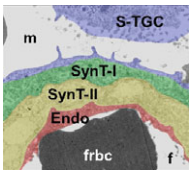
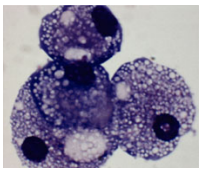


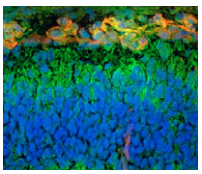
Secrets of the placental labyrinth unlocked

The inner compartment of the rodent placenta – the labyrinth – contains the villi where nutrients pass from the maternal blood into the foetal blood. These villi are covered with a layer of mononuclear sinusoidal trophoblast giant cells (S-TGCs) and two layers of multinucleated syncytiotrophoblast cells (SynT-I and SynT-II). Now, on p. 2083, Simmons and colleagues solve the long-standing mystery of the developmental origins of this trilaminar structure. By examining gene expression in the mid-gestation mouse labyrinth, the researchers identify specific markers for each layer. They show that these markers are expressed in distinct layers in the chorion (the embryo's outer membrane) before villous formation begins and that the induction of the S-TGC and SynT-I precursors does not require the presence of SynT-II precursors, the first of the precursors to appear. Thus, they conclude, the three differentiated trophoblast cell types in the rodent labyrinth arise from distinct, autonomous precursors in the chorion that are patterned before its morphogenesis begins.



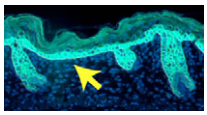
Eklf role in early haematopoiesis revealed

Throughout development, signalling pathways and transcription factor networks control the differentiation of stem cells and progenitor cells but how their effects are integrated is poorly understood. Now, on p. 2071, Lohmann and Bieker reveal how Bmp4 signalling and Gata transcription factors interact to control haematopoiesis in mice by studying the regulation of the erythroid-specific transcription factor Eklf during this process. In differentiating embryonic stem (ES) cells, they report, Eklf expression is initiated in haematopoietic progenitor cells before erythroid commitment. Using a new RNAi-based loss-of-function approach in embryoid bodies, among other approaches, they show that Gata2 and Smad5 (a downstream effector of Bmp4 signalling) cooperate to induce Eklf expression in erythroid-megakaryocytic progenitor cells. The maintenance of Eklf expression in committed erythroid cells, however, is regulated by Gata1 in a Smad-independent manner. These results suggest that Eklf is poised to regulate lineage fate decisions during early haematopoiesis and, more generally, show how the factors that govern early mouse development can be studied in ES cells undergoing in vitro differentiation.



Cortical migration converges on C3G

Cerebral cortex development involves a series of neuronal migrations that are regulated through neuronal cell-surface receptors (integrins) interacting with extracellular matrix (ECM) proteins and neighbouring cells (radial glia). Voss and colleagues now report that C3G, a guanine nucleotide exchange factor that can activate, by GTP exchange, signalling from the Ras-like Rap1, acts downstream of neuronal cell-surface receptors to regulate cortical neuron migration in mice (see p. 2139). In C3G-deficient embryos, they report, the cortical preplate does not split into the marginal zone and subplate because of defects in cortical neuron migration. Consequently, the cortical plate does not form, a phenotype that is common to reelin pathway mutants (reelin is an ECM protein that regulates neuronal migration). The attachment of radial glial cells and neurons to the ECM is also disrupted in C3G-deficient embryos, the researchers report. Thus, C3G is essential for two key processes in cortex development – neuronal migration and radial glial attachment – perhaps because reelin and integrin signalling converge at this Ras signalling molecule.

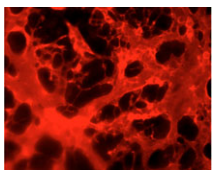


Hair-raising β-catenin signalling

Hair shaft differentiation and the induction of hair follicle placodes in the mammalian embryonic surface ectoderm require β-catenin signalling but can activation of this signal alone globally program ectodermal cells to a hair follicle fate? The answer, report Sarah Millar and co-workers on p. 2161, is yes. However, controlled downregulation of β-catenin signalling is needed for the development of a normal fur coat. The researchers found that hair follicle placodes are expanded and induced prematurely in mouse embryos that express a mutant dominant-active form of endogenous epithelial β-catenin. These premature placodes fail to invaginate but precociously express hair shaft keratins. Eventually, the whole epidermis adopts a hair follicle fate and epidermal stratification is disrupted. In addition, the mutant embryonic skin becomes prematurely innervated and pigmented. Thus, the researchers conclude, β-catenin not only promotes hair follicle placode and hair shaft fate, but also activates the signals that attract nerve fibres and melanoblasts into the developing hair follicles and suppresses epidermal differentiation.

Dpp on the brink(er)

In *Drosophila*, the morphogen Dpp patterns developing structures by directly regulating the expression of its target genes, which it also indirectly regulates by downregulating the transcription of the nuclear repressor *brinker* (*brk*). On p. 2183, Yao et al. describe the intricate way in which multiple modular *brk* promoter elements generate an inverse *brk* expression gradient in response to the Dpp gradient. The promoter region of *brk*, they report, contains multiple compact modules, each of which contains one or more binding sites for the Schnurri/Mad/Medea (SMM) complex (which mediates the repression of some Dpp target genes) linked to regions that activate *brk* transcription. Because the SMM complex represses these activator regions in a distance-dependent manner, each module responds autonomously to Dpp signalling. However, unlike other modular promoters (for example, the promoter in the segmentation gene *eve*), the outputs from the regulatory modules in *brk* are integrated to generate the final *brk* expression pattern. This unique promoter organisation, the researchers suggest, ensures a robust and precise response to Dpp signalling.



Angiogenesis and β1 integrin stick together

Integrins – heterodimeric cell-surface receptors that bind to laminin, collagen and other ligands in the extracellular matrix (ECM) – propagate many intracellular signals during development. For example, integrin-ECM interactions regulate the formation of new blood vessels (angiogenesis). But which integrin-ligand pairs are required in endothelial cells (ECs) to mediate this process? Carlson and co-workers now report that β1 integrin is needed for EC adhesion, migration and survival during angiogenesis (see p. 2193). Lineage-specific deletion of *Itgb1* (which encodes β1 integrin) in ECs in mouse embryos causes embryonic lethal vascular defects, they report, including the formation of a discontinuous endothelium in blood vessels. Furthermore, isolated *Itgb1*-null ECs behave in a disorganised manner, fail to adhere to or migrate on laminin or collagen substrata and have reduced survival. These findings highlight the essential role that β1 integrin plays during angiogenesis and suggest that targeted therapies that block the function of β1 integrins in ECs could control the growth and survival of cancers by preventing neovascularisation.

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