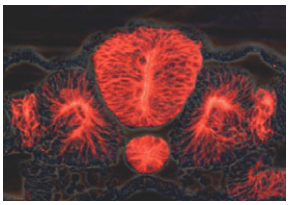
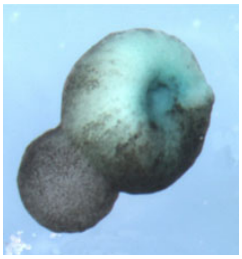
What a cell *Wnts* to regenerate

The functions of Wnt/β-catenin signalling during embryogenesis have been well documented, but much less is known about its role in the adult. Now, Randall Moon and colleagues show how distinct Wnt signalling pathways have opposing roles in zebrafish tail fin regeneration. On p. 479, they report that, following injury, *wnt10a* activates the β-catenin signalling pathway, leading to *fgf20a* expression, which is required for blastema formation and tail fin regeneration. *Wnt5b*, however, acts independently of, and antagonistically to, the β-catenin pathway, thereby inhibiting regeneration. Because its expression is regulated by the β-catenin pathway via *wnt10a* expression, the authors propose that these opposing Wnt pathways establish negative-feedback loops that modulate β-catenin signalling to ensure the correct level, location and duration of this signalling pathway in tail fin regeneration. As the authors discuss, Wnt/β-catenin signalling is also upregulated in the development of vertebrate liver and heart, although its precise role is unclear. Nevertheless, these findings may provide targets for therapeutic regenerative medicine in the future.



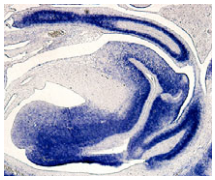
Neural crest cells set free by BMP

Neural crest (NC) cells are progenitors that delaminate away from the neural tube once specified. An epithelial to mesenchymal transition is required in these cells before dispersal can occur. These cells then migrate to new locations where they form the peripheral neurons and glia, in addition to several other cell types. On p. 491, Kalcheim and colleagues show how BMP4 promotes the ADAM10-mediated cleavage of N-cadherin along the neural tube, thus alleviating the inhibitory effect of N-cadherin on NC delamination. Full-length N-cadherin protein inhibits NC delamination by promoting cell-adhesion mechanisms and by repressing Wnt signalling, which acts downstream of BMP4 and is required for delamination. Mutation analysis revealed that N-cadherin has three domains – the β-catenin, extracellular and juxtamembrane domains that are required for correct NC delamination. Interestingly, overexpression of the N-cadherin soluble cytoplasmic cleavage product stimulates both β-catenin and cyclin D1 transcription, leading to enhanced Wnt signalling and NC delamination.



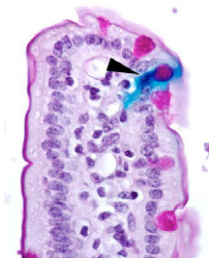
LRP6: axing axin

The LDL receptor-related protein 6 (LRP6) was first identified as a Wnt co-receptor in mice. However, the precise role that LRP6 plays in Wnt signalling has remained unclear. On p. 503, Janet Heasman's group now reveal that LRP6 degrades axin – an essential event in the Wnt11-activated formation of the dorsal axis in *Xenopus* embryogenesis. They also reveal that LRP6 regulates axin levels in the oocyte and maintains β-catenin expression in a low steady state – Wnt signalling has previously been believed to exist in either an on or off state. Axin is a negative regulator of Wnt signalling that targets β-catenin for degradation, so preventing Wnt target gene activation. LRP6 depletion in the embryo, in this study, led to increased axin and decreased β-catenin levels. In wild-type oocytes, exogenous β-catenin degradation was prevented by the co-injection of *LRP6* mRNA, whereas in axin-depleted oocytes, β-catenin levels increased. This study reveals a novel role for LRP6 in axin degradation and highlights the complexity of Wnt signalling.



Urogenital development under the spotlight

Amphibians and birds excrete waste products through the cloaca, an endodermally lined chamber. In mammals, the cloaca gives rise to some of the more specialised structures of the urogenital and reproductive organs. Quite how the cloaca gives rise to these crucial organs has remained elusive and understudied. Now, on p. 525, Haraguchi et al. shed much-needed light on this developmental process. They reveal that Shh and Gli mutant mice display hypoplasia of the external genitalia, internal urethra and bladder, indicating a requirement for Hh signalling in their development. Using the *Gli1-CreER*^{T2} mouse, the authors have fate mapped Hh-responsive mesenchyme and found that the bladder mesenchyme and external genitalia derive from Shh-responsive peri-cloacal mesenchyme, revealing how the coordination of urogenital formation is regulated by Hh signalling. The precise source, targets and ligands required for urogenital and reproductive development require further investigation, especially because future treatments of congenital urogenitary defects that are less invasive than reconstructive surgery may stem from these and future findings.



Notches marked up

The ligand-activated Notch receptor undergoes proteolytic cleavages, which release an intracellular fragment that activates target genes. Notch signalling regulates many cell fate decisions, but determining where and when it is activated has proven problematic. Now, on p. 535, Raphael Kopan and colleagues reveal a novel genetic approach in mice to locate Notch activation during development. Using an N_1IP-CRE allele, in which the Notch1 intracellular fragment is replaced by Cre, they have mapped Notch activity via β-galactosidase expression. This approach is particularly novel as this transgene marks descendents of a progenitor cell. Using this technique, they identify novel roles for Notch1 signalling in the heart, vasculature, retina and stem cell compartments of self-renewing epithelia. Interestingly, high levels of Notch1 activation do not always correlate with it having an essential role, as is revealed for intestinal stem cells. Together, these findings provide new insights into Notch activation and subsequent cell fate choice. Similar studies on the other Notch receptors in the mouse should provide further new information.

IN *JOURNAL OF CELL SCIENCE*

New home for β-cells

β-cells, the insulin-producing cells lost in type I diabetes, were thought to reside only in the pancreas. Now, another source of β-cells has been revealed in the liver. These β-cells are located within extra-hepatic bile ducts and have elevated levels of insulin mRNA, of the proteolytically cleaved insulin C-peptide and insulin-containing secretory granules characteristic of pancreatic β-cells. The cells are derived from liver epithelium rather than the pancreas and can secrete insulin in response to glucose. These findings offer renewed hope for the treatment of diabetes, where previous attempts to replace or increase the number of β-cells have been hindered by the limited supply of pancreatic islets. (For more on β-cell development and pancreatic cell specification, see Charles Murtaugh's review on p. 427 and Lori Sussel's research article on p. 515 of this issue of *Development*.)

Dutton, J. R., Chillingworth, N. L., Eberhard, D., Brannon, C. R., Hornsey, M. A., Tosh, D. and Slack, J. M. W. (2006). β cells occur naturally in extrahepatic bile ducts of mice. *J. Cell Sci.* **120**, 239-245.