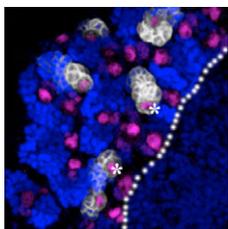
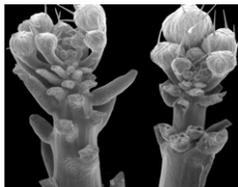


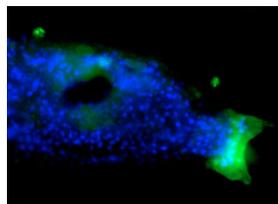
### Phyllotactic patterning: microRNAs made redundant?

Plant microRNAs regulate gene expression in a sequence-specific manner by binding to target mRNAs, leading to their degradation. Unlike animal microRNAs, plant microRNAs have a high degree of complementarity to their targets, and the scarcity of microRNA loss-of-function phenotypes in plants implies that redundancy exists between microRNA family members. Now, two papers provide new insights into this redundancy and into microRNA-regulated shoot development in *Arabidopsis*. Elliot Meyerowitz and colleagues show how the activity of redundant *miR164* family members is crucial for the spatial positioning of flowers on the *Arabidopsis* stem, and for the number and size of floral organs (see p. 1051). And Patrick Laufs and co-workers on p. 1045 report how the continued expression of *CUP-SHAPED COTYLEDON2* (*CUC2*), a *miR164* target, regulates correct flower positioning. In their study, Meyerowitz and colleagues report that the elimination of all three, but not of individual, *miR164* family members severely disrupts flower and shoot development in *Arabidopsis*. In the absence of the three *miR164* microRNAs, the expression domains of their transcription factor-encoding targets, *CUC1* and *CUC2*, become enlarged in the inflorescence meristems of mutant plants. This result, together with other findings reported here, indicate that the *miR164* microRNAs not only act to reduce target transcript levels but can also spatially limit target mRNA accumulation – functions, the authors propose, that hint at their possible involvement in developmental robustness. The study also reveals that the *miR164* family members are not fully redundant but show some functional diversification, raising questions as to whether microRNA gene families evolve in the same way as protein-coding gene families do through gene or genome duplication. Laufs and co-workers' complementary study shows that the *miR164*-regulated expression of *CUC2* is crucial for organ patterning in the stem rather than in the apical meristem. They report that the pattern of flower primordia is irregular in the fully grown stems of plants that express a *miR164*-resistant version of *CUC2*. These plants effectively overexpress *CUC2*, indicating that the timing and level of *CUC2* expression is crucial for patterning. Together, these results indicate that patterning is not completely determined in the apical meristem and that redundancy between microRNAs provides the platform for this unexpected level of complexity.



### A death sentence for neuroblasts

What causes *Drosophila* larval neuroblasts to self-renew with each round of cell division? Insights into this are not only of interest to neurobiologists but also to stem cell researchers. Polycomb group (PcG) genes in mammals are known to regulate stem cell fate and proliferation. Now on p. 1091 of this issue, Bello et al. show that mutations in five of the *Drosophila* PcG genes increase the expression of the posterior Hox genes *abd-A* and *Abd-B* and subsequently induce neuroblast death. This phenotype is rescued by blocking apoptosis. The segmental determination and lineage, but not cell death, of abdominal secondary neuroblasts relies on posterior Hox gene expression. Thus, PcG genes regulate neurogenesis differently in varying developmental contexts. The contributions that other known PcG target genes, such as cell cycle regulators, make in this setting remain to be determined. Individual PcG genes regulate different processes both in mammals and flies; however, the deregulation of Hox gene expression is a common feature of PcG mutants.



### Metamorphosis – the end of a tail

How a tadpole metamorphoses into an adult is a captivating process. But how does the tail disappear? Now Chambon et al., on p. 1203, identify a gene network together with a cell-cell communication protein called Ci-sushi that are required for apoptosis in the regressing tail of *Ciona* tadpoles. From a microarray expression profiling analysis of *Ciona* larvae treated with inhibitors of the MAP kinase and JNK pathways, which regulate apoptosis, these investigators uncovered a network of genes that show expression changes during metamorphosis. *Ci-sushi*, one such gene, is expressed in the tail epithelia and is downregulated by JNK inhibitors – when knocked down by a morpholino, tail cell death and regression are prevented. The authors propose that JNK activity in the CNS (which escapes cell death) causes apoptosis in adjacent cells through Ci-sushi activity. Given their basic chordate body plan, similar studies of *Ciona* larvae might shed light on the regulation of apoptosis in other vertebral column tissues, such as the neural tube.



### Mammary development: from normal to pathological

How the mammary gland develops from buds in the ventral embryonic epidermis and how subsequent ducts develop are poorly understood. Now Hens et al. (p. 1221) report on the role that parathyroid hormone-related protein (PTHrP) and its cooperation with BMP signalling plays in some of these events. By studying various individual and combined mutant and reporter mice, the authors discovered that PTHrP secreted by mammary epithelial cells present in mammary buds leads to the upregulation of BMP4 on the mesenchymal cells that surround them, making these mesenchymal cells responsive to BMP4 that is present within the ventral epidermis. The authors found that as a result of this cooperation between PTHrP and BMP signalling, *Msx2* expression is upregulated in the mammary mesenchyme, which then suppresses hair follicle formation in the epithelium immediately surrounding the nipple. In this way, paracrine BMP signalling regulates the fate choice between hair and mammary gland. The authors also propose from their findings that this cooperative PTHrP and BMP signalling enables the mesenchyme to initiate the outgrowth of the mammary epithelial buds. In a separate study focused on later ductal development (p. 1231), Moraes et al. report on the dysplastic effects that sustained smoothened (Smo)-mediated hedgehog (Hh) signalling has during ductal elongation in virgin transgenic mice. They studied this by expressing activated human SMO (SmoM2) under the control of the mouse mammary tumour virus promoter in transgenic mice. This constitutively active form of Smo induces a pre-cancerous state in the mammary ductal cells of the transgenic mice, in which the increased proliferation of mammary epithelium and differentiation defects are seen, while in vitro, an increased proportion of these cells can undergo anchor-independent growth. From these and other results, the authors put together a model in which Hh signalling must be prevented in the mature ducts of virgin mice, and possibly in the mature ducts of humans as well. Under such a model, ectopic Hh signalling could contribute to early human breast cancer development by stimulating proliferation and by increasing the pool of division-competent cells that are capable of anchorage-independent growth.

