evidence of increased responsiveness to this cytokine. IL-21 is a recently identified member of the γc cytokine family, other members of which (such as IL-7) mediate T-cell proliferation and survival. However, in contrast to IL-7, IL-21 did not support the survival of T cells *in vitro*. The IL-21R$^+$ T cells of NOD mice proliferate rapidly but do not survive, leading to low numbers of long-lived memory T cells. The observation that stimulated T cells have a short life was supported by their failure to upregulate expression of the anti-apoptotic molecules Bcl-2 or Bcl-X_L. The important role of IL-21 in autoimmune susceptibility in this model ties in with the fact that the gene encoding IL-21 lies in a known NOD susceptibility locus on chromosome 3.

Sarvetnick and colleagues suggest that a lymphopenic environment favours the proliferation of those T cells specific for readily available antigens. In most cases, this will be autoreactive T cells that have escaped deletion in the thymus. Being 'too clean', particularly during childhood, could create such a lymphopenic environment in humans by reducing the constant stimulation of our immune systems by bacteria and viruses in the environment. This could explain the increasing prevalence of autoimmune diseases in modern 'hygienic' societies.

Kirsty Minton

References and links

ORIGINAL RESEARCH PAPER King, C. *et al.* Homeostatic expansion of T cells during immune insufficiency generates autoimmunity. *Cell* **117**, 265–277 (2004)

Finally, by targeting HIV-1 directly with neutralizing gp120-specific antibodies and a CD4–immunoglobulin fusion protein, both localized infection of cervical tissue and transfer of infectious virus by migratory cells were inhibited.

The design of novel microbicides that provide effective protection from sexual transmission of HIV relies on a detailed understanding of viral attachment and infection. This report indicates the main receptors involved in these processes in human cervical tissue and so might help towards the development of highly specific microbicides.

Lucy Bird

References and links

ORIGINAL RESEARCH PAPER Hu, Q. *et al.* Blockade of attachment and fusion receptors inhibits HIV-1 infection of human cervical tissue. *J. Exp. Med.* **199**, 1065–1075 (2004)

FURTHER READING Davis, C. W. & Doms, R. W. HIV transmission: closing all the doors. *J. Exp. Med.* **199**, 1037–1040 (2004)

IN BRIEF

STRUCTURE

Supine orientation of a murine MHC class I molecule on the membrane bilayer.

Mitra, A. K. *et al. Curr. Biol.* **14**, 718–724 (2004)

Previous studies looking at the structure of MHC molecules have used recombinant forms consisting of only the extracellular domains. However, these structures do not take into account interactions with specific lipid microdomains of the plasma membrane. To address this, Luc Teyton and colleagues used electron microscopy to analyse the extracellular domains of the MHC class I molecule H–2K^b tethered to a lipid bilayer by a histidine tag. Surprisingly, the MHC molecule was shown to lie on its side parallel to the membrane, rather than standing up perpendicular to the membrane as is usually depicted. This orientation was maintained by ionic interactions between lipid head groups in the membrane and the length of the MHC protein. As the supine orientation was shown to be optimal for binding of the co-receptor CD8, changes in MHC orientation might be another way to regulate T-cell-receptor signalling.

SIGNALLING

The cell-surface receptor SLAM controls T cell and macrophage functions.

Wang, N. *et al. J. Exp. Med.* **199**, 1255–1264 (2004)

In this study, mice deficient for signalling lymphocyte activation molecule (SLAM, also known as CD150) were generated and used to analyse the specific contribution of SLAM to immune responses. SLAM-mediated signalling occurs through SLAM-associated protein (SAP), and SAP-deficient mice have a severe X-linked immunodeficiency. As SAP also mediates signalling through five other SLAM-related receptors, the precise contribution of SLAM to the immunodeficiency was unknown. The SLAM-deficient mice had impaired macrophage responses to lipopolysaccharide and increased susceptibility to infection with *Leishmania major*, as well as defective T_H2-cell responses. This indicates that SLAM functions as a co-receptor for signalling through Toll-like receptor 4 and the T-cell receptor.

INNATE IMMUNITY

Nucleic acid is a novel ligand for innate immune pattern recognition collectins surfactant proteins A and D and mannose-binding lectin.

Palaniyar, N. *et al. J. Biol. Chem.* 15 May 2004 (doi:10.1074/jbc.M403763200)

Collectins, including surfactant protein D (SP-D), are extracellular innate immune proteins known to bind microbial carbohydrate patterns. In this study, SP-D was shown to bind linear plasmid DNA directly, as well as synthetic oligonucleotides, even at high salt concentrations. Whereas this strong interaction was mediated largely by the collagen-like region of SP-D, electron microscopy indicated that the globular regions of the molecule also associated with DNA. Furthermore, because SP-D co-localized with the DNA of apoptotic cells, the authors suggest that SP-D functions as an opsonin, binding the DNA of apoptotic cells to enhance their clearance.