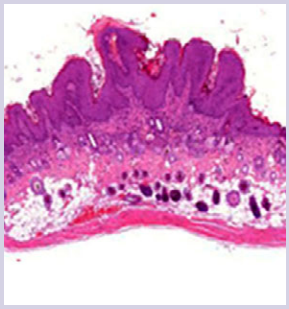


Flower protein: biomarker for early cancer detection?

It is thought that selection determines which cells in a tissue give rise to a tumour through clonal expansion. Identifying biomarkers that detect this early precancerous process might enable prevention before tumours form. Based on findings that Flower protein marks pretumoral cells in *Drosophila*, Petrova et al. set out to study whether the mouse homologue (mFwe) has the same function. They show that mFwe expression is increased in skin cells surrounding papillomas in mice, and that mFwe-deficient mice develop normally but are resistant to chemically induced skin papillomas, suggesting that mFwe promotes the expansion of pretumoral cells. These data suggest that Flower protein might be a biomarker for early skin cancer detection and a potential drug target. **Page 553**

Pancreatic diseases: β-catenin essential in adult acinar cells

Controversy surrounds the role of the Wnt pathway – and particularly its key mediator, β-catenin – in pancreatic exocrine and endocrine cells. Keefe et al. set out to conclusively address the role of β-catenin in adult pancreatic acinar cells using a transgenic labelling approach. They show that loss of β-catenin impairs acinar cell proliferation during postnatal growth and adult homeostasis, as well as during regeneration following injury. By contrast, loss of β-catenin does not affect islet cells, suggesting that diabetes-associated mutations affecting the Wnt pathway have effects elsewhere in the body. These data should help to better understand and develop treatments for diseases of the pancreas, including diabetes, pancreatitis and pancreatic cancer. **Page 503**

Fine-tuning candidate therapy for RASopathies

RASopathies, such as cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, are rare developmental diseases caused by germline mutations that lead to overactivation of the RAS-MAPK pathway. Anastasaki et al. build on previous work to test whether fine-tuning doses of PD0325901, an inhibitor of this pathway that is in clinical use for cancer treatment, can minimise the developmental defects of RASopathies. Using zebrafish embryos, they show that continuous, low doses of PD0325901 during development prevents the detrimental effects of a CFC-associated mutation without inducing the side effects observed when inhibiting the pathway using higher doses of the drug. Thus, anti-cancer agents that target the RAS-MAPK pathway might hold promise for these devastating developmental diseases. **Page 546**

Salmonella virulence factor Stn: role in membrane integrity

Much effort has been invested in determining how *Salmonella* virulence factors cause acute gastroenteritis. There has been debate about whether and how the *Salmonella* enterotoxin Stn contributes to the virulence of the bacteria. Nakano et al. find that a *Δstn* strain is no less virulent in vitro or in vivo than wild type. However, proteomic profiling shows that *Δstn* has abnormal membrane localisation of OmpA, a highly immunogenic outer membrane protein that is important for bacterial homeostasis. In addition, Stn and OmpA are found to directly interact. Thus, Stn might be important for bacterial cell membrane integrity through regulating the localisation of OmpA. **Page 515**

Paneth cell ablation induces neonatal necrotizing enterocolitis in mice

Neonatal necrotizing enterocolitis (NEC) is a major cause of mortality and morbidity in preterm infants. The cause is unclear and, despite significant research, little progress has been made in developing treatments. Based on findings that infants with NEC lack Paneth cells in the small intestine, Zhang et al. developed a new mouse model to test the role of this cell type in the disease. They show that selective ablation of Paneth cells followed by infection with *Klebsiella pneumoniae* causes intestinal pathology that resembles that of human NEC. Advantages of this model over existing models of NEC include its simplicity and the fact that it can be applied in mice at a developmental stage that is relevant to human NEC. This work furthers knowledge regarding NEC pathology and provides a new model for testing potential treatments. **Page 522**

Functional and metabolic impairments in cancer cachexia

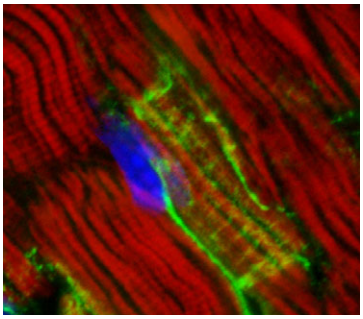
Cachexia, characterised by weight loss, muscle atrophy and fatigue, occurs in many individuals with cancer and causes more than 20% of cancer-related deaths. Animal models of the condition exist, but many of their phenotypes have not been comprehensively characterised. Murphy et al. analysed colon-26 (C-26) tumour-bearing mice, a common mouse model of cancer cachexia, for functional and metabolic defects: they find impairments in tests of physical activity, as well as reduced strength and increased fatigability of muscle tissues. Moreover, these mice have metabolic impairments such as reduced oxygen uptake and increased fat oxidation. This characterisation should help to identify relevant end points for future studies, and supports the continued use of C-26 tumour-bearing mice as model for human cancer cachexia. **Page 533**

Newly identified medaka *myc17* gene induces liver hyperplasia

Dysregulated Myc expression is observed in many types of cancer, in line with the known role of this transcription factor in regulating cellular processes such as apoptosis, proliferation and differentiation. Investigating the function of Myc in diverse biological models provides clues to its role in cancer. Menescal et al. analyse a newly identified, unusual version of Myc (*myc17*) found in the medaka genome, which also contains a conventional, conserved version of Myc (*myc20*). Although Myc17 lacks protein-regulatory sequences found in other reported versions of Myc, studies of two inducible transgenic medaka lines

show that Myc17 is functional and, like other versions of Myc, drives apoptosis and proliferation in vivo. In addition, long-term *myc17* induction causes liver hyperplasia. These transgenic medaka lines can be further used to probe the role of Myc in liver tumorigenesis. **Page 492**

Heart-specific deletion of CENP-F causes dilated cardiomyopathy



It has been proposed that disruption of the microtubule (MT) cytoskeleton can contribute to heart disease. Dees et al. now provide genetic evidence to support this hypothesis by characterising mice with cardiomyocyte-specific knockout of CENP-F, a multifunctional MT-binding protein whose decreased expression was recently linked to end-stage dilated cardiomyopathy in humans. Mutant mice have smaller hearts with multiple defects including thinner ventricular walls, reduced myocyte proliferation and fewer intercalated discs (myocyte-specific junctional complexes responsible for electrical and force transduction). Mutant mice also develop progressive dilated cardiomyopathy, arrhythmias and cardiac fibrosis. These results reveal a new disease mechanism and suggest that mutations in other MT-associated proteins could also contribute to heart disease. **Page 468**

Retinoids exacerbate IBD in a new zebrafish model

Retinoids, which are commonly used to combat acne, have several side effects, including the development of inflammatory bowel disease (IBD). To investigate the effect of retinoids on the gastrointestinal system in vivo, Oehlers et al. developed a model of IBD by immersing zebrafish larvae in dextran sodium sulfate (DSS), a chemical commonly used to induce colitis in rodents. As occurs in individuals with IBD, DSS exposure induced a protective mucosecretory response in zebrafish larvae. Both endogenous and DSS-induced mucus secretion were suppressed by exogenous retinoic acid, which promoted inflammation and exacerbated enterocolitis. These findings introduce a new model of IBD and provide evidence for how the disease might be triggered in patients treated with retinoids. **Page 457**

Dilated cardiomyopathy: antifibrotic effect of IGF1

Despite recent progress in developing treatments for dilated cardiomyopathy (DCM), mortality remains high. Given that insulin-like growth factor-1 (IGF1) improves myocardiocyte function in other pathological settings, Touvron et al. investigated whether IGF1 would also be beneficial in an established mouse model of DCM. The model involves cardiac-specific inducible knockout of serum response factor (*Srf*), encoding a transcription factor important for heart development and function; fatal DCM occurs within 10 weeks of inducing *Srf* deletion. Crossing these to mice that overexpress IGF1 in cardiomyocytes resulted in a strain that showed delayed DCM, better cardiac function and longer lifespan after *Srf* deletion. Overexpression of IGF1 also markedly reduced cardiac fibrosis and inflammation, partly by counteracting the increased expression of connective tissue growth factor (CTGF) caused by *Srf* deletion. These results further understanding of how *SRF* contributes to heart failure and suggest that IGF1 might be a promising therapeutic. **Page 481**