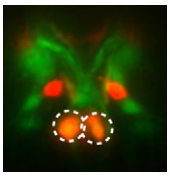
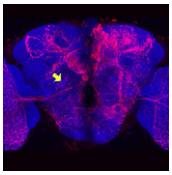
IN THIS ISSUE



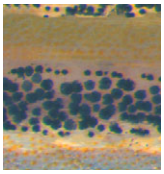
Roadmap for neuronal specification

Neuronal subtype specification is regulated by the coordinated action of transcription factors. Any one factor may be expressed in multiple subtypes, but specification is achieved based on the precise combination of factors and is therefore context dependent. In this issue (p. 422), Oliver Hobert and colleagues explore neuronal differentiation in *C. elegans* and focus on the role of the TTX-3 LIM homeodomain transcription factor in regulating neural subtype specification. The authors find that TTX-3 is broadly required in multiple neuron classes of relatively unrelated identity, but that the interacting partners and downstream targets of TTX-3 are subtype specific. TTX-3 is required for cholinergic AIY interneuron specification, while an interaction with the POU domain protein UNC-86 leads to the specification of serotinergic NSM neurons. Furthermore, UNC-86 itself can specify cholinergic IL2 sensory and URA motoneurons via cooperation with the ARID-type transcription factor CFI-1. This detailed analysis of transcriptional cascades reveals a programming roadmap for neuronal subtype specification.



Neural progenitors divide and conquer

Neuronal diversity in *Drosophila* is generated by the temporal specification of type II neuroblasts (NBs) and their progeny, the intermediate neural progenitors (INPs). Multiple transcription factors are expressed in a birth order-dependent manner within each INP lineage, but whether this temporal patterning gives rise to discrete neuronal sets from each individual INP cell is unclear. Now, on p. 253, Tzumin Lee and colleagues describe extensive fate-mapping of individual neurons derived from specific type II NB lineages. The authors use targeted clonal labelling to specifically label neurons in individual INP clones, and by restricting the clonal induction to specific time windows they are able to generate and characterise clones of neurons that are born from two successively produced INPs. The resulting analyses demonstrate that the temporal specification of INPs does indeed translate to distinct types of neurons, suggesting that neuronal fate diversification might operate as a function of age.



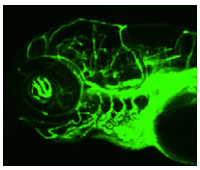
How the zebra(fish) got its stripes

The striped pattern of the zebrafish skin offers an excellent model system in which to study biological pattern formation. Previous studies have shown that the interactions between melanophores and xanthophores are crucial for pattern formation, but little is known regarding the molecular mechanisms that regulate this phenomenon. Now, on p. 318, Shigeru Kondo, Masakatsu Watanabe and colleagues uncover a role for long-range Delta/Notch signalling between the melanophore and xanthophore pigmented cell types that is crucial for proper stripe formation. The authors show that Delta/Notch signalling is required for melanophore survival, since disruption of the pathway by DAPT treatment results in loss of melanophores, while constitutive Notch activation in transgenic fish rescues this effect. The authors use targeted laser ablation to show that the source of this survival signal is the xanthophore. Interestingly, the authors observe long protrusions that originate from the melanophores and extend to the xanthophores, which might serve as a means to mediate the Delta/Notch signalling over long distances.

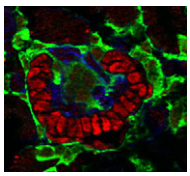
Peri important role for Notch

Pericytes are specialised cells that wrap around the endothelial cells of the vasculature to regulate vascular integrity, permeability and blood flow. Despite this crucial role, the molecular mechanisms that control pericyte development are not well understood. In this issue, two papers identify a requirement for Notch in pericyte development in the brain and kidney vasculature.

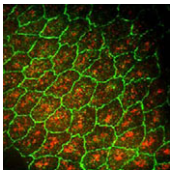
On p. 307, Bruce Appel and colleagues investigate the role of Notch in regulating pericyte number in the developing zebrafish brain vasculature. The authors interrogate a panel of Notch genes and identify



notch3 as expressed in the developing vasculature, specifically in cells positive for *pdgfrb*, a known pericyte marker. Loss-of-function of Notch3 leads to disruption of the blood-brain barrier and cerebral haemorrhaging, which is likely to be due to the reduction in pericyte number. Importantly, the authors show that Notch3 is required for pericyte development and specifically for promoting proliferation and expansion of the cells. Using *pdgfrb* expression as a readout, the authors observe that overexpression of the Notch3 intracellular domain is associated with increased numbers of pericytes, whereas interference with Notch3 activity causes a reduction. Based on varying levels of *pdgfrb* expression observed throughout the study, the authors hypothesize that Notch3 may positively regulate *pdgfrb* in order to regulate pericyte proliferation.



The role of Notch signalling in pericyte development is also investigated by Raphael Kopan and colleagues (p. 346), who report a critical requirement for Notch during the development of the pericytes of the mammalian kidney, known as mesangial cells. These cells, along with the smooth muscle and interstitial cells of the kidney, derive from Foxd1^{+} stromal precursors; however, Notch signalling appears to be only required for the emergence of the mesangial cells. Inactivation of Notch specifically in the stromal precursors results in the formation of glomeruli that lack mesangial cells, leading to glomerular aneurism and kidney failure at birth. The authors go on to show that, in this case of pericyte development in the kidney, Notch1 and Notch2 appear to act redundantly.



Case closed: ion channels mediate dorsal closure

Dorsal closure is a morphogenic process that involves the interplay of mechanical forces as two opposing epithelial sheets come together and fuse. These forces impact cell shape and the rate of morphogenesis, but the molecular pathways that translate mechanical force into phenotype are not well understood. Now, on p. 325, Daniel Kiehart and colleagues demonstrate a role for calcium signalling via mechanically gated ion channels (MGCs) in *Drosophila* dorsal closure. Using UV-induced calcium release, the authors show that increased calcium levels stimulate contractility during dorsal closure, whereas treatment with a calcium-chelating agent disrupts closure. Via a series of pharmacological perturbations, the authors demonstrate that MGCs regulate actomyosin contraction that, in turn, is required for force production and successful dorsal closure. The authors support their findings by knocking down two separate MGC subunits, which also leads to a failure to generate sufficient force for dorsal closure. This study paves the way for investigating MGCs in other morphogenic processes, for example during wound repair.