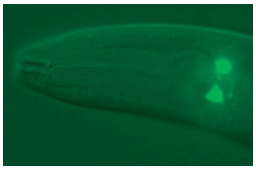
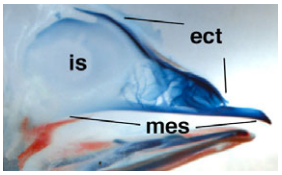


Worming into steroid and insulin signal intersection

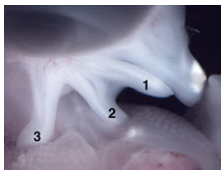
In *C. elegans* larvae, steroid hormone signalling functions with insulin/IGF-1-like signalling to promote reproductive development and to prevent dauer arrest – in hostile conditions, larvae enter the dormant diapausal dauer stage instead of becoming adults. Now, Patel and colleagues have discovered a key enzyme in the biosynthetic pathway used by *C. elegans* to make steroid hormones – HSD-1, which is orthologous to vertebrate 3β-hydroxysteroid dehydrogenases (3β-HSDs; see p. 2239). They found HSD-1 by screening for mutations that enhance the dauer phenotype of *ncr-1* mutants; NCR-1 and NCR-2 are intracellular cholesterol transporters that prevent dauer arrest. *hsd-1*; *ncr-1* double mutants, they report, fail to inhibit dauer arrest; feeding these worms with certain steroid hormone precursors rescues this defect. They also show that reduction of the HSD-1-mediated steroid signal alters the subcellular localization of the DAF-16/FOXO transcription factor, a component of the insulin signalling pathway. This important result reveals a novel way in which steroid hormone and insulin/IGF-1-like signalling can intersect to direct development.

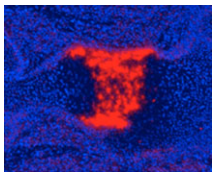
Shh noses into craniofacial development… …and creates a ZPA in the jaw

Noses come in many shapes and sizes, and some human conditions are marked by characteristic nasal malformations. Facial morphogenesis depends on inductive interactions between cephalic neural crest cells (NCCs, which give rise to the nasal capsule and other head structures) and cephalic epithelia, but which molecules provide the instructive signals? Benouaiche and co-workers now report that sonic hedgehog (Shh) signalling from the foregut endoderm patterns the avian nasal capsule (see p. 2221). The surgical removal in ovo of the most rostral zone of the endoderm (EZ-I), they report, prevents the formation of mesethmoid cartilage (a ventral part of the nasal capsule that forms the upper beak), but this defect can be rescued by the implantation of Shh-loaded beads. Correspondingly, when the authors grafted an extra EZ-I into developing embryos, an ectopic mesethmoid formed, the development of which they inhibited by suppressing Shh signalling. These results support the notion that early endodermal regionalization drives normal facial morphogenesis and suggest that its disruption might result in craniofacial defects.



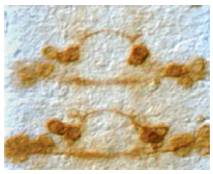
Another head structure that cephalic NCCs give rise to is the lower jaw, which forms when these cells migrate into the first branchial arch (BA1) of avian and mammalian embryos. Shh expression in the ventral foregut endoderm is crucial for the survival and development of these NCCs. Now, on p. 2311, Nicole Le Douarin and colleagues unexpectedly report that the transplantation of Shh-expressing quail cells into the presumptive territory of BA1 before NCCs migrate into this region induces mirror-image supernumerary jaws to form in the mandibular mesenchyme (the embryonic tissue that gives rise to the lower jaw). They show that the development of these extra jaws is preceded by the expression of *Fgf8*, *Bmp4* and *Shh* in the caudal BA1 ectoderm in a spatial pattern similar to that normally seen in the oral epithelium. The activation of these genes leads to the formation of two extra lower-jaw-organizing centres with opposite rostrocaudal polarities. Thus, the researchers suggest, Shh-producing cells create a zone of polarizing activity (ZPA) in mandibular buds just as they do in developing limb buds.





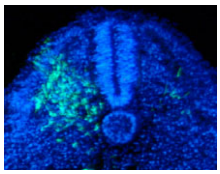
Out of joint with JAWS

Synovial joints provide skeletons with flexibility but what controls where these fluid-filled structures form during bone development? On p. 2215, Sohaskey and colleagues report that the novel protein JAWS (joints abnormal with splitting) coordinates cartilage formation and synovial joint positioning in mice. *Jaws*$^{-/-}$ mice, they report, have many skeletal defects (including stunted limbs and short, round faces) that indicate that the development of the endochondral skeleton (the part of the skeleton in which a cartilage template directs bone formation) requires JAWS. Most strikingly, they note, *Jaws*$^{-/-}$ mice have ectopic joints within their digits. Furthermore, JAWS deficiency delays chondrocyte maturation and impairs the metabolism of chondroitin sulphate and the proteoglycan aggrecan, two components of cartilage. Thus, the researchers suggest, JAWS limits joint formation to specific locations in the embryonic skeleton by acting as a key regulator of chondrogenesis and synovial joint positioning. Future studies of *Jaws*$^{-/-}$ mice might, therefore, provide insights into what causes joint degeneration in osteoarthritis and other debilitating joint conditions.



Wnt signal transduction via Src kinases in developing CNS

During nervous system development, axons are guided by many attractive and repulsive cues. For example, members of the RYK/Derailed family of inactive receptor tyrosine kinases guide axons in the *Drosophila* ventral nerve cord and in the mammalian brain by acting as Wnt receptors. On p. 2277, Wouda et al. reveal how these kinase-inactive RYKs might transduce Wnt signals by reporting that WNT5-mediated signalling through Derailed in the *Drosophila* embryonic CNS involves the non-receptor Src family tyrosine kinases SRC64B and SRC42A. *Src64B*/*Src42A* double mutants, they show, have defects in the formation of the nerve fibre tracts that connect the two sides of the brain (commissures) similar to those seen in *Wnt5* and *derailed* mutants. Derailed and SRC64B, they report, form a complex, the formation and/or stability of which requires SRC64B activity. Furthermore, the mammalian orthologues of these proteins also form complexes together. Thus, Src family kinases might play novel roles in Wnt5/Derailed signalling during CNS development in flies and in mammals.



A tail of axial progenitors

The vertebrate tail bud is thought to contain multipotent progenitor cell populations that generate the embryo's axial structures (the neural tube, notochord and paraxial mesoderm). Now, by grafting tissue from a new transgenic chick line in which all embryonic cells express GFP into unlabelled embryos, McGrew and colleagues identify three progenitor cell populations in the avian tail bud (see p. 2289). Cells from the embryonic chordoneural hinge, they report, contribute descendants to all of these axial structures, whereas cells from the dorsoposterior tail bud yield mesodermal tissue only. Both these populations are likely to be 'long-term axial progenitors' because they are retained in the tail bud after serial transplantation. By contrast, a ventral tail bud cell population, which also generates paraxial mesoderm, is not retained after serial transplantation. Finally, by showing that transplantation of tail bud progenitor cells into earlier embryos resets their Hox expression (which determines the anteroposterior identity of axial cells), the researchers challenge the idea that Hox identity is fixed during gastrulation.

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