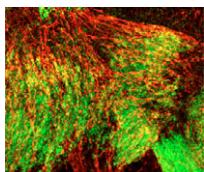


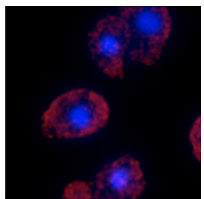
### Proliferation and fate choice in the liver

Identifying the factors that contribute to organ progenitor cell maintenance and differentiation is of crucial importance to developmental and disease-related research. In their study of liver development, Suzuki et al. have now identified such a factor, the transcription factor *Tbx3*, and investigated its functions in hepatoblast proliferation and cell fate determination (see p. 1589). The authors discovered that *Tbx3* is expressed in mouse hepatoblasts (which differentiate into hepatocytes and bile duct epithelial cells) using a fluorescence flow cytometry-based technique to identify different embryonic liver cell populations, which they assayed for the expression of numerous T-box genes. *Tbx3* is a known transcriptional repressor of *p19<sup>ARF</sup>*, so the researchers next investigated the expression of *p19<sup>ARF</sup>* in normal and *Tbx3*-null hepatoblasts and found that *Tbx3* loss results in a *p19<sup>ARF</sup>*-induced growth arrest, which pushes hepatoblasts towards a bile duct epithelial fate. These findings thus show that in hepatoblasts, *p19<sup>ARF</sup>*-induced growth arrest is important for activating biliary differentiation, whereas its repression by *Tbx3* promotes an alternative (hepatocytic) fate.



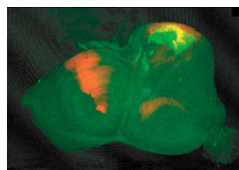
### Cranial neural crest wanders without guidance

Neuropilin (NRP) receptors and their class 3 semaphorin (SEMA) ligands have well-established roles in axon guidance. On p. 1605, Christiana Ruhrberg and colleagues now report that these proteins also direct cranial neural crest cells (NCCs) during sensory nervous system development. Cranial NCCs differentiate into glia, bone and cartilage, but also contribute sensory neurons to the cranial ganglia, the source of nerve bundles that carry sensory information to the brain. Using double *Nrp1/Nrp2* mutant mice, the authors show that the ordered positioning of these sensory neurons requires NRP1 and NRP2 and their ligands SEMA3A and SEMA3F. From these and other findings, the authors conclude that these proteins act synergistically to prevent migrating cranial NCCs from wandering into the wrong part of the head. They are also required to maintain the organisation of cranial sensory axons during development, leading the researchers to propose a model in which class 3 SEMAs act on NRP receptors both to direct cranial NCCs and to repel the axonal projections of sensory neurons.



### Dicty cell cycle comes into view

Several factors have conspired against the imaging of the *Dictyostelium* cell cycle, not least the lack of markers to distinguish its different phases. But on p. 1647, Muramoto and Chubb announce the creation of transgenic *Dictyostelium* that carry a live-cell fluorescent marker for the S phase. The role of the cell cycle during *Dictyostelium* development is controversial – whether differentiating cells replicate their DNA during development and the cell-cycle phase that the spores are in are matters of debate. Here, the authors report that after development is initiated, differentiating cells undergo a wave of DNA synthesis. Most spores, they reveal, are in G<sub>2</sub>, which begins after DNA synthesis and before mitosis starts. Furthermore, by inducing double-strand DNA breaks, they describe the first identified *Dictyostelium* checkpoint – at the G<sub>2</sub>–M transition. Since *Dictyostelium* has vertebrate DNA repair enzymes not present in yeast or invertebrates, these findings should illuminate future studies of the cell cycle's role in developmental processes in both *Dictyostelium* and other organisms.



### Hox links to transcriptional machinery

Although Hox proteins have fundamental roles in development, researchers have long been puzzled by what creates their binding specificity. Now, Walter Gehring and co-workers add a piece to that puzzle (see p. 1669). The Hox DNA-binding homeodomain has low sequence specificity, and co-factors are thought to contribute to this specificity by binding to a conserved YPWM motif (found in most Hox proteins). Gehring's lab previously demonstrated that ectopic expression of the *Drosophila* Hox gene *Antennapedia* (*Antp*) causes cells of the eye to adopt the developmental fate of the wing. Now they show that YPWM is required for this eye-to-wing transformation and, using a yeast two-hybrid system, have identified a YPWM-binding protein called BIP2. Using gain-of-function experiments and a new *bip2* mutant allele, the authors show that the ANTP–BIP2 interaction is required for the ectopic formation of wing structures. BIP2 is a TATA-binding protein associated factor (TAF), making this the first demonstration of a link between a Hox protein and the basal transcription machinery.



### Tbx18 charges cochlea for sound

The cochlea translates mechanical sound into electrical stimulus. Crucial to this is the voltage potential between the sensory hair cells and the cochlea endolymph, in which the correct ionic composition is maintained by fibrocytes in the cochlea wall. Now Andreas Kispert and colleagues report that otic fibrocyte differentiation requires the T-box transcription factor *Tbx18* – without it, the endocochlear potential essential for sound conduction by sensory hair cells breaks down and profound deafness occurs (see p. 1725). As *Tbx18*-null mice die soon after birth owing partly to defective somite development, the researchers studied transgenic *msd::Tbx18* mice, which express *Tbx18* throughout the presomitic and somitic mesoderm but not the inner ear. These mice are deaf, have abnormal otic mesenchyme compartmentalization and defective otic fibrocyte differentiation, which might, the authors argue, be secondary to *Tbx18*'s earlier role in otic mesenchyme compartmentalization. These findings highlight the crucial role of non-epithelial otic cell types in normal hearing and in the aetiology of deafness.

Jenny Bangham

### IN JOURNAL OF CELL SCIENCE Nestin' instincts in NP cells

During brain development, neural progenitor (NP) cells extend radial processes across the thickening brain wall to form a scaffold for migrating neurons. The processes grow only during G<sub>1</sub>–S phase, and NP cells undergo mitosis before and after process extension. The intermediate-filament protein nestin is strongly expressed in NP cells, but does it have a role in coordinating morphological alteration with cell-cycle progression? To investigate this, Hideyuki Okano and colleagues have generated a transgenic mouse line in which a *Nes* enhancer (*Nes* encodes nestin) controls the expression of a rapidly degraded fluorescent protein called dVenus. In *Journal of Cell Science*, these researchers now report that *Nes*-enhancer-driven expression of dVenus is high in NP cells during G<sub>1</sub>–S phase, but is downregulated during G<sub>2</sub>–M phase. Moreover, strong *Nes* expression correlates with the elongation of radial processes. These and other results reported in this study suggest that nestin has a role in coordinating cell-cycle progression and radial-process formation in NP cells.

Sunabori, T. et al. (2008). Cell-cycle-specific nestin expression coordinates with morphological changes in embryonic cortical neural progenitors. *J. Cell Sci.* 121, 1204–1212.