

IN BRIEF

EPIGENETICS**Tumour suppressive HIF2 α**

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 2 α (HIF2 α) levels but not HIF1 α , and a transcriptional response characterized by increased neuronal and decreased cell cycle gene expression. Given the correlation between high HIF2 α and better prognosis in patients, this suggests that HIF2 α 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 HIF2 α 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 SIRP α . Alvey *et al.* investigated the potential of SIRP α -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-SIRP α TAMs.

ORIGINAL ARTICLE Alvey, C. M. *et al.* SIRP α -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 (IFN γ)-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 IFN γ -induced tissue signature, mediates peripheral immune surveillance, and this is exploited by tumours.

ORIGINAL ARTICLE Nirschl C. J. *et al.* IFN γ -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)