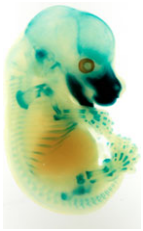
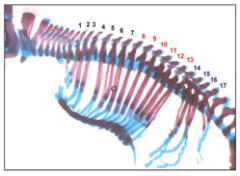


About face

Ellis-van Creveld (EvC) syndrome causes severe skeletal and craniofacial abnormalities, and Victor Ruiz-Perez, Judith Goodship and colleagues previously cloned two genes – *EVC* and *EVC2* – that underlie this disorder. Now, on p. 2903, the researchers confirm that Evc ablation in mice results in an EvC-like phenotype and they use this mouse model to determine the molecular and developmental roles of Evc. They show that Evc is expressed in developing bones and in the orofacial region (the mouth and face). Within chondrocytes, the protein is localised to the primary cilium – an organelle that is central to hedgehog (Hh) signalling – which piqued the researchers' interest in Evc's relationship with Indian hedgehog (Ihh), a 'master regulator' of bone development. Ihh itself is unaffected in $Evc^{-/-}$ mice, but downstream genes, such as *Ptch1* and *Gli1*, have reduced expression, and the researchers conclude that Evc is required for transducing the Ihh signal. Curiously, $Evc^{-/-}$ mice have normal Gli3 processing. Next, the authors are going to use their model to find out whether other cell lineages rely on Evc for Hh signal transduction.

Branching through semaphorin

Branching morphogenesis is a complex developmental process that has been studied thoroughly in the kidney, lung and mammary gland. But Pei-Hsin Huang and colleagues have been investigating branching morphogenesis in the mouse submandibular gland (SMG) – the salivary gland under the floor of the mouth – and on p. 2935, report the role of semaphorin signalling during the first step of SMG branching morphogenesis: the process of cleft formation. Semaphorin, together with its receptors neuropilin (Npn) and plexin (Plxn), is well known for its role in the nervous system and is involved in branching morphogenesis in other tissues. By downregulating or overexpressing combinations of these molecules in ex vivo SMG culture, the researchers show that the semaphorins Sema3A and Sema3C, the neuropilin Npn1 and the plexins PlxnA2 and PlxnD1, are specifically required for cleft formation. But the researchers were surprised to find that Sema3A and Sema3C function additively, with Npn1 mediating signals from both semaphorins, which contrasts with their antagonistic interactions in the lung and nervous system. The authors conclude that while semaphorin signalling has roles in branching morphogenesis in different tissues, it functions very differently in different contexts.



Cracking the rib cage code

Patterning of the rib cage is complex, not least because it derives from two different tissues – the somitic mesoderm (which forms the vertebrae and ribs) and the lateral plate mesoderm (which forms the sternum). On p. 2981, Deneen Wellik and colleagues shed light on the 'Hox code' that orchestrates development of the thoracic skeleton. They made mutant mice lacking whole groups of paralogous Hox genes – *Hox5*, *Hox6* and *Hox9* – which had dramatic effects on rib cage morphology. Surprisingly, the phenotypes do not fit with the simplest version of the model of 'posterior prevalence', in which posterior groups of Hox genes are functionally dominant over the next-most anterior group. Consistent with Hox genes in other tissues, the phenotypes in the somite-derived skeleton do have consistent colinearity – the genomic distribution of the genes is reflected in their spatial and temporal expression and function during development. However, no such colinearity is seen in the sternum. The authors conclude that Hox patterning of the thoracic skeleton occurs through different mechanisms depending on the mesodermal tissue from which it derives.

METs orchestrate cell fate

Just as chromatin structure influences gene expression, molecules that orchestrate chromatin remodeling can influence cell fate by regulating the transcription of cell-fate specification genes. On p. 2991, Erik Andersen and H. Robert Horvitz investigate the roles of histone methyltransferases (HMTs) in cell-fate specification in *Caenorhabditis elegans* vulval development. They used RNAi or deletion alleles to systematically probe the phenotypes of all 38 SET-domain-containing HMTs in *C. elegans*. They found that double mutants in the genes *met-1* and *met-2* cause ectopic vulva induction, and show that the two HMTs act redundantly to repress the transcription of the EGF gene *lin-3*, which induces vulval development. This makes *met-1* and *met-2* so-called synMuv genes, which negatively regulate vulval development. But how do they work? The authors show that MET-1 and MET-2 are homologous to HMTs that methylate histones at H3K36 and H3K9, respectively, and both proteins are required for normal histone trimethylation. They propose a model for the way that these HMTs act with other chromatin-remodeling factors to repress transcription and to inhibit vulval cell fates.

Jenny Bangham

IN *JOURNAL OF CELL SCIENCE*

Miz1 – the bald facts

The transcription factor Miz1 is expressed in hair follicles and keratinocytes. It controls cell proliferation and is involved in the regulation of gene expression by TGFβ. Now, in a paper published in *Journal of Cell Science*, Hans-Peter Elsässer and colleagues reveal its important role in hair morphogenesis and follicle structure. The researchers created conditional mutants lacking Miz1 expression in keratinocytes. These mice have rough fur owing to an alteration in the orientation and structure of hair follicles. They also have a pronounced delay in the onset and progression of catagen (the regression phase of hair development), something also seen in mice lacking TGFβ. Furthermore, the epithelium in these mice is thicker at the top of the hair follicles (where the hair follicle epithelium becomes the interfollicular epithelium), owing to increased keratinocyte proliferation. This prompted the authors to investigate the roles of Miz1 in TGFβ-mediated gene regulation. They observe reduced expression of several TGFβ targets in cultured Miz1-deficient keratinocytes, and discuss the roles of Miz1 and TGFβ in controlling proliferation and differentiation during hair morphogenesis and generation of follicle structure.

Gebhardt, A., Kosan, C., Herkert, B., Möröy, T., Lutz, W., Eilers, M. and Elsässer, H.-P. (2007). Miz1 is required for hair follicle structure and hair morphogenesis. *J. Cell. Science* **120**, 2586-2593.