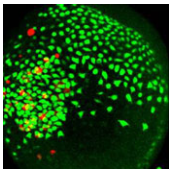
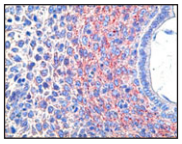


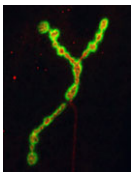
Mesodermal chemokine signals for endodermal migration

During vertebrate gastrulation, mesodermal and endodermal cells internalise through the blastopore and then migrate in different ways to establish the internal and external organisation of the embryo. Wnt/planar cell polarity signalling controls the mesodermal cell migration but what regulates the endodermal cell movements? Mizoguchi and colleagues now report that, during zebrafish gastrulation, the chemokine Sdf1, which is released by mesodermal cells, controls the dorsal migration of endodermal cells, which express the Sdf1 receptor Cxcr4 (see p. 2521). Morpholino knockdown of *cxcr4a* or *sdf1a/sdf1b* (*sdf1*) inhibits the directional migration of *cxcr4a*-expressing endodermal cells, whereas misexpressed Sdf1 attracts *cxcr4a*-expressing endodermal cells. Using a transgenic line that expresses GFP in the endodermal cells, they also show that Sdf1/Cxcr4 signalling regulates the formation and orientation of the characteristic filopodial processes that, the researchers suggest, may help the endodermal cells decide their direction of migration. These results provide important new insights into the control of endodermal migration during zebrafish gastrulation.



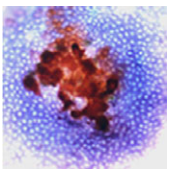
Gap junctions: maternal role in implantation

Over 50% of fertilised mammalian eggs fail to implant in the uterus. These failures are generally blamed on embryonic defects. Now, however, Laws and colleagues report that gap junction communication between uterine stromal cells drives the formation of new maternal blood vessels and is, therefore, crucial for embryo survival (see p. 2659). During early pregnancy, the steroid hormones oestrogen and progesterone control both the differentiation of uterine stromal cells into decidua (a secretory tissue) and uterine neovascularisation, two processes needed for successful embryo implantation. Oestrogen, the researchers report, stimulates the expression of the gap junction protein connexin 43 (Cx43) in mouse uterine stromal cells in vivo, and Cx43 expression, they show, is necessary for decidual differentiation, uterine neovascularisation and embryo survival. In vitro, human endometrial stromal cells do not differentiate into decidual cells or secrete the angiogenic factor VEGF when CX43 expression is ablated. Thus, the researchers conclude, Cx43-containing stromal gap junctions play a conserved and crucial role during implantation.



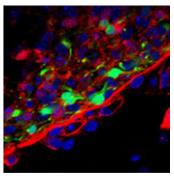
Fragile X marks synaptic defects

The fragile X syndrome (FraX) mental retardation and autism spectrum disorder is caused by loss of *FMR1* function. FMRP, the RNA-binding translation regulator encoded by *FMR1*, modulates synapse structure and function, but where and when its loss causes synaptic defects is unclear. Now, on p. 2637, Gatto and Broadie reveal FMRP's spatiotemporal roles in synaptogenesis by conditionally driving its expression in a FraX fly model. The constitutive presynaptic expression of dFMRP in these flies rescues their synaptic architectural defects but not normal neurotransmission. From these and other findings, they conclude that dFMRP has a crucial presynaptic role in regulating neuromuscular junction synaptic architecture, but acts post-synaptically in regulating neurotransmission strength. The authors also rescued synaptic structural defects in FraX flies by expressing dFMRP in early and late larval development; the rescue of defects in later development indicates that dFMRP can mediate late-stage plasticity to reverse some synaptic impairments. Thus, although FraX is primarily a developmental disease, late-stage therapeutic intervention might prove to be beneficial.



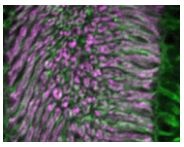
Nodal pro-domain sends the right signals

Nodal proteins are TGFβ-related, secreted signalling proteins that play essential roles in vertebrate embryonic development. In zebrafish, the Nodal-related factors Cyclops (Cyc) and Squint (Sqt) have overlapping functions during mesoderm induction and behave as short- and long-range morphogens, respectively. But what determines their different signalling activities? On p. 2649, Tian and co-workers report that the pro-domain of Cyc (like other TGFβ-related proteins, Cyc contains a pro-domain and a mature domain) regulates its activity. Unlike other Nodal proteins, Cyc requires its pro-domain for its activity. They identify several pro-domain regions that regulate Cyc signalling activity, including a lysosome-targeting region that, by destabilising the Cyc precursor, restricts the distance over which Cyc acts. Finally, they report that a mutation in a conserved arginine in the Cyc pro-domain increases Cyc activity. This last observation hints at a possible aetiology for human congenital heterotaxia, a defect in left-right asymmetry caused by an identical mutation in human NODAL.



bHLH genes seal neural and non-neural fates

In mammalian brains, the choroid plexus secretes cerebrospinal fluid and functions as a blood-brain barrier. Now, on p. 2531, Imayoshi and colleagues reveal that the Hes genes and neurogenin regulate the specification of this uniquely non-neural brain tissue in mouse embryos. The researchers show that the prospective choroid plexus region in the dorsal telencephalic midline of the developing brain expresses the proneural basic helix-loop-helix (bHLH) gene neurogenin 2 (*Ngn2*) and the bHLH repressor genes *Hes1* and *Hes5*. This region, they report, gives rise to choroid plexus epithelial cells and to Cajal-Retzius cells, specialised neurons that guide neuronal migration. Inactivation of *Hes1* in the dorsal telencephalon of *Hes3*/*Hes5*-null mice upregulates *Ngn2* expression and leads to increased formation of Cajal-Retzius cells and to a complete loss of choroid plexus epithelial cells; *Ngn2* overexpression has similar effects. Thus, the researchers conclude, Hes and *Ngn2* genes antagonistically regulate non-neural versus neural fate specification in the developing mouse brain, a new role for mammalian bHLH genes.



Fly view of ROS and neurodegenerative disease

Mitochondrial dysfunction occurs in many late-onset neurodegenerative disorders (including Alzheimer's disease) and in developmental neurodegenerative disorders, such as Leigh syndrome, which is caused by mutations in the electron transport chain (ETC). But how does mitochondrial dysfunction cause neurodegeneration? Mast and co-workers perturbed the ETC in the *Drosophila* retina and now report that reactive oxygen species (ROS) overproduction in the photoreceptor cell body causes synaptic degeneration (see p. 2669). Mutations in the ETC component succinate dehydrogenase do not affect the early stages of photoreceptor development but cause degeneration of the photoreceptor synapses and cell bodies in late pupal and adult animals. ROS production, not energy depletion, causes this synaptic degeneration. Furthermore, ROS production in the cell body is sufficient to cause synaptic degeneration. These results establish the first animal model for Leigh syndrome and, more generally, suggest that excessive ROS production might cause some of the pathological changes seen in other neurodegenerative disorders.

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