IN BRIEF

TUMOUR SUPPRESSORS

An X chromosome gene, *WTX*, is commonly inactivated in Wilms tumour

Rivera, M. N. *et al. Science* 4 January 2007 (doi: 10.1126/science.1137509)

Daniel Haber and colleagues have identified mutations in *WTX*, a newly identified gene on the X chromosome, in approximately one third of patients with the childhood kidney cancer Wilms tumour. *WTX* mutations did not coincide with *WT1* mutations, which account for 5–10% of patients with Wilms tumour. The authors show that *WTX* undergoes monoallelic inactivation, whereby the single X chromosome of males or the active X chromosome of females is mutated.

TUMORIGENESIS

Selective requirements for E2f3 in the development and tumorigenicity of Rb-deficient chimeric tissues

Parisi, T. *et al. Mol. Cell Biol.* 8 January 2007 (doi: 10.1128/MCB.01854-06)

Jacqueline Lees and colleagues have generated retinoblastoma 1 ($Rb1^{-/-}$;$E2f3^{-/-}$ chimeric mice to investigate how E2F3 influences tumorigenesis in $Rb1^{-/-}$ tissues, which was previously impossible because of $Rb1^{-/-}$;$E2f3^{-/-}$ embryonic lethality. The authors show that the loss of *E2f3* does not prevent the development of pituitary and thyroid tumours that result from *Rb1* ablation. However, pre-neoplastic lesions that arise in $Rb1^{-/-}$ mice, which are thought to develop into the equivalent of human small-cell lung cancer, were completely suppressed by *E2f3* inactivation.

THERAPY

Targeting TACE-dependent EGFR ligand shedding in breast cancer

Kenny, P. A. & Bissell, M. J. *J. Clin. Invest.* 11 January 2007 (doi: 10.1172/JCI129518)

Paraic Kenny and Mina Bissell show that the inhibition of tumour necrosis factor-α-converting enzyme (TACE) activity prevents an autocrine loop that normally leads to the shedding of a growth-factor ligand that functions as an oncogenic stimulus in a 3D tissue-culture model of breast cancer progression. TACE-dependent ligand shedding was shown to be active in breast cancer cell lines, and TACE expression in human breast tumour samples was indicative of poor prognosis. This could explain constitutive growth-factor receptor activity without mutations in the corresponding genes, and provides a new oncogenic pathway worth targeting for anticancer drug development.

SENESCENCE

The DNA damage signalling pathway is a critical mediator of oncogene-induced senescence

Mallette, F. A. *et al. Genes Dev.* **21**, 43–48 (2007)

Gerrado Ferbeyre and colleagues show that inhibition of a DNA-damage response kinase, ataxia telangiectasia mutated (ATM), in human fibroblasts prevents p53-dependent senescence induced by the oncogenes *E2F1*, *RASV12* or *STAT5* (signal transducer and activator of transcription 5). Oncogene-induced senescence (OIS) was associated with the activation of DNA-damage signalling pathways and could not be bypassed by the inactivation of *TP53* or *RB1*, indicating that the DNA-damage response and OIS are functionally related barriers to tumorigenesis.