RESEARCH HIGHLIGHTS

Re-routing junctions to invade the brain

Pathogens that are able to cross the blood-brain barrier can cause cerebrospinal meningitis. Pili on the surface of *Neisseria meningitidis* mediate adhesion to endothelial cells in the brain and are required for crossing the blood-brain barrier, but the mechanism was unclear. A recent report (*Science* **325,** 83–87; 2009) describes how the bacterium breaches the blood-brain barrier.

N. meningitidis hijacks cell-polarity proteins to mislocalize cell-junction components that make up the endothelial cell barrier, allowing bacterial transfer. The authors infected cultured brain endothelial cells with *N. meningitides,* which adhered to cells, formed microcolonies and recruited actin — events that are known to be triggered by type IV pili. They also found that components of adherens and tight junctions, which are normally located between the cells, appeared underneath bacterial microcolonies. These structures were connected to actin and required the prior recruitment of the polarity proteins Par3 and Par6, as is the case for normal adherens junctions. The adherens junction protein VE-cadherin was shown to relocalize, through endocytosis, from intercellular junctions to the location of the bacteria. Bacterial infection increased cell permeability and resulted in the appearance of gaps between the cells in a manner dependent on the activity of the polarity kinase PKCzeta and bacterial pili. Thus, *N. meningitidis* subverts a normal polarization pathway to invade the brain. CKR

Wnt sets up kidney tubule diameter

Defective tubule morphogenesis is associated with polycystic kidney diseases in humans. Carroll and colleagues (*Nature Genet.*, **41,** 793–799; 2009) have found that in mice, Wnt9b signalling controls kidney tubule diameter by regulating the orientation of embryonic tubule wall cells and the divisions of post-natal tubule epithelial cells.

When impairing Wnt9b function through inducible knockout during kidney tubule morphogenesis, the authors noticed the formation of cysts. Although post-natal maintenance of tubule diameter relies on Wnt9b-dependent oriented cell divisions, embryonic epithelial kidney cells divided in random orientations, suggesting that alternative mechanisms regulate tubule diameter in the embryo. As an embryonic tubule grows, elongated epithelial cells re-orient perpendicular to the tubule longitudinal axis, a process analogous to the convergent-extension movements that lead to thinning and lengthening of tissues at various stages of development. This process was disrupted in Wnt9b mutants independently of canonical β-catenin signalling. Instead, Rho and Jnk signalling, which have been linked to the planar cell polarity (PCP) pathway that controls convergent extension, are impaired in Wnt9b mutants. How Wnt9b regulates Rho/Jnk through the PCP pathway to control the re-orientation of elongated cells early in development and orientated divisions in post-natal kidney tubules remains to be explored. NLB

Yeast meiosis gets rusty with age

In humans, the fidelity of meiotic chromosome segregation decreases with age. Amon and colleagues now show that even budding yeast are not immune to the deleterious effects of ageing on meiotic chromosome segregation (*Dev. Cell* **16,** 844–855; 2009).

The authors found that aged yeast cells were unable to form spores — the haploid end-products of the yeast meiotic programme — and that the expression of genes required for meiosis was perturbed. Aged yeast cells failed to induce expression of Ime1, a transcription factor required for entry into meiosis. However, re-expressing Ime1 in these cells only partly restored sporulation efficiency, indicating that it is not the sole reason for the meiotic defect. Aged cells that did enter meiosis were found to show defective chromosome segregation and a concomitant decrease in spore viability. Extending replicative lifespan in yeast by manipulating levels of Fob1, a replicative fork barrier protein, and Sir2, a NAD-dependent histone deacetylase, rescued sporulation efficiency and other meiotic defects of aged yeast cells. Extrachromosomal ribosomal DNA circles are known to accumulate and contribute to ageing and the authors suggest that they may also account for the reduced sporulation efficiency of aged cells as their ectopic introduction into young cells similarly decreased sporulation efficiency. SS

Total recall

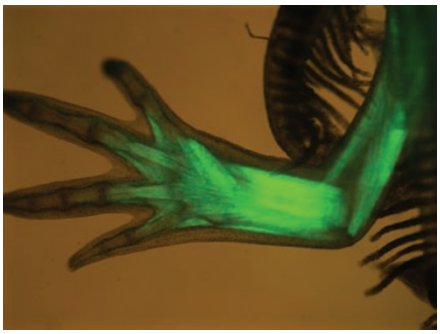

Image kindly provided by D. Knapp and E. Tanaka

Following amputation, salamanders regenerate fully functional limbs through the dedifferentiation of adult tissues into a zone of undifferentiated progenitors called the blastema. Which tissues contribute to the blastema and whether blastema cells are pluripotent remains unclear. Tanaka and colleagues tracked the major limb tissues during regeneration in the salamander *Ambystoma mexicanum* using a GFP transgene, and found that the blastema is composed of a heterogeneous collection of progenitors with restricted potential that retain memory of their tissue of origin (*Nature* **460,** 60–65; 2009).

Tissue labelling was achieved by using GFP-expressing donors, and transplanting a given GFP$^+$ limb tissue, or the embryonic region that produces that given tissue, into a GFP- host intact limb. Following amputation at a GFP-expressing site and blastema formation, thousands of individual labelled cells were tracked in several animals, revealing that the regenerating cells are not pluripotent. Muscle, epidermal, cartilage and Schwann cell-derived progenitors all maintained their developmental origins and gave rise to cells with their own tissue and, in some cases, positional identity. Dermal cells were an exception and generated both dermis and bone.

Although it remains unclear whether lineage restriction also applies to other salamander species, this study shifts current views of the blastema as a pool of homogeneous progenitors, and represents a technical advance in mapping cell fate *in vivo* in complex tissues. SG

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