IN BRIEF

RADIOTHERAPY

FLASHing tumours

A new study in mice suggests that radiation delivered in short pulses at ultrahigh dose rates (FLASH) is as effective against lung tumours as conventional protracted single lower dose rates and has fewer side effects. Using both orthotopic lung tumours in immunocompetent mice and human lung tumour xenografts in nude mice, Favaudon *et al.* showed that FLASH irradiation caused less lung fibrogenesis and less apoptosis in normal tissue than conventional radiation. Although this technique was only tested in one tumour type, it suggests that delivery methods are crucial to minimizing radiation treatment side effects, and it has implications for therapeutic protocols.

ORIGINAL RESEARCH PAPER Favaudon, V. *et al.* Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice. *Sci. Transl Med.* **6**, 245ra93 (2014)

METASTASIS

Regulating brain metastasis

Sevenich *et al.* have shown that the protease cathepsin S regulates breast cancer metastasis to the brain in mice by cleaving junctional adhesion protein B (JAM-B) in cells that form the blood–brain barrier (BBB) to facilitate extravasation of breast cancer cells across the BBB. Moreover, high expression levels of cathepsin S in human breast tumours were associated with decreased brain metastasis-free survival. Collectively, these results suggest that cathepsin S is a potential therapeutic target for breast cancer-related brain metastasis.

ORIGINAL RESEARCH PAPER Sevenich, L. *et al.* Analysis of tumour- and stroma-supplied proteolytic networks reveals a brain-metastasis-promoting role for cathepsin S. *Nature Cell Biol.* http://dx.doi.org/10.1038/ncb3011 (2014)

TUMOUR SUPPRESSORS

p53 and cellular plasticity

Suppression of the liver cancers hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC) by p53 was investigated by Tschaharganeh *et al.* p53 loss promoted dedifferentiation of mature hepatocytes by indirectly promoting the expression of nestin, a protein associated with stem and progenitor cells. The resulting progenitor-like cells were then primed to develop into HCCs or CCs, depending on the acquisition of lineage-specific oncogenic mutations. Furthermore, increased nestin expression correlated with p53 loss in human HCCs and CCs. These data suggest that p53 can suppress tumours in part through preventing the 'reprogramming' of differentiated cells.

ORIGINAL RESEARCH PAPER Tschaharganeh, D. F. *et al.* p53-dependent nestin regulation links tumor suppression to cellular plasticity in liver cancer. *Cell* **158**, 579–592 (2014)

PROTEOMICS

Connecting genotypes to phenotypes

Zhang *et al.* carried out proteomic analyses of 95 human colorectal cancer (CRC) samples previously characterized at the genomic level by The Cancer Genome Atlas (TCGA). This proteogenomic analysis found that mRNA levels often did not reliably predict protein levels. Therefore, potential driver genes could be prioritized as those with greater changes in protein levels. CRCs were classified into five proteomic subtypes; these were similar to the three transcriptomic subtypes identified by TCGA but also identified additional characteristics that might better explain CRC biology and patient prognosis.

ORIGINAL RESEARCH PAPER Zhang, B. *et al.* Proteogenomic characterization of human colon and rectal cancer. *Nature* http://dx.doi.org/10.1038/nature13438 (2014)