IN BRIEF

TUMOUR MICROENVIRONMENT

Clearing the air for T cells

Antitumour T cells are suppressed by hypoxic tumour areas enriched in extracellular adenosine through activation of A2A adenosine receptors (A2ARs). Hatfield *et al.* found that mice with lung tumours given supplementary oxygen have improved tumour oxygenation. This enhanced intratumoural infiltration of T cells, reduced immunosuppression by regulatory T cells, and increased tumour regression and long-term survival. As respiratory hyperoxia is used in the clinic, the authors postulate that it can be easily combined with existing immunotherapies for cancer and with available synthetic antagonists of A2ARs.

ORIGINAL RESEARCH PAPER Hatfield S. M. *et al.* Immunological mechanisms of the antitumor effects of supplemental oxygenation. *Sci. Transl Med.* **7**, 277ra30 (2015)

CIRCULATING TUMOUR CELLS

Breaking free

By analysing the phenotype of circulating tumour cells in the bone marrow of patients with early-disseminated breast cancer, Werner *et al.* have shown that dissemination might be driven by low levels of retinoic acid-induced 2 (RAI2). Depletion of RAI2 in luminal breast cancer cell lines resulted in dedifferentiation and increased invasiveness. RAI2 interacts with C-terminal-binding proteins (CTBPs), which control the expression of target genes involved in breast cancer. These results suggest that RAI2 maintains differentiation of luminal breast epithelial cells and might prevent metastasis initiation.

ORIGINAL RESEARCH PAPER Werner S. *et al.* Suppression of early hematogenous dissemination of human breast cancer cells to bone marrow by retinoic acid induced 2 *Cancer Discov.* http://dx.doi.org/10.1158/2159-8290.CD-14-1042 (2015)

TUMOUR IMMUNOLOGY

If the mountain will not come to Muhammad…

Natural killer (NK) cells use receptors such as NKG2D to recognize and eliminate cancer cells that overexpress ligands for these receptors. Deng *et al.* have studied a mouse NKG2D ligand — MULT1, which is commonly upregulated in primary tumours — and shown that shedding of MULT1 causes NK cell activation and tumour rejection. Secreted MULT1 reverses the desensitization of NK cells caused by membrane-bound NKG2D ligands on tumour-associated cells, such as myeloid cells. Recombinant soluble MULT1 also stimulated tumour rejection in mice, so this could be an approach for cancer immunotherapy.

ORIGINAL RESEARCH PAPER Deng W. *et al.* A shed NKG2D ligand that promotes natural killer cell activation and tumor rejection. *Science* http://dx.doi.org/10.1126/science.1258867 (2015)

TREATMENT RESPONSE

Stay warm

Eng *et al.* have found that the standard temperature at which mice are housed has an effect on treatment response. The sensitivity of several pancreatic tumour models to cytotoxic therapies was increased when mice were housed at a temperature of 30 °C compared with the standard temperature of 22 °C. Mice housed at 30 °C have decreased levels of norepinephrine, which mediates the physiological response to cold stress. Increased therapeutic sensitivity correlated with decreased levels of norepinephrine in tumours; therefore, sensitivity could be increased by administration of an adrenergic receptor antagonist at that temperature.

ORIGINAL RESEARCH PAPER Eng, J. W-L. *et al.* Housing temperature-induced stress drives therapeutic resistance in murine tumour models through β_2-adrenergic receptor activation. *Nature Commun.* **6**, 6426 (2015)