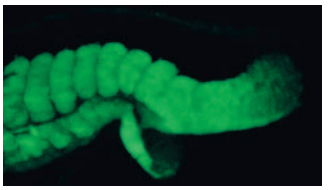
In this issue

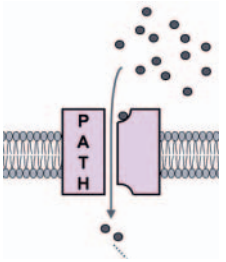
A late tail of Bmp signalling

The Bmp signalling pathway is required for proper tissue patterning and formation during embryogenesis, but because it is essential for early development, it has been very difficult to investigate its specific functions at later stages. To circumvent this problem, Pyati et al. (see p. 2333) generated transgenic zebrafish containing an inducible dominant-negative Bmp receptor with which they inactivated Bmp signalling at selected time points in development. Their results show that during early gastrulation, Bmp signalling is important for tail organizer formation and for patterning the ventral mesoderm. However, from mid-gastrulation to early somitogenesis, the role of Bmp signalling changes – at these stages, Bmp signalling promotes ventral fin formation and, unexpectedly, prevents additional tails from forming. These findings thus reveal a specific late requirement for Bmp signalling during tail patterning, and highlight the dynamic temporal roles that this pathway plays during development.



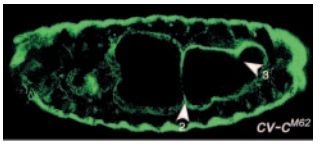
Transporting food into growth

Cell and tissue growth can be altered during development by an embryo's nutritional status. Varying nutrient levels cause changes in intracellular amino acid levels and trigger signalling from the insulin receptor (InR) pathway, resulting in the subsequent modulation of intracellular TOR kinase activity. On p. 2365, Goberdhan et al. report two new *Drosophila* proton-assisted amino acid transporters (PATs), CG3424 (also called PATH) and CG1139, that modulate tissue growth in many non-endocrine tissues. These PATs genetically interact with TOR and with other InR signalling components. CG3424, which is widely expressed, also activates a TOR target in an amino acid-dependent manner when expressed in a *Xenopus* oocyte system. Surprisingly, it has a very low capacity for transporting amino acids, but a high affinity compared with CG1139 and other mammalian PATs, suggesting that growth control via this process is conserved but does not require bulk amino acid transport into a cell.



Actin reorganisation during morphogenesis

The Rho family of small GTPases function in many morphogenetic processes that shape an embryo. Their activity is partly modulated by RhoGAP proteins, which switch RhoGTPases to an inactive state. By searching for genes that regulate *Drosophila* embryo morphogenesis, Denholm et al. have discovered that the *crossveinless-c* (*cv-c*) gene encodes a RhoGAP that is expressed in, and is required by, multiple embryonic tissues undergoing morphogenesis, such as the Malpighian tubules (MpTs) and the epidermis during dorsal closure (see p. 2389). Genetic interactions between *cv-c* and RhoGTPase mutants indicate that the small GTPases, Rho1, Rac1 and Rac2, are Cv-c substrates. The authors' loss- and gain-of-function studies reveal that Cv-c regulates actin cytoskeleton dynamics during MpT convergent extension movements. From these and other data, they conclude that Cv-c functions to organise the actin cytoskeleton in tissues undergoing morphgenesis by regulating the activity of specific RhoGTPases.



Tbx20: orchestrating heart development

Although ~1% of humans are born with structural heart malformations, we know relatively little about the transcriptional programs that underpin the complex, orchestrated process of heart development. Now three papers in *Development* report that the T-box transcription factor Tbx20 occupies a central position in the pathways that control heart lineage specification and morphogenesis, from where it acts dose-dependently to influence embryonic heart development and adult heart function. Richard Harvey's (see p. 2451) and Sylvia Evans' (see p. 2475) groups both used gene targeting in mice to investigate *Tbx20*'s role in cardiogenesis. Both report that *Tbx20* null mice die in mid-gestation with severely malformed, underdeveloped hearts in which heart chamber formation had failed. Underlying these defects is a perturbed transcriptional program that alters cell proliferation patterns, the expansion of cardiac progenitors and the acquisition of tissue identity. In particular, both teams found that Tbx2 – a transcriptional repressor that inhibits chamber-specific gene expression programs in non-chamber heart tissue – is inappropriately activated throughout the heart in *Tbx20* null mice. These and other data lead Harvey and co-workers to propose that hierarchical, repressive interactions between Tbx20 and other T-box factors underlie the early lineage split between chamber and non-chamber myocardium on which subsequent heart morphogenesis depends. These conclusions are strengthened by the findings of Evans' team, who show that Tbx2 is a direct target of Tbx20. Moreover, they report that Tbx2 directly binds to Nmyc1, which it represses in vitro and which is required for early myocardial proliferation. Nmyc1 expression is also downregulated in *Tbx20*$^{-/-}$ mice. From their findings, these authors conclude that Tbx20 regulates cell proliferation in a region-specific manner by repressing Tbx2, which in turn represses *Nmyc1*. Thus, these two studies reveal how Tbx20 co-ordinates the transcriptional programs that control heart tissue specification and growth. Harvey and co-workers' further finding that heart function is compromised in adult *Tbx20*$^{+/-}$ mice adds additional complexity to this picture. The dose-dependent effects of Tbx20 are elegantly expanded upon by Benoit Bruneau and co-workers (see p. 2463). This group knocked down *Tbx20* in ES cells using RNAi, and then generated mouse embryos from cell lines in which *Tbx20* was expressed highly, moderately or not at all. Their findings show that Tbx20 acts in a dose-dependent manner during heart and motoneuron development – the complete knockdown of *Tbx20*, for example, mirrors the null mutant, while a mild knockdown causes right ventricle underdevelopment and persistent truncus arteriosus, defects associated with human heart congenital conditions. The breakdown of cardiac transcription factor networks also features in this study. Specifically, this team found that Tbx20 might act synergistically with the cardiac transcription factors Isl1 and Gata4 to activate *Mef2c* and *Nkx2.5* expression – genes that are required for anterior heart field formation, a region that gives rise to the heart's outflow tract and ventricles. Together, these papers shed new light on how tissue specification, morphogenesis and proliferation are co-ordinated in early heart development by Tbx20, and provide new candidates for the study of both congenital heart defects and adult cardiomyopathies.