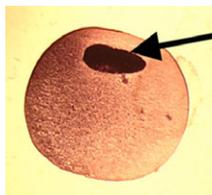


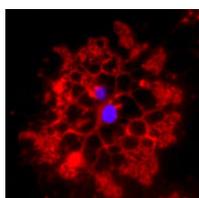
### Ventral leg fate (T)boxed in

In the developing fly leg, events downstream of the Wnt ligand Wingless (Wg) and the BMP ligand Decapentaplegic (Dpp) determine dorsoventral fate choices. But how do distal cells, which are exposed to high levels of both Wg and Dpp, discriminate between the two when choosing dorsoventral fates? The answer, report William Brook and colleagues, lies with the T-box transcription factors H15 and Midline (Mid) (see p. 2689). The authors demonstrate that activation through ventral Wg and repression through dorsal Dpp determines the ventral expression of both factors. Whereas neither *mid* nor *H15* alone are essential for leg development, loss-of-function mutations in both genes lead to the loss of Wg-dependent ventral leg structures. By contrast, the ectopic expression of *mid* alone can induce ventral fates in dorsal cells; however, this effect is reduced by attenuated Wg signalling, indicating that Wg acts both upstream of and in parallel with *mid*. Together, these results suggest that *mid* and *H15* act as selector genes for ventral leg fate.



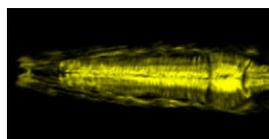
### Nuclear reprogramming the oocyte way

Transplanting somatic nuclei into *Xenopus* oocytes that are in first meiotic prophase is an effective way to reprogram them to a multipotent state. On p. 2695, John Gurdon and co-workers reveal that the activation of muscle genes in such nuclei occurs independently of known muscle transcription factors. When the authors injected nuclei from a range of mouse cell types into *Xenopus* oocytes, they found that muscle gene transcription was activated to almost the same extent as in muscle cells. This transcriptional activation occurred independently of maternally provided MyoD (a myogenic factor) and of protein synthesis, ruling out that myogenic transcription factors were being transcribed and translated from the transplanted nuclei. Interestingly, the transcription of non-muscle lineage genes was also activated. From their findings, the authors conclude that nuclear reprogramming by oocytes is achieved through a different mechanism to that of virus-induced transcription factor overexpression, as used in other reprogramming approaches, perhaps reflecting the activity of a new type of transcriptional control in certain organisms' oocytes.



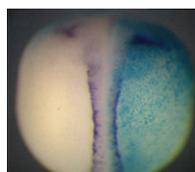
### $\beta 1$ integrin wraps up CNS myelination

In the central nervous system (CNS), specialised cells called oligodendrocytes produce the myelin sheath that insulates axons and enables fast nervous conduction. As seen in multiple sclerosis, myelination defects can lead to severe neurological problems. Now, Colognato, Müller and colleagues report findings that support the disputed notion that the extracellular matrix receptor  $\beta 1$  integrin is crucial for CNS myelination (see p. 2717). They report that in two mouse mutants in which  $\beta 1$  integrin was conditionally ablated in the CNS, CNS myelination defects were present that were not due to aberrant oligodendrocyte differentiation or survival. Instead, their *in vitro* experiments show that  $\beta 1$  integrins regulate myelin sheet outgrowth by activating the serine/threonine kinase AKT, and that constitutively active AKT can rescue the outgrowth defects caused by  $\beta 1$  integrin loss. Together these findings reveal that  $\beta 1$  integrin promotes the myelin wrapping of CNS axons in an AKT-dependent manner, opening the door to future studies into the downstream effectors of AKT and their role in myelination.



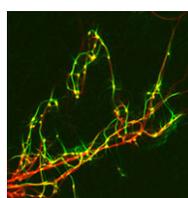
### CEH-51 muscles in on mesoderm development

Many mesodermal cell types, including pharynx and body muscle cells, are derived from a single cell, the MS blastomere, in *Caenorhabditis elegans*. Mesoderm specification involves the activation of the T-box factor gene *tbx-35*; *tbx-35* mutation results in a severe decrease in MS-derived tissue. On p. 2735, Morris Maduro and co-workers now identify the NK-2 homeobox gene *ceh-51* as a novel regulator of mesoderm development. The researchers report that *ceh-51* is expressed in mesoderm cells and is a direct target of TBX-35. Its overexpression causes embryonic arrest and promotes MS-derived tissue specification, whereas a null mutation results in larval arrest and pharyngeal defects. Embryos with loss-of-function mutations in both *ceh-51* and *tbx-35* have a more severe phenotype than do single mutants, indicating that the functions of TBX-35 and CEH-51 in mesoderm development partially overlap. Given that T-box and NK-2 factors are also crucial for heart development in flies and vertebrates, their role in regulating mesoderm development might be evolutionarily conserved.



### aPKC's fateful nuclear journey

Several well-conserved molecules, such as the apical kinase aPKC, determine apicobasal epithelial polarity. But how do they influence cell fate determination, particularly in vertebrates, in which the aPKC-Par polarity complex's role in neural cell fate diversification has been controversial? Now, on p. 2767, Nancy Papalopulu and colleagues illuminate this issue with their study of *Xenopus* primary neurogenesis, during which the two cell layers of the frog neural plate adopt different fates – deep, non-polar cells become neurons and superficial, polarised cells remain as progenitors. They show that a membrane-tethered form of aPKC suppresses primary neurogenesis in deep cells, while promoting cell proliferation, effects that are mimicked by a nuclear-localised, activated form of aPKC. Blocking endogenous aPKC with a nuclear, dominant-negative form had the opposite effect: it enhanced neurogenesis. Surprisingly, the researchers detected both endogenous and membrane-tethered aPKC in the nucleus, leading them to propose that aPKC acts as a nuclear cell fate determinant during primary neurogenesis, perhaps by transmitting polarity information from membrane to nucleus.



### Wash meshes linear and branched actin

Wiskott-Aldrich Syndrome (WAS) proteins, such as Wasp and Wash, regulate branched actin networks by activating Arp2/3 in response to Rac and Cdc42 GTPases. By contrast, the linear actin nucleators Spire and Cappuccino (Capu) function downstream of Rho1 GTPase. But now, Susan Parkhurst and colleagues demonstrate that Rho1 and Wash regulate both linear- and branched-filament actin networks (see p. 2849). *In vitro*, Wash activates Arp2/3 to nucleate actin, but also bundles F-actin and microtubules (MTs). *In vivo*, Wash is essential for *Drosophila* oocyte development and functions in the Rho1/Capu/Spire pathway. It physically interacts with all three factors, the authors report, and its actin- and MT-bundling activity is regulated by both Rho1 and Spire, and intriguingly also by Arp2/3, *in vivo*. As Wash requires Arp2/3 to regulate the actin cytoskeleton during oogenesis, Arp2/3 might thus act as a molecular switch for Wash function. Future work should shed light on how the different actin networks are coordinated and how, when misregulated, these processes contribute to disease.