**TUMOUR SUPPRESSORS**

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


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


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


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


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.