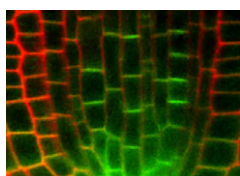


Dopaminergic differentiation progresses with β -catenin

The loss of dopaminergic (DA) neurons is a hallmark of Parkinson's disease (PD), a common human neurodegenerative disorder. Stem cell replacement therapy is a promising strategy for alleviating PD, but one current limitation is generating large enough numbers of DA neurons. Now, on p. 2027, Eric Huang and co-workers reveal that several stages of DA neurogenesis depend on β -catenin. The authors show, using conditional gene knockout approaches, that regionally deleting β -catenin in the neurogenic niche of the mouse ventral midbrain (vMB), which gives rise to DA progenitors, disrupts progenitor cell adherent junctions and radial glial cell integrity. This leads to reduced DA neurogenesis and defects in DA neuron polarity, migration and segregation. By contrast, removing β -catenin from DA neural progenitors does not perturb vMB structure, but rather reduces DA neurogenesis by impairing the later progression of committed progenitors to DA neurons. From these findings, the authors suggest that β -catenin-mediated regulation of DA differentiation could be exploited in the development of cell-based therapies for PD.



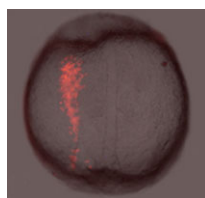
Auxin signalling hits the BRX

In plants, the balance between auxin nuclear activity and polar auxin transport (PAT) between cells determines each cell's transcriptional response to auxin. Mutations in *BREVIS RADIX* (*BRX*), a root growth regulator, disturb auxin-responsive gene expression, but what is the function of *BRX*? Now, Christian Hardtke and colleagues determine that *BRX* is a plasma membrane-associated protein that translocates to the nucleus in response to auxin exposure or auxin flux (see p. 2059). Using *BRX*-GFP fusion proteins, the researchers demonstrate that *BRX* is membrane-associated and translocates to the nucleus after auxin stimulation, where it might associate with transcription factors to regulate gene expression. *BRX* localization is polarized in vascular cells, as is that of the *PIN* family of auxin efflux carriers; expressing *BRX* under the control of a *PIN* promoter rescues *brx* root phenotypes, whereas inhibiting PAT mimics *brx* mutants. Auxin also induces *BRX* degradation. Together, these findings highlight how *BRX* might function in a novel auxin signalling pathway and how gene expression could be modulated in response to an auxin gradient.



Dual switch turns on zygotic genes

At a certain point in the development of most animal embryos, the mid-blastula transition (MBT), cell cycle progression slows down, and developmental control switches from maternal factors to zygotic transcripts. How are these two concurrent events controlled? Here, Eric Wieschaus and colleagues report that in *Drosophila*, total DNA content regulates both cell cycle slowing (CCS) and the zygotic transcription of select genes, whereas most zygotic transcription begins after a set timespan (see p. 2101). CCS depends on the ratio of nuclear content to cytoplasmic volume (the N/C ratio); using chromosome rearrangements, the researchers now demonstrate that CCS is independent of any particular genome region and requires an N/C ratio above 70% of that in wild-type embryos. They also demonstrate that, whereas most zygotic transcription depends on a timing mechanism independent of the N/C ratio, a set of 88 genes is N/C ratio-regulated. Thus, the researchers propose two independent mechanisms exist that control the onset of zygotic transcription, one of which correlates with CCS.

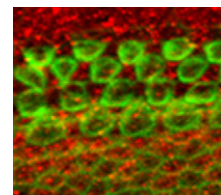


Converging on convergent extension regulators

Convergent extension (CE) is a morphogenetic process during which cells within a layer intercalate (converge), making the layer longer and thinner (extended) as a result. CE is important for diverse morphogenetic events, from gastrulation to organogenesis. In this issue, two articles identify new regulators of CE with potential implications for human hereditary disorders.

On p. 2121, Zhang, Shi and colleagues report that Down syndrome critical region protein 5 (*Dscr5*) regulates CE through non-canonical Wnt/planar cell polarity (PCP) signalling during zebrafish gastrulation. *Dscr5* is encoded on a chromosomal region crucial to Down syndrome pathogenesis in humans and functions in glycosylphosphatidylinositol (GPI) biosynthesis. The authors show that both *dscr5* overexpression and morpholino knockdown impair CE, but not embryonic patterning. *Dscr5* is also required for the cell surface localization of Knypek/Glypican 4. Glypicans, heparan sulfate proteoglycans that promote PCP signalling by facilitating Wnt interactions with signalling receptors, contain GPI membrane anchors, and these findings indicate for the first time that glypican function is linked to GPI biosynthesis. *Dscr5* knockdown also promotes endocytosis of the Wnt receptor Frizzled 7 and the degradation of the PCP pathway component Dishevelled. Thus, *Dscr5* appears to regulate CE by allowing glypican and Wnt receptor interaction at the cell surface, thereby also preventing Dishevelled degradation.

On p. 1977, Norio Yamamoto and colleagues identify CE as being important for mouse inner ear patterning. Mammals detect sounds through the organ of Corti (OC), an inner ear structure that contains highly ordered rows of auditory sensory cells, but the mechanisms that control OC cellular patterning are unclear. By measuring tissue and cell size and shape, the authors establish that during OC development, CE movements occur. They also find that non-muscle myosin II (NMII) is distributed asymmetrically in the developing sensory cells, and that inhibiting NMII genetically and pharmacologically leads to defects in OC CE movements. Based on these data, the authors propose that NMII is a key regulator of OC patterning and suggest that this might explain the hearing defects of humans with myosin mutations. The results of these two studies shed new light on CE regulation and on its importance in development and disease.



IN JOURNAL OF CELL SCIENCE The path to lumenogenesis

During vascular morphogenesis, a complex signalling network controls endothelial-cell (EC) lumen formation. George Davis and colleagues have shown previously that protein kinase C (PKC), Rho GTPases and the downstream kinases Pak2 and Pak4 are essential components of this network. In *J. Cell Sci.*, the researchers now show that EC lumen formation in a 3-dimensional collagen matrix requires the Src-family nonreceptor tyrosine kinases (SFKs) Src and Yes, which regulate the actin cytoskeleton and cell migration, as well as PKC ϵ , which activates SFKs. SFKs regulate Rho GTPase activity in many contexts, and the authors report that, during EC lumen formation, an SFK-containing multiprotein complex directly associates with the Rho GTPase Cdc42. This association depends on PKC ϵ . PKC ϵ and Cdc42, in turn, trigger a downstream kinase cascade involving Pak2, Pak4, B-Raf, C-Raf, ERK1 and ERK2. As each kinase in this pathway is essential, these results define a linear signalling pathway required for EC lumen formation.

Koh, W. et al. (2008). Formation of endothelial lumens requires a coordinated PKC ϵ , Src-, Pak- and Raf-kinase-dependent signaling cascade downstream of Cdc42 activation. *J. Cell Sci.* 122, 1812-1822.