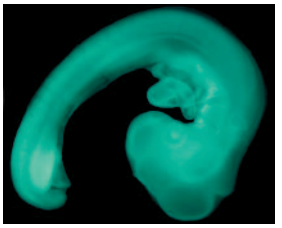
In this issue

By Jane Bradbury

Myc maintains ES cell pluripotency

The LIF (leukaemia inhibitory factor)/STAT3 signalling pathway is crucial for the self-renewal of mouse embryonic stem (ES) cells, but the downstream effectors of this pathway are not known. Now, Cartwright and co-workers show that LIF/STAT3 controls mouse ES cell self-renewal and pluripotency through the transcription factor Myc (see p. 885). The researchers report that *Myc* is a target gene for STAT3 – a transcription factor activated by LIF signalling – in these cells. They show that *Myc* mRNA levels in ES cells fall rapidly following LIF withdrawal and that the Myc protein becomes phosphorylated on threonine 58, making it a target for degradation by GSK3β. Based on their results, the researchers propose that LIF and STAT3 control ES cell self-renewal and pluripotency by regulating Myc activity, thus identifying Myc as a key regulator of mouse ES cell self-renewal.

Transgenic chickens get the green light



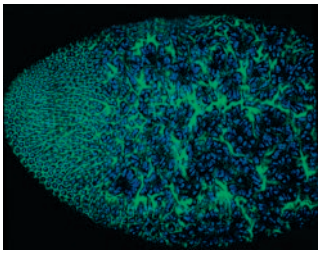
Hens that lay transgenic eggs could both greatly facilitate the study of embryonic development and provide bioreactors for the pharmaceutical industry; however, generating them has proved technically difficult. Chapman and colleagues have now cracked this challenge to produce homozygous roosters and hens that ubiquitously express enhanced green fluorescent proteins (eGFP; see p. 935). By injecting a replication-defective lentiviral vector expressing eGFP under the control of the phosphoglycerol kinase promoter into fertilised eggs, the researchers managed to create a rooster that carried the transgene in his germline. From this starting point, the authors then bred homozygous individuals that expressed eGFP uniformly throughout their tissues, which could be detected by in situ hybridization and immunocytochemistry. This paper thus shows that ubiquitous transgene expression is achievable in chickens and opens the way to deriving other transgenic chickens for use in developmental studies.

Arterial differentiation: the nerve connection

Tissue vascularisation is a highly coordinated process requiring angiogenesis, arteriovenous differentiation and the patterning of the vascular network, but the signals responsible for its control, which come from neighbouring tissues, are largely unknown. On p. 941, Mukouyama and co-workers provide the first in vivo evidence that VEGF (vascular endothelial growth factor) from the peripheral nervous system is necessary for arteriogenesis. By using transgenic mice in which *Vegfa* is conditionally deleted in sensory neurons, motoneurons and/or Schwann cells, the researchers show that nerve-derived VEGFA is required for arterial differentiation in the skin of embryonic mouse limbs. Endothelial expression of neuropilin 1 (NRP1) – a VEGF-induced artery-specific VEGF co-receptor – is also required, suggesting that a NRP1-mediated positive feedback loop may promote arteriogenesis. Surprisingly, nerve-vessel alignment is normal in these mutants, indicating that this alignment, which subsequently patterns the vasculature, must be mediated by residual levels of VEGFA or by another nerve-derived signal.

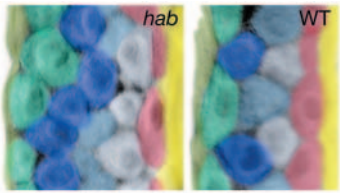
Ploughing a straight furrow

Precise changes in plasma membrane shape underlie many morphogenetic processes. During the cellularisation of *Drosophila* embryos, furrow canal formation – a specialised process of membrane invagination – and actin cytoskeleton reorganisation enclose the nuclei of the syncytial blastoderm into cells. On p. 1009, Großhans and colleagues report that the guanyl-nucleotide exchange factor RhoGEF2 and the formin Diaphanous (Dia) play a crucial role in regulating the position, shape and stability of the furrow canal by controlling actin filament assembly. They show that *RhoGEF2* or *dia* mutant embryos have enlarged furrows – both proteins normally localise to the invagination site before furrow formation – and that F-actin levels at the furrow canal are reduced in these mutants. As *RhoGEF2* and *dia* appear to act in a parallel genetic pathway to *nullo* and *sry-α*, early furrow canal markers that are involved in junction formation, these two pathways might control complementary aspects of furrow canal formation.



E-cadherin: expanding the fish embryo

The first morphogenetic movement of teleost embryos is epiboly, when the embryonic cell mass spreads over the yolk. Kane and co-workers now provide new insights into this process in their analysis of zebrafish mutants with arrested epiboly (p. 1105). These mutants were found to have different versions of the *half baked* (*hab*) locus, which the authors report here encodes the zebrafish homolog of E-cadherin. They identify two cell layers in the epiblast, the outer of which expresses *hab* mRNA at higher levels, and show that during normal epiboly, inner layer cells radially intercalate into the outer cell layer and flatten, thus expanding the area of the epiblast. In *hab* mutants, the interior cells intercalate normally but fail to flatten and sometimes return to the inner layer. The researchers conclude that E-cadherin is required for the cell movements of epiboly and possibly for similar movements in mammalian embryos.



Oncogene effects and developmental state

A woman's susceptibility to breast cancer is influenced by the timing of normal developmental events, such as her first full-term pregnancy, suggesting that the effects of oncogene activation might be modulated by the developmental state of the breast. On p. 1147, Blakely and colleagues provide in vivo molecular evidence for this hypothesis by showing a developmental stage-specific effect of aberrant MYC activation in the mouse mammary gland. The researchers use a doxycycline-inducible transgenic mouse model to show that MYC overexpression during a specific 72-hour window in mid-pregnancy inhibits post-partum lactation. Unexpectedly, MYC overexpression does this by inducing precocious lactation via Stat5 activation; the absence of a suckling stimulus then causes the gland to involute prematurely to a non-lactating state. The researchers conclude that the oncogenic effects of MYC may similarly depend on the developmental stage of the mammary gland when the oncogene is activated.