IN BRIEF

EPIGENETICS

Tumour suppressive HIF2α

Westerlund *et al.* found that combining the DNA demethylating drug 5-aza-deoxycytidine with the differentiation-promoting therapy retinoic acid inhibited tumour growth and prolonged survival in mouse xenograft models of high-risk neuroblastoma. This treatment resulted in high hypoxia-inducible factor 2α (HIF2α) levels but not HIF1α, and a transcriptional response characterized by increased neuronal and decreased cell cycle gene expression. Given the correlation between high HIF2α and better prognosis in patients, this suggests that HIF2α inhibitors may not be a viable therapeutic option.

ORIGINAL ARTICLE Westerlund, I. *et al.* Combined epigenetic and differentiation-based treatment inhibits neuroblastoma tumor growth and links HIF2α to tumor suppression. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1700655114 (2017)

TUMOUR IMMUNOLOGY

Feeding frenzy

Tumour cells are thought to avoid being phagocytosed through expression of the 'self' marker CD47, which ligates the macrophage receptor SIRPα. Alvey *et al.* investigated the potential of SIRPα-inhibited bone marrow-derived macrophages, primed with tumour-targeting antibodies, to clear tumours *in vivo*. Systemic injection of these macrophages into tumour-bearing mice increased engulfment of tumour cells compared with host tumour-associated macrophages (TAMs), and tumours regressed. However, anti-tumour effects were limited as donor macrophages eventually underwent mechanosensitive-mediated differentiation into non-phagocytic, high-SIRPα TAMs.

ORIGINAL ARTICLE Alvey, C. M. *et al.* SIRPA-inhibited, marrow-derived macrophages engorge, accumulate, and differentiate in antibody-targeted regression of solid tumors. *Curr. Biol.* http://dx.doi.org/10.1016/j.cub.2017.06.005 (2017)

TUMOUR IMMUNOLOGY

Tumours copy to escape

How tumours escape the immune system is not well defined. Nirschl *et al.* show that immune phagocytes in human melanoma share a physiological gene signature, which co-enriches and correlates with interferon-γ (IFNγ)-directed gene transcripts, and which is induced across multiple human cancers. Suppressor of cytokine signalling 2 (SOCS2) was highly expressed in melanoma-infiltrating mononuclear phagocytes and required for immune escape. SOCS2 loss *in vivo* led to robust immune-mediated tumour rejection. This indicates that SOCS2, as part of an IFNγ-induced tissue signature, mediates peripheral immune surveillance, and this is exploited by tumours.

ORIGINAL ARTICLE Nirschl C. J. *et al.* IFNγ-dependent tissue-immune homeostasis is co-opted in the tumor microenvironment. *Cell* **170**, 127–141 (2017)

LEUKAEMIA

Multiple origins of relapse

The origin of relapse in acute myeloid leukaemia (AML) is thought to be due to drug-promoted mutagenesis or to the selection of drug-resistant cells. Shlush *et al.* provide evidence for the latter and propose at least two distinct patterns of relapse in AML. In some patients, relapse can occur from a small subpopulation of a genetically diverse pool of leukaemia stem cells already present at diagnosis. In other patients, relapse can occur from larger subpopulations of phenotypically committed leukaemia cells that have a stem cell-like transcriptional signature. This shows that targeting stem cell properties is crucial to prevent relapse.

ORIGINAL ARTICLE Shlush, L. I. *et al.* Tracing the origins of relapse in acute myeloid leukaemia to stem cells. *Nature* **547**, 104–108 (2017)