IN BRIEF

GENETICS

Germline mutations in *WTX* cause a sclerosing skeletal dysplasia but do not predispose to tumorigenesis

Jenkins, Z. A. *et al. Nature Genet.* **41**, 95–100 (2009)

Somatic inactivation of *WTX*, which encodes a repressor of Wnt signalling, is thought to drive Wilms' tumour development in a subset of patients. However, this study shows that germline mutations in *WTX* cause X-linked osteopathia striata congenita with cranial sclerosis (OSCS) but do not predispose to Wilms' tumour or other malignancies. This suggests that loss of *WTX* alone is not sufficient for tumorigenesis, and that mutations at other loci are required for tumour development.

TUMORIGENESIS

Disruption of the *SRC-1* gene in mice suppresses breast cancer metastasis without affecting primary tumor formation

Wang, S. *et al. Proc. Natl Acad. Sci. USA* **106**, 151–156 (2009)

Expression of steroid coactivator 1 (SRC1) is associated with poor prognosis in breast cancer. In this study, $Src1^{-/-}$ mice were crossed with mice expressing a transgene encoding mouse mammary tumour virus polyoma middle T antigen (PyMT). The mammary tumours that developed in these mice were more differentiated than those in $Src1^{+/+}$ PyMT mice and the frequency of metastasis was reduced, suggesting that targeting SRC1 could improve the prognosis of patients with advanced breast cancer.

ANGIOGENESIS

PDGF-C mediates the angiogenic and tumorigenic properties of fibroblasts associated with tumors refractory to anti-VEGF treatment

Crawford, Y. *et al. Cancer Cell* **15**, 21–34 (2009)

This study provides evidence indicating that tumour-associated fibroblasts (TAFs) mediate resistance to vascular endothelial growth factor A (VEGFA) inhibitors. Platelet-derived growth factor C (PDGFC) was upregulated in TAFs from mouse tumours that developed resistance to VEGFA inhibition. Treatment of these mice with PDGFC-neutralizing antibodies inhibited the angiogenic effects of TAFs, and concomitant treatment with anti-PDGFC neutralizing antibodies and a VEGFA inhibitor synergistically reduced tumour growth. Therefore, targeting stromal mediators such as PDGFC could temper the development of resistance to VEGFA inhibition.

STEM CELLS

Cell-cycle restriction limits DNA damage and maintains self-renewal of leukaemia stem cells

Viale, A. *et al. Nature* **457**, 51–56 (2009)

New insights into the mechanisms that underlie the self-renewal of leukaemia stem cells have been provided by a mouse model of acute promyelocytic leukaemia (APL) that expresses the oncogenic fusion PML–RAR. Upregulation of the cell cycle inhibitor p21 was observed in haematopoetic stem cells from the mice. This led to cell cycle arrest and DNA repair, thus maintaining a pool of quiescent leukaemic stem cells. p21 was essential for leukaemogenesis, identifying it as a potential therapeutic target.