IN BRIEF

TUMOUR IMMUNOLOGY

Keeping virus-driven lymphomas in check

Epstein–Barr virus (EBV) is rapidly cleared by the immune system, but it can persist in some cells for life. Under conditions of immunosuppression, B cells that are latently infected with EBV can undergo marked proliferation and malignant transformation. EBV latent membrane protein 1 (LMP1) is essential for the transformation of human B cells. Here, the authors generated a mouse model in which all B cells expressed LMP1. $LMP1^+$ B cells were efficiently deleted by T cells in immunocompetent animals, but they underwent marked clonal expansion and formed large B cell lymphomas in immunocompromised animals. Both $CD4^+$ and $CD8^+$ T cells contributed to immune surveillance of $LMP1^+$ B cells. Natural killer (NK) cells were also activated by $LMP1^+$ B cells, which expressed ligands for the NK cell receptor NKG2D. Indeed, treatment of tumour-bearing mice with an NKG2D–Fc fusion protein caused efficient lysis of $LMP1^+$ tumour cells, suggesting a possible new therapy for EBV-driven B cell lymphomas.

ORIGINAL RESEARCH PAPER Zhang, B. *et al.* Immune surveillance and therapy of lymphomas driven by Epstein-Barr virus protein LMP1 in a mouse model. *Cell* **148**, 739–751 (2012)

IMMUNOTHERAPY

A killer combination

In this study, a combination of the tumour-targeting antibody trastuzumab (which is specific for human epidermal growth factor receptor 2 (HER2)) and a natural killer (NK) cell-activating antibody specific for CD137 is shown to be highly effective in treating breast cancer. Trastuzumab leads to the elimination of $HER2^+$ breast cancer cells mainly through antibody-dependent cell-mediated cytotoxicity by NK cells. NK cells exposed to trastuzumab-coated $HER2^+$ tumour cells upregulate the co-stimulatory molecule CD137, and subsequent treatment with a CD137-specific agonistic antibody improved their ability to kill trastuzumab-coated $HER2^+$ tumour cells *in vitro*. Moreover, athymic mice (which lack T cells but have normal NK cells) that were engrafted with human breast cancer cells and treated with trastuzumab followed by the CD137-specific antibody showed a marked reduction in tumour size and mortality compared with mice treated with only one antibody. The enhanced cytotoxicity was restricted to antibody-coated tumour cells, which suggests that this combined therapy could be applicable to other cancer-targeting antibodies.

ORIGINAL RESEARCH PAPER Kohrt, H. E. *et al.* Stimulation of natural killer cells with a CD137-specific antibody enhances trastuzumab efficacy in xenotransplant models of breast cancer. *J. Clin. Invest.* **122**, 1066–1075 (2012)

TUMOUR IMMUNOLOGY

Hope in a sticky situation

During tumorigenesis, the hypoxic tumour environment promotes the formation of new blood vessels that show many abnormalities compared with healthy vasculature. Leukocyte adhesion to endothelial cells lining the tumour-associated vasculature is impaired and, consequently, effector immune cells cannot gain access to the tumour. In this study, the authors treated tumour-bearing mice with a tumour necrosis factor (TNF)–peptide fusion protein that targets TNF to the tumour-associated vasculature. They found that this therapy promoted the upregulation of adhesion molecules on endothelial cells and increased the infiltration of $CD8^+$ T cells into tumours. In mice with ovalbumin-expressing tumours, delivery of the fusion protein markedly increased the antitumour responses of adoptively transferred ovalbumin-specific $CD8^+$ T cells. The authors suggest that a similar approach could be used to improve the efficacy of adoptive T cell transfer-based therapies for cancer.

ORIGINAL RESEARCH PAPER Calcinotto, A. *et al.* Targeting TNF-α to neoangiogenic vessels enhances lymphocyte infiltration in tumors and increases the therapeutic potential of immunotherapy. *J. Immunol.* **188**, 2687–2694 (2012)