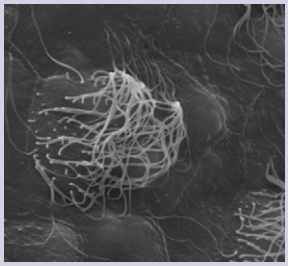

Uncovering ionocytes in *Xenopus* epithelia

An important function of specialised epithelia is to regulate ion homeostasis. Dysfunction of epithelial ion homeostasis can give rise to several human diseases, such as distal renal acidosis (when kidney epithelia are affected) or cystic fibrosis (when lung and gut epithelia are affected). Dubaissi and Papalopulu investigate the use of *Xenopus* larval skin as a model to study epithelial ion homeostasis, and show that this tissue contains ionocytes that depend on the transcription factor foxi1e for development and are highly similar to intercalated cells of the human kidney. Furthermore, *Xenopus* ionocytes are required for normal development of multiciliated cells. This work demonstrates the utility of *Xenopus* larval skin as a model for investigating complex cell interactions in intact tissue. *S.A.* **Page 179**

A role for LKB1 in preventing neurodegeneration in mice

The molecular processes underlying axon degeneration in many neurodegenerative diseases are not well understood. Sun et al. now uncover a neuroprotective role for LKB1, a protein kinase previously shown to have a role in axon differentiation in worms, by investigating mice conditionally lacking LKB1 in regions of the CNS and in the endocrine pancreas. They identify that the LKB1 downstream target sporadic Alzheimer's disease (SAD) A/B kinase and its subsequent phosphorylation of tau protein are involved in preventing axonal degeneration. These results indicate that LKB1 promotes neuronal survival and controls motor function in a vertebrate system. *S.A.* **Page 193**

tsc2 mutant zebrafish model of tuberous sclerosis complex

Tuberous sclerosis complex (TSC), a disease caused by mutation of the *TSC1* or *TSC2* genes, is a multi-organ disease whose severity depends upon the number and location of benign tumours known as hamartomas that grow in the brain, kidney, lung, heart and skin of affected patients. By using a novel zebrafish model, Kim et al. introduce a new experimental approach to studying mutant *tsc2* gene function during normal development, as well as the mechanisms leading to hamartoma formation and disease progression. *K.W.* **Page 255**

A role for Trpm7 in pancreatic cancer?

Chemical mutagenesis approaches in zebrafish have created an important resource of mutant fish that have defects in organ development. Yee et al. demonstrate that a line of fish with abnormal pancreatic development carries a mutation in the ion channel receptor Trpm7. This protein is overexpressed in human pancreatic adenocarcinoma cell lines, and interfering with its expression inhibits cell growth, so it might be a potential biomarker and/or therapeutic target for pancreatic adenocarcinoma. *K.W.* **Page 240**

Visualising β-cells in the pancreas

In both type 1 and type 2 diabetes, the β-cells of the islets of Langerhans in the pancreas are either destroyed or defective, resulting in insufficient insulin production. To study β-cells in development and disease, Shimajiri et al. generated a mouse in which expression of green fluorescent protein and secreted alkaline phosphatase is driven using the regulatory regions of the β-cell-specific neurogenin-3 gene. Pancreatic organ cultures derived from these mice allow developing β-cells to be visualised. In addition, this model system enables tracking the fate of developing β-cells in response to various stimuli. *K.W.* **Page 268**

Skeletal malformation and the SHP-2 pathway

In humans, gain- and loss-of-function mutations of the SHP-2 protein tyrosine phosphatase cause Noonan syndrome and LEOPARD syndrome, respectively. Patients that suffer from either of these diseases have skeletal abnormalities, among other symptoms. Bauler el al. show in mice that loss of SHP-2 function causes defective skeletal morphogenesis by inhibiting bone remodelling. It is probable that similar defects underlie LEOPARD syndrome in humans, so these mice should be useful for identifying and dissecting the signalling pathways affected by SHP-2 mutations. They may also yield new information about mechanisms of bone regulation. *K.W.* **Page 228**

ECM remodelling: a tale of two tissues

Remodelling of the extracellular matrix (ECM) occurs during normal development, following tissue damage and is key in establishing metastatic niches for invading cancer cells. Matrix metalloproteinases (MMPs) have an important role in ECM degradation, although attributing a specific role for individual MMPs has been difficult owing to functional overlap with other proteases. Hald et al. now demonstrate that double-knockout mice lacking both plasmin and MMP9 suffer from lethal colonic inflammatory mass lesions that resemble lesions seen after mucosal prolapse in humans. By contrast, wound healing in skin is normal, indicating tissue-specific differences in ECM remodelling that might be clinically exploitable. *K.W.* **Page 212**

Breaking point: metalloproteinases and fracture repair

Lieu et al. examine MMPs during bone repair in mice, and show that there are both spatial and temporal differences in expression. They find that MMP2, which is mutated in multicentric osteolysis with arthritis in humans, is required during the remodelling phase of fracture repair, at later stages than MMP9 and MMP13. These distinct functions of different MMPs during bone repair suggest that some might be relevant therapeutic targets in inflammation and angiogenesis, whereas others, such as MMP2, could be targeted to enhance bone remodelling. *K.W.* **Page 203**