In this issue

Six1 and ear development

Mammalian inner ear development begins with the induction of the otic placode, an ectodermal thickening on either side of the hindbrain. Placode invagination forms the otic vesicle, which differentiates into the inner ear. Many genes are involved in this developmental program but their function during inner ear morphogenesis is poorly understood. On p. 3989, Zheng et al. investigate the role of the mammalian homeobox gene Six1 in auditory system development. They report that Six1 is expressed in all the sensory epithelia of the developing ear in normal mice. By examining auditory system development in Six1−/− mice, they also show that Six1, similar to Eya1, is not required for initiation of inner ear organogenesis but rather regulates important signalling molecules (including Fgf3, Fgf10 and Bmp4) that are involved in the specification of the inner ear sensory organs.

Combinatorial specification of motoneurons

Somatic and ventral motoneurons (sMNs and vMNs, respectively) are both required for the central control of vertebrate body movement and homeostasis. But although much is known about how the differentiation of sMNs is controlled, less is known about vMN specification in the developing hindbrain. On p. 4149, Pattyn and his colleagues describe how the Nkx6 and Nkx2 classes of homeodomain proteins have complementary roles in vMN specification in mice and chicks. While Nkx2.2 is sufficient to induce vMNs, Nkx6 proteins are not needed for vMN generation but instead prevent these cells from differentiating into interneurons and direct later aspects of their differentiation. The authors also show that Nkx6 proteins and the motoneuron determinant Olig2 act in parallel in sMN differentiation, a result that leads them to conclude that sMN and vMN cell fate specification requires a combination of transcription factors rather than a single master regulator.

A lucky break: bone development reactivated

Bone repair after injury seems to closely resemble embryonic bone development: for example, both processes involve progenitor cell recruitment, vascular network establishment and the differentiation of precursor cells into bone or cartilage. But just how similar are the two processes? To find out, Colnot et al. (see p. 4123) examined fracture repair in the absence of matrix metalloprotease 9 (MMP9), a key regulator of bone development. They report that the skeletal defects that occur during bone repair in adult Mmp9−/− mice are very similar to those that occur during bone development in these mutants and that, as in development, MMP9 mediates the vascularisation of hypertrophic cartilage. These parallels between endochondral bone formation during development and fracture repair strongly indicate that the embryonic bone differentiation program is reactivated during adult fracture repair.

Apoptosis in C. elegans: the molecular details

During C. elegans neurogenesis, the NSM cells differentiate into serotonergic neurons while their sister cells undergo programmed cell death (PCD). On p. 4057, Thellmann et al. show that transcriptionsal regulation of the most upstream gene in the C. elegans central cell-death pathway—the cell-death activator gene egl-1—is involved in this PCD event. They also define a regulatory element that is required for egl-1 expression. Their findings show that the SNAIL-like protein, CES-1, which blocks NSM sister cell death, and a heterodimer of the helix-loop-helix proteins, HLH-2 and HLH-3, which is required for NSM sister PCD, both bind to this regulatory element. The authors propose that HLH-2/HLH-3 is a cell-type specific activator of egl-1 transcription and suggest that CES-1 and HLH-2/HLH-3 determine NSM sister cell fate by competing to bind to the egl-1 locus.

Screening for new AP axis determinants

In Drosophila, the establishment of the anteroposterior (AP) axis occurs during oogenesis and is determined by the localisation of bicoid and oskar mRNA to the anterior and posterior of the oocyte, respectively, via microtubule cytoskeleton polarisation. To uncover additional genes involved in this process, Martin et al. performed an elegant genetic screen that, unlike previous genetic screens of AP axis determination, permits the recovery of lethal mutations (see p. 4201). By identifying, in living oocytes, chemical-induced mutations that disrupt the localisation of GFP-Staufen in germline clones (because Staufen binds to both bicoid and oskar mRNA, GFP-Staufen is a marker for both poles of the oocyte at different developmental times), Martin et al. discovered 23 new complementation groups on chromosome 3R that disrupt AP axis formation. As a forerunner of what their results could eventually reveal about AP axis formation, the authors’ characterisation of several mutations reported here indicate their involvement in microtubule organisation.

In Journal of Cell Science

Superoxide: the route to multicellularity?

Reactive oxygen species (ROS), such as superoxide ions, are an important signalling mechanism in mammals and plants. Yeast and bacteria respond to ROS produced during oxidative stress but do not actively produce them as messengers. So when did ROS generation become a signalling mechanism and why? Bloomfield and Pears suggest this occurred with multicellularity. They show that Dictostelium, which can be uni- or multicellular, can generate superoxide in response to a secreted factor produced early in development during the transition to multicellularity that occurs with food scarcity. They report that superoxide scavengers can block Dictostelium aggregation during this transition and reduce the expression of genes important for early development. They conclude therefore that a superoxide-dependent signal is critical for the initiation of Dictostelium development and that this mechanism might have arisen to provide the signalling diversity that multicellularity demands.