IN BRIEF

NATURAL KILLER CELLS

Cutting edge: Distinct NK receptor profiles are imprinted on CD8 T cells in the mucosa and periphery during the same antigen challenge: role of tissue-specific factors.

Laouar, A. *et al. J. Immunol.* **178**, 652–656 (2007)

In this study, the authors examined the factors that control the expression of natural killer (NK)-cell receptors by $CD8^+$ T cells. $CD8^+$ intraepithelial lymphocytes (IELs) express high levels of the NK-cell receptor 2B4 but not NK group 2, member A (NKG2A). By contrast, $CD8^+$ peritoneal exudate lymphocytes (PELs) did not express 2B4 but expressed high levels of NKG2A during the same antigen challenge. Inhibition of co-stimulation by CD70 (expressed by antigen-presenting cells) blocked the expression of 2B4 by $CD8^+$ IELs. In addition, treatment with retinoic acid (which has been shown to be produced by intestinal dendritic cells) attenuated the expression of NKG2A by PELs. So, tissue-specific factors differentially regulate the expression of NK-cell receptors on $CD8^+$ T cells, which could potentially regulate T-cell effector activity at specific sites.

ANTIVIRAL IMMUNITY

Regulation of innate antiviral defenses through a shared repressor domain in RIG-I and LGP2.

Saito, T. *et al. Proc. Natl Acad. Sci. USA* **104**, 582–587 (2007)

Retinoic-acid-inducible gene I (RIG-I) is an intracellular sensory molecule that binds double-stranded (ds) RNA. But how is RIG-I signalling controlled? In resting cells, RIG-I is maintained as a monomer, but following binding to dsRNA RIG-I self-associates to form a multimeric complex. RIG-I then interacts with interferon-β-promoter stimulator 1 (IPS1) to signal to downstream effector molecules. This process was shown to be tightly regulated by an internal repressor domain. Indeed, deletion of this repressor domain resulted in constitutive signalling by RIG-I. The RIG-I-like RNA helicase LGP2 also contains a repressor domain, and it associates in *trans* with RIG-1 to prevent self-association. So, this study identifies a repressor domain in RIG-I and LGP2 that controls signalling to downstream effectors in response to dsRNA.

IMMUNOTHERAPY

Induced sensitization of tumor stroma leads to eradication of established cancer by T cells.

Zhang, B. *et al. J. Exp. Med.* 8 January 2007 (doi:10.1084/jem.20062056)

One reason why attempts at treating cancer with immunotherapy often fail is because cancer cells can lose expression of MHC molecules, thereby allowing them to escape lysis by the transferred cytotoxic T lymphocytes (CTLs). This study shows that CTLs can be effective at eliminating established tumours, even those expressing low levels of antigen, when administered after a bout of irradiation or chemotherapy. Using high-affinity T-cell-receptor tetramers, the authors showed that two days after irradiation therapy, tumour-associated stromal cells expressed tumour-specific peptide–MHC complexes and became susceptible to CTL lysis. This was due to stromal-cell uptake, and subsequent cross-presentation, of tumour antigens released by irradiation-induced necrosis of the cancer cells. Elimination of the tumour-associated stromal cells meant that any remaining tumour cells could no longer survive.