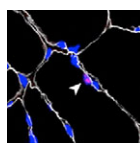


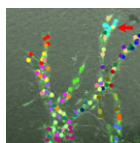
### New blood: vasculature restrains pancreas growth

Although the primary function of blood vessels is to provide organs with the oxygen and nutrients that are essential for tissue growth and maintenance, blood vessels also provide positive paracrine signals during early pancreas development. Now, Yuval Dor and colleagues report that, surprisingly, non-nutritional signals from blood vessels restrain pancreas growth later in development (see p. 4743). In gain-of-function experiments, they show that VEGF-induced hypervascularisation restrains pancreatic growth in embryonic mice. Conversely, the elimination of endothelial cells increases the size of embryonic pancreatic buds. Blood vessels, they report, restrict the formation of pancreatic tip cells, reduce pancreatic lateral branching and prevent differentiation of the pancreatic epithelium into endocrine and exocrine cells both *in vivo* and *ex vivo*. The researchers propose, therefore, that the vasculature controls pancreas morphogenesis and growth by reducing branching and by maintaining the undifferentiated state of primitive epithelial cells. These unexpected findings might have important implications for the derivation of insulin-producing  $\beta$ -cells from embryonic stem cells for the treatment of diabetes.



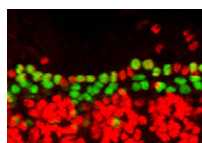
### Hesr1 and Hesr3 regulate satellite cell fate

During postnatal growth, satellite cells (skeletal muscle stem cells) divide to provide new myonuclei for growing muscle fibres, but in adult muscle they are maintained in an undifferentiated quiescent state except during muscle regeneration. Notch signalling regulates stem cells in many tissues, including skeletal muscle, and here, So-ichiro Fukuda and co-workers investigate whether the Notch target genes *Hesr1* and *Hesr3* are involved in the generation of satellite cells (p. 4609). They report that *Hesr1* and *Hesr3* are expressed simultaneously in neonatal and adult mouse satellite cells and show that, although *Hesr1* and *Hesr3* single-knockout mice have no obvious satellite cell or muscle regeneration abnormalities, the postnatal generation of undifferentiated quiescent satellite cells is impaired in *Hesr1/3* double-knockout mice. Moreover, satellite cell numbers gradually decrease in *Hesr1/3* double-knockout mice because of premature differentiation, and the mice develop an age-dependent muscle regeneration defect. Thus, the researchers conclude, *Hesr1* and *Hesr3* play crucial roles in skeletal muscle homeostasis by regulating the undifferentiated quiescent state of satellite cells.



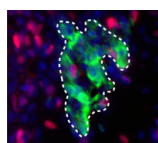
### Endothelial cell movements during angiogenesis

During angiogenesis, new blood vessels sprout from an existing vascular network, elongate and bifurcate to form a new branching network. The individual and collective movements of vascular endothelial cells (ECs) during angiogenic morphogenesis are poorly understood but, on p. 4763, Koichi Nishiyama and colleagues provide some new insights into these movements. Using time-lapse imaging and a computer-assisted analysis system to quantitatively characterise EC behaviours during sprouting angiogenesis, they show that ECs move backwards and forwards at different velocities and change their positions relative to each other, even at the tips of elongating branches *in vitro*. This 'cell mixing', which also occurs *in vivo* at the tips of developing mouse retinal vessels, is counter-regulated by EC-EC interplay via DLL4-Notch signalling and might be promoted via EC-mural cell interplay. Finally, the researchers show, the dynamic behaviour and migration of ECs contribute to effective branch elongation. Thus, cell behaviours during angiogenesis and other forms of branching morphogenesis might be more complex and variable than previously thought.



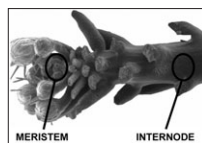
### JAK/Stat signals touch Tinman's heart

During *Drosophila* heart development, intercellular signalling pathways activate a conserved cardiac-specific gene regulatory network by inducing the expression of the transcription factor Tinman (Tin) in the dorsal mesoderm. Stat92E, the transcriptional effector of the JAK/Stat signalling pathway, is a direct target of Tin and, on p. 4627, Eric Olson and colleagues characterise JAK/Stat signalling during cardiogenesis for the first time. They show that *Drosophila* embryos with mutations in the JAK/Stat ligand *upd* or in *Stat92E* have non-functional hearts with luminal defects and inappropriate cell aggregations. The JAK/Stat pathway, they report, is active in the dorsal mesoderm when the initially broad mesodermal expression pattern of *tin* becomes restricted to cardiac and visceral muscle progenitors, which occurs after dorsal mesoderm progenitor specification. Finally, they show that JAK/Stat signals activate Enhancer of Split complex genes to restrict Tin expression, thereby regulating heart precursor diversification. Overall, these findings show that JAK/Stat signalling regulates heart development and identify an autoregulatory circuit by which *tin* restricts its own expression domain.



### Careless tALK predisposes to neuroblastoma

Neuroblastoma, the most common extracranial solid tumour in childhood, arises from cells of the developing sympathoadrenergic lineage. Activating mutations in the gene encoding the tyrosine kinase receptor anaplastic lymphoma kinase (ALK) have been identified in both familial and sporadic cases of neuroblastoma so might Alk signalling control proliferation in this lineage? On p. 4699, Hermann Rohrer and colleagues report that forced expression of wild-type ALK or neuroblastoma-related constitutively active mutant ALK increases the proliferation of cultured immature chick sympathetic neurons and their expression of the proto-oncogene *NMyc* and of the neurotrophin receptor *trkB*. By contrast, *Alk* knockdown both *in vitro* and *in vivo* reduces sympathetic neuron proliferation. Furthermore, the Alk ligand Midkine (Mk) is expressed in immature sympathetic neurons, they report, and *in vivo* knockdown of *Mk* also reduces sympathetic neuron proliferation. Together, these results indicate that Mk/Alk signalling controls the extent and timing of sympathetic neurogenesis. Thus, the predisposition to neuroblastoma that is associated with activating ALK mutations might be the result of aberrant neurogenesis.



### (Bell)ringing the changes in plant phyllotaxis

Complex networks of regulatory genes control morphogenesis but how are these networks translated into the local changes in tissue growth that shape multicellular organisms? Jérôme Pelloux and co-workers (p. 4733) have been investigating the modulation of phyllotaxis (the arrangement of leaves and flowers along plant stems) in *Arabidopsis* by the transcription factor BELLRINGER (BLR). In plants, the formation of new lateral organs depends on demethylesterification of homogalacturonan (HG), a major component of plant cell wall pectins. The researchers show that ectopic primordia form in the floral meristem of *Arabidopsis blr* mutants because of ectopic expression of the pectin methyltransferase *PME5*, which changes the demethylesterification state of HG. Thus, BLR normally represses *PME5* expression in the meristem, thereby influencing the establishment of the phyllotactic pattern. However, in the elongating stem, the researchers report, BLR activates *PME5* expression to maintain phyllotaxis. These results identify BLR as an important component of the regulatory network that controls HG demethylesterification and, in turn, phyllotaxis in *Arabidopsis*.

Jane Bradbury