IN BRIEF

PANCREATIC CANCER

Splicing a metastatic switch

Alternative splicing generates two isoforms of the transcription factor paired-related homeobox 1 (PRRX1): PRRX1a and PRRX1b. Takano *et al.* show that in pancreatic ductal adenocarcinoma (PDAC), both isoforms have distinct roles in metastasis. Both *in vitro* and in PDAC mouse models, PRRX1b promotes epithelial–mesenchymal transition, invasion and tumour de-differentiation, whereas PRRX1a promotes the reverse mesenchymal–epithelial transition, differentiation and metastatic growth in the liver. Evidence of a similar PRRX1 switch was also observed in human PDAC samples. One transcriptional target of PRRX1b was the hepatocyte growth factor gene (*Hgf*), and inhibition of HGF in combination with gemcitabine reduced tumour growth and metastasis in an orthotopic PDAC mouse model.

ORIGINAL ARTICLE Takano, S. *et al.* Prrx1 isoform switching regulates pancreatic cancer invasion and metastatic colonization. *Genes Dev.* **30**, 233–247 (2016)

SENESCENCE

Preventing ageing

The tumour suppressor $p16^{INK4A}$ is expressed by senescent cells, which accumulate in tissues over time, and might have a role in ageing. By specifically inducing apoptosis of $p16^{INK4A}$-expressing cells in mice, Baker *et al.* demonstrate that clearance of these cells extends their lifespan: it reduces tumorigenesis as well as other features associated with ageing, with no evidence of side effects. It will be interesting to determine how clearance of these cells prevents tumour formation and whether this can be exploited for cancer therapy.

ORIGINAL ARTICLE Baker, D. J. *et al.* Naturally occurring $p16^{Ink4a}$-positive cells shorten healthy lifespan. *Nature* **530**, 184–189 (2016)

LEUKAEMIA

Not all stem cells are equal

Lechman, Gentner *et al.* identified a prognostic microRNA (miRNA) signature from leukaemia stem cells (LSCs) in human acute myeloid leukaemia (AML) samples. One miRNA in this signature, miR-126, promoted LSC stem cell characteristics (such as self-renewal) and chemotherapy resistance of LSCs in part through targeting PI3K–AKT–mTOR signalling. However, in normal haematopoietic stem cells (HSCs), miR-126 blocked self-renewal, suggesting that miR-126 inhibition could target LSCs while preserving HSCs.

ORIGINAL ARTICLE Lechman, E. R., Gentner, B. *et al.* miR-126 regulates distinct self-renewal outcomes in normal and malignant hematopoietic stem cells. *Cancer Cell* **29**, 214–228 (2016)

IMMUNOTHERAPY

Biomarkers of immunotherapy-induced colitis

Despite the therapeutic efficacy of immune checkpoint inhibitors against some tumours, immune-related side effects remain a large concern. Dubin *et al.* show in a prospective study of patients with melanoma that new-onset colitis associated with the cytotoxic T lymphocyte-associated antigen 4 (CTLA4) inhibitor ipilimumab correlates with the pre-treatment faecal microbiota. An increase in bacteria from the Bacteroidetes phylum and in microbial pathways of polyamine transport and B vitamin synthesis correlated with increased colitis resistance.

ORIGINAL ARTICLE Dubin, K. *et al.* Intestinal microbiome analyses identify melanoma patients at risk for checkpoint-blockade-induced colitis. *Nat. Commun.* http://dx.doi.org/10.1038/ncomms10391 (2016)