecture.



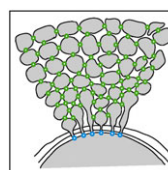
### Wnt and FGF act jointly in limb growth

Growth, patterning and cellular differentiation are inextricably linked during development, but what coordinates these processes? To find out, ten Berge and colleagues have been studying how the skeletal core, connective tissues and muscles of the vertebrate limb develop from a proliferating mass of mesenchymal cells. On p. 3247, they report that Wnt and FGF signals coordinate growth with lineage specification during limb development. FGFs from the apical ectodermal ridge (AER) of the limb bud and Wnts from the AER and the surface ectoderm, they report, act synergistically to promote proliferation and maintain the limb mesenchymal cells in an undifferentiated state, but act separately to specify cell lineages. Thus, withdrawal of both signals causes cell-cycle withdrawal and chondrogenic differentiation, whereas Wnt exposure alone maintains proliferation and favours connective tissue differentiation. The authors incorporate these results into a new model for limb development in which localized Wnt and FGF signals coordinate growth, patterning and cellular differentiation, and guide the growing limb's spatial organization.



### Neuronal specification: a BAPTISM of fluorescence

The vertebrate somatosensory system recognizes many chemical, mechanical and thermal stimuli but how this sensory diversity is established during development is poorly understood. Caron and colleagues now reveal that neuronal diversity in the zebrafish trigeminal sensory ganglia, which innervate the head, depends on the timing of neurogenesis (see p. 3259). To analyze neuronal birthdate (the time of a precursor's last division before it differentiates into a neuron) and cell fate, the researchers developed BAPTISM, a method in which the photoconvertible fluorescent protein Kaede marks neurons born at different times; birthdate is then correlated with fate using other nonconvertible fluorescent markers to label neural subpopulations. Their analyses show that the trigeminal sensory ganglia are formed from both early-born and late-born neurons. However, whereas the early-born neurons give rise to multiple classes of sensory neurons, the late-born neurons are restricted in their fate. The researchers speculate that this rapid multimodal neuronal specification is needed to produce functional trigeminal sensory ganglia by the time zebrafish hatch, two days after fertilization.



### LH frees oocytes from meiotic arrest

Meiosis in mammalian oocytes pauses in prophase until luteinizing hormone (LH) releases this arrest. One suggestion is that LH does this by closing the gap junctions between the somatic cells that surround the oocyte, thus blocking the transmission of a meiosis-inhibitory signal to oocytes. Now, Norris and co-workers show that LH-induced MAP kinase-dependent gap junction phosphorylation and closure is one of two paths to meiotic resumption in mouse ovarian follicles (see p. 3229). By monitoring the diffusion of fluorescent tracers in intact follicles, the researchers show for the first time that LH decreases the permeability of connexin 43-containing gap junctions between the somatic cells before nuclear envelope breakdown (NEBD; the start of the prophase–metaphase transition) occurs in oocytes. MAP kinase-dependent phosphorylation of connexin 43 causes this decreased permeability, they report. However, surprisingly, inhibition of MAP kinase activation does not prevent NEBD. Thus, they suggest, another pathway functions in parallel to MAP kinase-dependent gap junction closure to trigger meiosis resumption in response to LH.

Jane Bradbury

### IN JOURNAL OF CELL SCIENCE CSPGs show axons the way

During neural development and regeneration, chondroitin sulfate – the glycosaminoglycan (GAG) component of chondroitin sulfate proteoglycans (CSPGs) – is believed to guide axonal growth by acting as a chemorepellent. Chondroitin can be sulfated at several sites on its backbone – but can CSPG sulfation patterns affect its axon-guiding activity? In *J. Cell Sci.*, Geller and colleagues suggest it can. They show that chondroitin-4-sulfate, but not chondroitin-6-sulfate, repels growing axons of mouse cerebellar granule neurons. Moreover, reactive astrocytes (which inhibit axonal growth) upregulate CSPG expression and produce more 4-sulfated than 6-sulfated GAG chains. Knocking down endogenous chondroitin-4-O-sulfotransferase 1 (C4ST1) in these astrocytes depletes 4-sulfation and reduces the repellent activity of the conditioned medium; conversely, astrocytes in which C4ST1 is overexpressed have more 4-sulfated GAG chains and are less permissive to neuronal growth. Importantly, the expression of 4-sulfated GAG chains by reactive astrocytes is acutely increased in a mouse spinal injury model. Thus, the site of chondroitin sulfation affects its role in axon guidance.

Wang, H. et al. (2008). Chondroitin-4-sulfation negatively regulates axonal guidance and growth. *J. Cell Sci.* 118, 3083–3091.