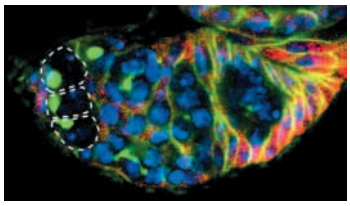
In this issue

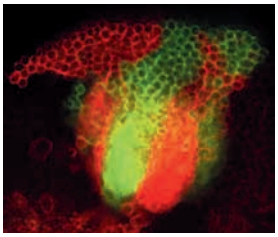
Clonal expansion in stem cell niches

Stem cell-associated stromal cells create a signalling microenvironment – a niche – that sustains the self-renewing and asymmetric properties of stem cell divisions. The *Drosophila* ovary is an ideal system for investigating how these niches form and recruit stem cells. In their careful study on p. 2579, Zhu and Xie have analysed the occupation of the ovarian niche in flies by primordial germ cells (PGCs). They report that, as niche formation begins, one population of PGCs directly differentiates, while an anterior population, which lies adjacent to the cells that create the niche, develop into germline stem cells. These anterior PGCs exhibit distinctive division patterns and require *dpp* signalling to maintain normal proliferation. Importantly, lineage-tracing analyses revealed that a single PGC can occupy a whole niche through clonal expansion. Such findings offer valuable insights into how other niches might form.



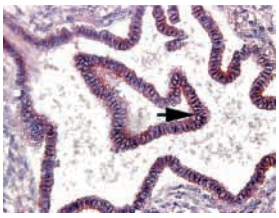
Dendrite elaboration in mushroom bodies

Mushroom bodies (MBs) are bilaterally symmetrical, fly brain structures required for olfactory learning and memory. Each one is derived from four neuroblasts and consists of ~2000 Kenyon cells (KCs) that project dendrites into the calyx where olfactory inputs are received and processed. Zhu et al. have used a clonal system to visualize neurons in whole-mount brain preparations to address key questions about the organization of these dendrites, such as: do KC dendrites of different clonal origin occupy the same or different territories in the larval and adult calyx? Their results on p. 2603 shed light on these important questions. For example, they find that MB dendrites of different clonal origins, although well mixed in larval brains, become restricted to distinct calycal spaces in adults, and that various subtypes of MB dendrites contribute differentially to calycal regions.



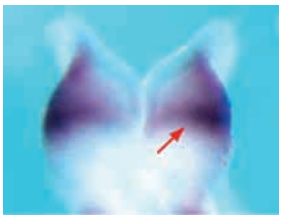
Branching morphogenesis and renal dysplasia

The mammalian kidney develops by a process called branching morphogenesis, which is driven by reciprocal inductive interactions between the metanephric blastema and ureteric bud (UB) embryonic tissue. To further investigate the inhibitory role of the BMP2 receptor ALK3 in kidney branching morphogenesis, Hu et al. generated mice expressing a constitutively active form of ALK3 in the UB (see p. 2753). As expected, mutant kidneys undergo less branching, but this surprisingly leads to medullary cystic dysplasia rather than to kidney hypoplasia. The transition from decreased branching to cystic dysplasia is accompanied by the increased expression of β-catenin and TCF, and by the formation of β-catenin/SMAD1 (an ALK3 effector) complexes. As such, ALK3 signalling appears to upregulate β-catenin expression via an unknown mechanism during this pathogenic event, providing new directions for studies of human renal dysplasia.



FGF8 function: patterning or cell survival?

The isthmic organizer (IsO) is a signalling centre that lies between, and patterns, the mesencephalon (mes) and rostral metencephalon (met) regions of the neural tube, which give rise to the midbrain and cerebellum, respectively. FGF8 and WNT1 are key components of the signalling activity of this centre, although their exact functions here remains unclear. To further investigate the role of FGF8 in the IsO, Gail Martin and colleagues conditionally inactivated *Fgf8* in the midbrain/hindbrain region of mice. The progressive loss of FGF8 here resulted in a dose-dependent loss of tissue; by E17.5, the entire midbrain, isthmus and cerebellum were absent in mutant embryos (see p. 2633), owing to ectopic cell death in the progenitors of these structures. FGF8 is also required to maintain gene expression in this region, including that of *Wnt1* and *Gbx2*. These findings highlight an essential role for FGF8 in regulating gene expression and cell survival in this region. Whether it also directly functions in the patterning of these tissues, as previously believed, remains to be resolved.



Tbx4 and Tbx5: dual roles in limb development revealed

Three papers in this issue together show, for the first time, that the T-box transcription factors Tbx4 and Tbx5 have critically important roles in specifying limb identity and in maintaining limb outgrowth through their regulation of genes that are essential for limb development. Toshihiko Ogura and colleagues misexpressed dominant-negative forms of these genes in the prospective limb fields of chick embryos (see p. 2729). This misexpression produced limbless phenotypes, and the repression of the *Wnt2b*, *Wnt8c*, *Fgf8* and *Fgf10* genes. By contrast, when *Tbx5* and *Tbx4* were misexpressed in chick embryo flanks, additional wing- (in response to *Tbx5*) and leg-like (in response to *Tbx4*) structures were induced, accompanied by the upregulation of Wnts and Fgfs. Thus, each Tbx gene confers a specific limb identity – *Txb5* the forelimb/wing and *Tbx4* the hindlimb – and initiates limb development by activating a Wnt/Fgf signalling cascade, as also indicated in the accompanying papers. When Logan and colleagues conditionally inactivated *Tbx5* in the developing mouse forelimb (see p. 2741), the forelimb bud completely failed to grow and *Fgf10* expression was lost from the prospective forelimb bud mesenchyme, resulting in extensive apoptosis. This team also misexpressed dominant-negative and dominant-activated forms of Tbx5 in the chick wing to reveal that Tbx5 is also required at later stages of limb bud development for continued limb outgrowth. By contrast, when Papaioannou and colleagues inactivated *Tbx4* in mice (see p. 2681), the initial patterning of hindlimb buds occurred normally but hindlimb development subsequently failed, in vitro and in vivo. Together these findings shed new light on a conserved genetic network that controls vertebrate limb development, and on the position and function of these Tbx genes in this network.