

## CDK8 flower power

Plant organs form post-embryonically from the meristems, structures in which cell division and cell specification are closely integrated. In the floral meristem, three classes of homeotic genes interact to specify sepals, petals, stamens and carpels. On p. 3147, Wang and Chen report that *HUA ENHANCER3* (*HEN3*) acts in the pathway of *AGAMOUS*, an *Arabidopsis* homeotic gene required for stamen and carpel specification. By analysing *hen3* mutants, the researchers found that *HEN3*, which was isolated as an enhancer of the *hual hua2* double mutant phenotype, is required for cell-fate specification in floral meristems and cell expansion in leaves. They also show that *HEN3* is the homologue of mammalian cyclin-dependent protein kinase 8 (CDK8), which is known to be required for cell differentiation in yeast and *Dictyostelium*. However, this is the first demonstration that CDK8 has a developmental function in a higher eukaryote.



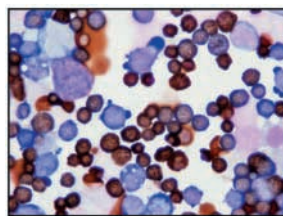
## Off with mitosis, on with endocycling

Usually, each step in the cell cycle depends on the completion of the previous stage. But some cells – for example, cardiomyocytes, *Drosophila* egg follicle cells and many cancer cells – can endocycle, where DNA synthesis continues without mitosis. On p. 3169, Shcherbata and colleagues investigate how Notch signalling controls the mitotic-to-endocytic transition in *Drosophila* follicle cells at mid-oogenesis. By identifying genes whose transcription is responsive to Notch at this transition, the researchers show that Notch activity: (1) blocks the mitotic (M) phase of the cycle by downregulating the G2/M regulator String; (2) allows G1 entry by activating *Hec/Cdh<sup>Frz</sup>*, a regulator of the APC ubiquitination complex; and (3) ensures S-phase entry by repressing Dacapo, a cyclinE/CDK complex inhibitor. As the researchers discuss, a better understanding of how external signalling pathways control physiological cell-cycle transitions could identify how abnormal cell-cycle control occurs in cancer cells.

## Signalling RED for terminal differentiation

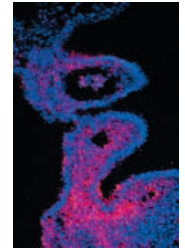
Gata1, a zinc-finger transcription factor, is essential for mammalian erythropoiesis. Erythroid cells that lack Gata1 apoptose, while Gata1 overexpression blocks differentiation. However, Gata1-overexpressing erythroid cells differentiate normally in vivo when wild-type cells are present, indicating that these cells produce a red cell differentiation signal (REDS) that rescues the defect in Gata1-overexpressing cells. On p. 3183, Gutiérrez et al. report that REDS is produced by committed erythroid cells. The researchers combine a tissue-specific Cre/*loxP* system and X inactivation to produce mice in which half the erythroid cells overexpress *Gata1* and half are *Gata1* null. These embryos are anaemic and die by E14, supporting a homotypic signalling mechanism in which mature erythroid cells produce REDS.

Importantly, these results indicate that terminal differentiation during erythropoiesis (and presumably during other differentiation programmes) is not achieved by simply turning off self-renewal signals, but also requires specific differentiation signals.



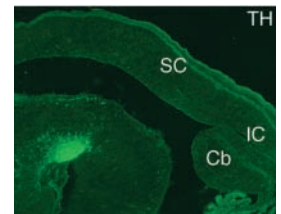
## Taking *Tbx1* to heart

Developmental defects in the cardiac outflow tract (OFT) cause many common human congenital heart diseases, including DiGeorge syndrome. *Tbx1*, a T-box transcription factor, is involved in the pathogenesis of this syndrome but a specific role for *Tbx1* in OFT morphogenesis has not been established. Now, Xu et al. show that *Tbx1* has a dual role in OFT development (see p. 3217). By studying genetically modified and conditional mouse mutants of *Tbx1*, the researchers show that correct separation of the aorta and pulmonary arteries in the OFT requires *Tbx1* function. This function also regulates OFT growth by supporting cell proliferation in the secondary heart field (SHF) – the source of cells that form the OFT. This is the first indication that a genetic defect related to human congenital heart disease directly affects SHF function and suggests that SHF malfunction may underlie other heart defects.



## Engrailed: preventing dopaminergic neuron loss

Parkinson's disease (PD) is caused by the loss of dopaminergic neurons in the substantia nigra, probably through apoptosis. Albéri and co-workers now report that the engrailed (*En*) genes are required to prevent apoptosis of newly-born mesencephalic dopaminergic neurons (see p. 3229). The homeobox transcription factors *En1* and *En2* are expressed in these neurons from early development to adulthood. In *En1/En2*-null mice, in which large areas of the brain are lost, mesencephalic dopaminergic neurons are generated and become postmitotic but are then lost by birth. The researchers show that this loss occurs by E14 through apoptosis. In vitro cell-mixing and RNAi experiments indicate that apoptosis induction occurs within 24 hours of *En* downregulation because of a cell-autonomous requirement for *En*. The researchers speculate that small changes in *En* expression could underlie the slow degeneration of dopaminergic neurons seen in PD.



## In *Journal of Cell Science*

### Pluripotent progenitors with potential

Cell transplantation has immense potential for treating inherited and degenerative diseases, but maintaining and directing the differentiation of stem-cell-like donor populations in culture has proven difficult. D'Ippolito et al. now report a human bone-marrow-derived cell type that might fit the bill: marrow-isolated adult multilineage inducible (MIAMI) cells. By culturing unfractionated bone marrow using conditions that mimic the stem cell microenvironment, they have derived cells that express mesodermal, endodermal and ectodermal markers, and those markers characteristic of embryonic stem cells, such as Oct4. These MIAMI cells have a greater potential for multilineage differentiation than do cells previously isolated from bone marrow, and continue to proliferate beyond 50 doublings, without signs of senescence. They thus represent a promising tool for cell transplantation to repair damaged, aged or diseased tissue.

D'Ippolito, G. et al. (2004). Marrow-isolated adult multilineage inducible (MIAMI) cells, a unique population of postnatal young and old human cells with extensive expansion and differentiation potential. *J. Cell Sci.* **117**, 2971–2981.