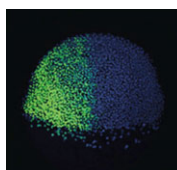


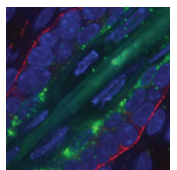
### Dynamics of human thymus development

The thymus is the primary organ responsible for generating T cells. Although thymus development has been studied in mice, little is known about how the human thymus develops. Here (p. 2015), Clare Blackburn and colleagues provide a comprehensive analysis of human thymus organogenesis. Using gene expression analyses, the researchers show that the spatial and temporal expression patterns of factors involved in thymus development in mice are conserved in humans. They also demonstrate that the human thymus arises from the third pharyngeal pouch, as in mice and in contrast to previous suggestions. Furthermore, they report, thymic epithelial cell differentiation as well as the immigration of mesenchymal cells and vascular progenitors into the human thymus occur after the onset of FOXP1 expression, consistent with the timing of these events in mice. Finally, the authors define precisely when the human thymus becomes colonised with haematopoietic cells, which are CD45<sup>+</sup>/CD7<sup>+</sup>/CD34<sup>int</sup> cells. Collectively, this study provides key insights into the conservation of thymus development between mice and humans, which has major clinical implications for enhancing or replacing thymus function.



### Coordinating head-to-tail with front-to-back

During embryogenesis, the anterior-posterior (AP) and dorsal-ventral (DV) axes are specified by the activity of key signalling pathways. FGF, Wnt and retinoic acid together pattern the AP axis: high activity defines more posterior tissues, which are specified later in development than anterior tissues. The BMP pathway specifies ventral fate; low BMP activity defines dorsal. Whether and how these pathways intersect to coordinate patterning of the two axes is poorly understood. On p. 1970, Megumi Hashiguchi and Mary Mullins provide evidence for synchronisation of DV and AP patterning in the zebrafish embryo. Upon temporally restricted inhibition of BMP in embryos anteriorised by inhibition of FGF or Wnt, the dorsalis tissue takes on the AP fate appropriate to the anteriorised embryo, rather than that corresponding to the time of BMP inhibition. The authors identify one mechanism mediating pathway cross-talk: MAPK, activated downstream of FGF, phosphorylates and inhibits the BMP effector Smad5. Thus, this work establishes the close temporal coordination of AP and DV patterning, and provides insights into how this is achieved.



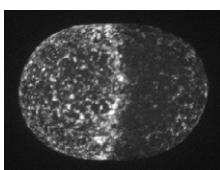
### miR-203 drives progenitor cell differentiation

MicroRNAs are important for the regulation of gene expression in a vast array of processes. In the skin, miR-203 has been shown to be crucial for the proper differentiation of the interfollicular progenitor cells, although the specific mechanism of this has remained elusive. In this issue (p. 1882), Rui Yi and colleagues investigate the precise timing of miR-203 activation during epidermal differentiation. They show that miR-203 is transcriptionally activated in the differentiating progeny of interfollicular progenitor cells upon asymmetric cell division. Using keratinocytes derived from miR-203-inducible mice, the authors found that miR-203 functions to promote an immediate exit from the cell cycle, leading to a complete loss of self-renewal after just 72 hours. They further identify a multitude of novel miR-203 targets *in vivo*, and demonstrate that co-repression by miR-203 of many of these, including Skp2, Msi2 and p63, is necessary for the function of miR-203 in inhibiting self-renewal. These data provide novel insights into the widespread role of miR-203 in differentiating interfollicular progenitor cells in the skin.



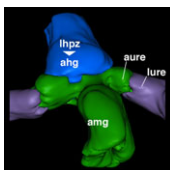
### Leaf patterning: AS1 far AS2 we know

The correct establishment of adaxial-abaxial patterning is crucial for leaf expansion and growth. The AUXIN RESPONSE FACTOR (ARF) family of proteins are key determinants of organ symmetry and abaxial patterning in *Arabidopsis thaliana* and are subject to complex regulatory control at both the transcriptional and translational level. Here (p. 1958), Chiyoko Machida and colleagues uncover an additional, dual mechanism for the regulation of ETT (also known as AFR3) by an ASYMMETRIC LEAVES1 (AS1)-AS2 complex. First, the authors show that the AS1-AS2 complex directly represses ETT expression via binding of AS1 to the promoter region. Second, they provide evidence for an indirect mechanism of regulation via miR390- and RDR6-dependent post-transcriptional gene silencing of both ETT and ARF4. The authors also suggest a possible epigenetic mechanism, as AS1-AS2 maintains the methylation status of ETT within the coding region. These discoveries shed light on the molecular framework of early leaf patterning events and help to uncover the events that lead to the specification of distinct adaxial and abaxial fates during leaf development.



### PAR-allele pathways for polarity

In the *C. elegans* embryo, anterior-posterior polarity is defined at the one-cell stage, via asymmetric and reciprocal localisation of cortex-associated PAR protein complexes: PAR-3, PAR-6 and aPKC localise to the anterior, whereas PAR-1, PAR-2 and LGL-1 are enriched at the posterior. Polarity maintenance involves mutual antagonism between the anterior and posterior complexes and may also involve CDC-42-dependent regulation of myosin activity. Kenneth Kemphues and co-workers (p. 2005) now provide evidence for multiple and partially redundant pathways acting at the posterior to maintain polarity once it has been established. Both PAR-2 and CDC-42, acting in separate pathways, have dual functions in independently regulating both anterior PAR complex localisation and myosin activity, whereas LGL-1 appears to have a buffering role in controlling PAR-6 protein levels. Although the molecular details of these pathways remain incomplete, the complex and overlapping mechanisms operating to maintain polarity in the early embryo underscore the importance of robust and efficient polarisation for subsequent development.



### Stem cells go out of bounds

Many animal tissues maintain populations of slowly proliferating stem cells that contribute to tissue homeostasis and repair. In *Drosophila*, for example, stem cells reside throughout the midgut and within the hindgut and renal tubules. But how and when do these cells arise? Volker Hartenstein and colleagues now show that *Drosophila* gut progenitors migrate across tissue boundaries and adopt the fate of the organ in which they come to reside (p. 1903). Using lineage tracing, the researchers demonstrate that a subset of adult midgut progenitors, which are initially located in the larval midgut, migrate posteriorly during development and contribute to the adult ureter and, subsequently, the renal stem cell population. In addition, they report, a population of hindgut progenitors migrates anteriorly into the midgut territory to differentiate and give rise to midgut enterocytes. These findings suggest that a stable boundary between the midgut (an endodermal tissue) and the hindgut/renal tubules (ectodermal tissues) does not exist and instead multipotent progenitors are able to cross the boundaries between these domains.