IN BRIEF

BREAST CANCER

Ferroportin and iron regulation in breast cancer progression and prognosis

Pinnix, Z. K. *et al. Science Trans. Med.* **2**, 43ra56 (2010)

Some cancers have been shown to have an increased requirement for iron, and a new study provides insights into the potential underlying mechanism by showing that the ferroportin iron transport system is important in breast cancer progression and prognosis. The authors showed that ferroportin and the hormone hepcidin, which regulates ferroportin stability, are expressed in cultured breast epithelial cells. However, compared with these cells, ferroportin expression was reduced in breast cancer cell lines, and this correlated with increased iron availability. Breast cancer cells transfected with ferroportin showed reduced growth in a xenograft mouse model. In addition, human breast tumour samples showed reduced ferroportin expression, which correlated with increased anaplasia, and increased ferroportin and decreased hepcidin expression predicted a favourable prognosis in patients with breast cancer, showing that the *in vitro* and mouse results can be extended to human breast cancer.

THERAPY

NF1 is a tumor suppressor in neuroblastoma that determines retinoic acid response and disease outcome

Hölzel, M. *et al. Cell* **142**, 218–229 (2010)

Retinoic acid therapy of neuroblastoma shows a variable clinical response, but the reasons for this have been unknown. Using a large-scale RNA interference (RNAi) screen, Bernards and colleagues have now identified crosstalk between the tumour suppressor *NF1* and the effects of retinoic acid on differentiation in neuroblastomas. They show that loss of NF1 in neuroblastoma activates Ras–MEK signalling, which represses ZNF423, a key transcriptional regulator of retinoic acid receptors. Mutations in *NF1* occur in primary neuroblastomas, and low levels of *NF1* and *ZNF423* in neuroblastoma are associated with a poor outcome. Treatment of *NF1*-deficient neuroblastoma cells with MEK inhibitors restores responsiveness to retinoic acid, suggesting that this might be a viable combination therapy for retinoic acid-resistant neuroblastomas that are deficient for *NF1*.

DNA DAMAGE

DNA damage signaling in response to double-strand breaks during mitosis

Giunta, S. *et al. J. Cell Biol.* **190**, 197–207 (2010)

The activation of DNA damage response signalling pathways by DNA double-strand breaks (DSBs) has been well characterized in interphase cells and leads to activation of cell cycle checkpoint arrest and the appropriate DNA repair pathway(s). However, DSBs that occur in mitotic cells do not induce checkpoint activation or repair, but is DNA damage response signalling activated? Jackson and colleagues showed that DSBs induced in mitotic cells activate upstream (apical) DSB signalling, including phosphorylation of histone H2AX at DSBs. Inactivation of the apical kinases ATM and DNA-PK hypersensitized cells to drugs that induce DSBs, suggesting that the activation of the apical pathway marks damage to be repaired in the following G1 phase.