IN BRIEF

SIGNALLING

The E3 ligase TRAF6 regulates Akt ubiquitination and activation

Yang, W. *et al. Science* **325**, 1134–1138 (2009)

Recruitment to the membrane is necessary for Akt activation, and Yang *et al.* show that Akt ubiquitylation by the E3 ubiquitin ligase TRAF6 is important for this process. Analysis of Akt activity in *Traf6*$^{-/-}$ mouse embryonic fibroblasts showed that loss of Akt ubiquitylation resulted in reduced phosphorylation and therefore reduced activation of Akt in the presence of insulin-like growth factor 1. Additionally, human prostate cancer cells, in which levels of TRAF6 were reduced using short hairpin RNAs, had low tumorigenic potential in xenograft mouse models, suggesting that TRAF6 may be a potential therapeutic target.

EPIGENETICS

LSD1 is a subunit of the NuRD complex and targets the metastasis programs in breast cancer

Wang, Y. *et al. Cell* **138**, 660–672 (2009)

Lysine-specific demethylase 1 (LSD1) catalyses histone demethylation. Wang *et al.* show that LSD1 is a component of the nucleosome remodelling and deacetylase (NuRD) complex, expanding the known functions of this complex in epigenetic regulation. Transcriptional target analysis revealed that LSD1-containing NuRD complexes repress the transcription of several important cellular regulators, including transforming growth factor-β1 (*TGFB1*). Subsequent LSD1 overexpression and knockdown studies, both *in vitro* and *in vivo*, indicated a role for LSD1 in suppressing breast cancer metastasis. In line with this, LSD1 was downregulated in a panel of breast carcinomas and inversely correlated with TGFβ1 expression.

DIABETES

A crucial role for adipose tissue p53 in the regulation of insulin resistance

Minamino, T. *et al. Nature Med.* 30 Aug 2009 (doi:10.1038/nm.2014)

Given that p53 has wide-ranging functions, it is perhaps not surprising that it is involved in diseases other than cancer. This paper documents the function of p53 in promoting senescent-like changes in adipose tissue from mice with type 2-like diabetes, which manifests as insulin resistance. Excessive calorie intake led to oxidative stress in adipose tissue in these mice, as well as increased expression of p53 and pro-inflammatory cytokines. Inhibition of p53 activity in adipose tissue suppressed the senescent changes and reduced insulin resistance. Adipose tissue from patients with type 2 diabetes showed similar changes.

NON-CODING RNAS

Repression of the *miR-17-92* cluster by p53 has an important function in hypoxia-induced apoptosis

Yan, H. l. *et al. EMBO J.* 20 Aug 2009 (doi:10.1038/emboj.2009.214)

Yan *et al.* show that expression levels of the *miR-17-92* microRNA cluster are reduced in cells under hypoxic conditions and that this is mediated by p53 binding to a proximal region in the *miR-17-92* promoter. Overexpression of *miR-17-92* suppressed hypoxia-induced apoptosis, indicating that p53 might induce apoptosis in hypoxic cells by repressing the expression of this microRNA cluster.