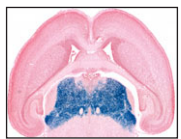


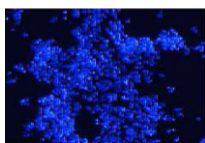
Syncytial nuclei go with the flow

Nuclear movements are important for a wide range of cellular and developmental processes, but whereas the intracellular mechanisms of nuclear movement have been studied in detail, the role of surrounding cells remains poorly understood. Now, on p. 1305, Carl-Philipp Heisenberg and colleagues reveal that, during zebrafish gastrulation, the nuclear movements seen in the yolk syncytial layer (YSL) are guided by surrounding tissues. Some yolk syncytial nuclei (YSN) are located below a tissue called the mesendoderm, which contains mesoderm and endoderm progenitors. During gastrulation, the movements of these YSN and of the mesendoderm are very similar. The authors demonstrate that these movements are coordinated, and that the mesendoderm directs YSN movements by modulating cortical flow (a concerted flow of actin filaments associated with the plasma membrane) within the YSL, which contains the YSN. They also find that the coordinated movement of the YSN and the mesendoderm requires E-cadherin. Thus, they propose, nuclear movements can be guided by surrounding tissues and are mediated by cortical flow.



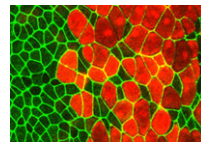
Gbx2 keeps thalamus within bounds

The thalamus relays information to the cortex and consists of dozens of distinct groups of neuronal cell bodies called thalamic nuclei. How do these separate nuclei form during development? On p. 1317, James Li and co-workers use an inducible genetic fate-mapping technique to demonstrate the importance of the homeobox transcription factor Gbx2 in the differentiation of thalamic nuclei. By tracing the fates of Gbx2-expressing cells and their descendants, the authors establish that these cells contribute to all thalamic nuclei, but that the precursors of different nuclei express Gbx2 at different times during development. Interestingly, Gbx2 seems to control this segregation of cells into different thalamic nuclei by acting on postmitotic neurons. The researchers also show that although the loss of Gbx2 does not lead to any obvious patterning defects in the forebrain, it results in disrupted dorsal and posterior thalamic boundaries, which normally separate the thalamus from neighbouring brain structures. From this and other data, the authors propose that Gbx2 functions cell-autonomously in regulating thalamic boundary formation.



Activin and Nanog: a pluripotent mix

Pluripotency, the ability to give rise to all the cell lineages of the body, is a hallmark of embryonic stem cells (ESCs), and understanding its regulation is essential for effectively controlling ESC differentiation. Ludovic Vallier, Roger Pedersen and colleagues now demonstrate a role for Nanog – a crucial component of the pluripotency transcriptional network – in safeguarding human ESCs (hESCs) against the differentiation-inducing effects of extracellular signals (p. 1339). They show that Activin/Nodal signalling, which maintains hESC pluripotency through SMAD2/3 activation, maintains NANOG expression through the binding of SMAD2/3 to the NANOG promoter, which blocks the differentiation of pluripotent cells into neuroectoderm. Conversely, NANOG appears to limit the Activin/Nodal-induced transcriptional activity of SMAD2/3 by forming a protein complex with it. This interaction prevents the differentiation of pluripotent cells from mesendoderm into endoderm, which is otherwise induced by exposure to BMP4 and Activin/Nodal signalling. From their findings, the researchers propose that a negative-feedback loop involving Nanog and Smad2/3 safeguards pluripotent cells against differentiation.

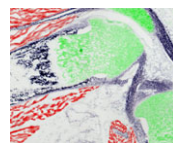
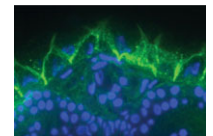


Cadherin function: right place, right time

Cadherins are a large family of cell-cell adhesion receptors, but despite intense research into their functions, many aspects of their activity remain somewhat elusive. Two papers in this issue of *Development* now shed new light on the significance of both cell-type specific cadherin expression and their subcellular localisation for their roles in development.

In the first study (p. 1327), Christopher Wylie and co-workers report that, in *Xenopus* ectoderm, distinct morphogenetic movements result from actin assembly mediated by differential cadherin expression. The authors show that the Type I sub-family members C-, E- and N-cadherin all assemble cortical actin. They then analysed the localisation of these three cadherins in the developing ectoderm, which separates into two parts (neural and non-neural). The cadherins, they find, are temporally and spatially differentially expressed in the neural and non-neural ectoderm; where expression domains overlap, the cadherins are predominantly found in different subcellular locations. In addition, whereas N-cadherin depletion affects actin assembly in, and the morphogenetic movements of, neural ectoderm, E-cadherin depletion has similar effects in the non-neural ectoderm. The two cadherins, however, cannot replace each other in rescue experiments. Thus, the researchers propose, cadherins are important for actin assembly during morphogenesis, and their differential expression is crucial for generating distinct morphogenetic movements.

In the second study, Mahendra Sonawane, Christiane Nüsslein-Volhard and colleagues investigate cellular junction assembly in zebrafish and report that E-cadherin is involved in regulating this process (p. 1231). The authors find that during the formation of hemidesmosomes, a type of cell junction that links the basal domain of epithelial cells to the extracellular matrix, E-cadherin and the polarity regulator Lgl2 localise to the lateral domain of epithelial cells. By contrast, the hemidesmosome component Integrin alpha 6 (Itga6) localises to both the lateral and the basal domain. The authors then demonstrate that Lgl2 promotes the targeting of Itga6 to the basal membrane during hemidesmosome formation, whereas E-cadherin negatively regulates this process. Thus, two proteins localised to the lateral domain act antagonistically to regulate basal hemidesmosome formation. Together, these two studies highlight the context-dependent nature of cadherin interactions and indicate that their function might be influenced by their subcellular localisation.



TGFβ tends to tendons

Tendons are tough fibrous connective tissue structures that connect muscles to bones and transmit muscle-generated forces to the skeleton. The assembly of tendon fibres has been studied intensively, but what are the molecular mechanisms that underlie tendon development? On p. 1351, Ronen Schweitzer and colleagues reveal that TGFβ signalling is crucial for tendon formation and for tendon progenitor (TNP) maintenance. The researchers find that tendons are missing throughout the body of mouse embryos in which TGFβ signalling is disrupted by mutating the genes that encode two TGFβ isoforms (TGFβ2 and TGFβ3) or the TGFβ type II receptor. Although TNPs form normally in these embryos, they are lost in later development, when the primordia of tendons would usually form. As no cell death accompanies this loss, the researchers suggest that TNPs assume an alternative fate. They also demonstrate that TGFβ is a potent inducer of TNP markers in tissue and organ culture. The source of TGFβ and its function in TNP specification and maintenance *in vivo* now await further investigation.