IN BRIEF

INNATE IMMUNITY

Dectin-1 mediates the biological effects of β-glucans.

Brown, G. D. *et al. J. Exp. Med.* **197**, 1119–1124 (2003)

Collaborative induction of inflammatory responses by dectin-1 and toll-like receptor 2.

Gantner, B. N. *et al. J. Exp. Med.* **197**, 1107–1117 (2003)

Dectin-1 — a recently identified receptor for fungus-derived β-glucan — is a transmembrane receptor that contains an extracellular lectin-like carbohydrate-recognition domain and an immunoreceptor tyrosine-based activation motif (ITAM) in its cytoplasmic tail. It is highly expressed by macrophages and neutrophils, and is also expressed by dendritic cells and some T cells. These two studies now show that dectin-1 collaborates with Toll-like receptors (TLRs) in the recognition of microorganisms. Signalling through dectin-1 results in phosphorylation of the ITAM and leads to phagocytosis and the production of reactive oxygen species, and TLR engagement leads to the production of pro-inflammatory cytokines. Simultaneous engagement of both receptors produces a synergistic effect. These results show that inflammatory responses to microorganisms result from collaborative recognition of distinct microbial components.

AUTOIMMUNITY

Immunoregulation of a viral model of multiple sclerosis using the synthetic cannabinoid R(+)WIN55,212.

Croxford, J. L. & Miller, S. D. *J. Clin. Invest.* **111**, 1231–1240 (2003)

Some patients suffering from multiple sclerosis (MS) use cannabis to alleviate symptoms of the disease, and several studies are on-going to investigate the basis of these effects. In this study, the immunoregulatory effects of a synthetic cannabinoid-receptor agonist were examined using Theiler's mouse encephalitis virus-induced demyelinating disease — a T helper 1 (T_H1)-mediated disease — as a model of MS. Treatment with the agonist at various timepoints inhibited progression of the clinical disease. This was associated with a reduced capacity to generate T_H1 cells and down-regulated T_H1-cell effector function.

T-CELL DEVELOPMENT

In vitro generation of T lymphocytes from embryonic stem cell-derived pre-hematopoietic progenitors.

de Pooter, R. F. *et al. Blood* 8 May 2003 (DOI: 10.1182/blood-2003-01-0224)

Embryonic stem (ES) cells can differentiate into all lineages of blood cells *in vivo*, and are useful tools for studying haematopoiesis *in vitro*. Although ES cell-derived precursors have been shown to develop into B cells and natural killer cells *in vitro*, their T-cell potential has not yet been shown. Here, an early ES cell-derived population of $Flk1^+CD45^-$ pre-haematopoietic precursors that can generate T cells *in vitro* was defined, which should aid future *in vitro* studies of T-cell commitment and differentiation.

HIV

Close encounters

HIV infection spreads through the closest of human interactions and now, new research shows that the virus can also take advantage of intimate contacts between cells of the immune system to aid infection of its principal target, the $CD4^+$ T cell.

Dendritic cells (DCs) are the main antigen-presenting cells (APCs) that are involved in the initiation of an immune response. They internalize antigens, which are processed and presented to T cells together with co-stimulatory signals that are essential for T-cell activation. But it seems that HIV has taken advantage of this essential immune interaction: DCs can bind and internalize HIV virions through C-type lectin receptors but, instead of becoming infected, the DCs assist in the infection of T cells. To find out exactly how this happens, David McDonald and co-workers pulsed myeloid-derived DCs with HIV-1, then observed their interactions with T-cell targets using time-lapse fluorescent imaging.

Before T-cell contact, the virus was distributed evenly on or inside the DC but, within minutes, most of it had concentrated in the T-cell–DC contact zone. Internalized HIV was also transported to this site. This redistribution is reminiscent of the formation of structured synapses at the contact region between T cells and APCs. T-cell–DC synapses are a special case, in that they can form in the absence of specific antigen — a process that does not lead to activation but might help T cells to 'sniff out' rare antigen-presenting DCs.

Immunostaining of conjugates between $CD4^+$ T cells and HIV-pulsed DCs showed that CD4 and the adhesion molecule LFA1 (leukocyte function-associated antigen 1) — which are both involved in the antigen-independent synapse — as well as the HIV co-receptors CCR5 (CC-chemokine receptor 5) and CXCR4 (CXC-chemokine receptor 4), were often concentrated at the cell–cell junction. In several of these conjugates, HIV was detected inside the T cell, indicating that infection had occurred across the synapse. This process was even more efficient when the DCs were matured with lipopolysaccharide.

Together, these observations support the idea that HIV has subverted the antigen-independent synapse for its own ends, which takes our appreciation of immune exploitation by HIV to a new level.

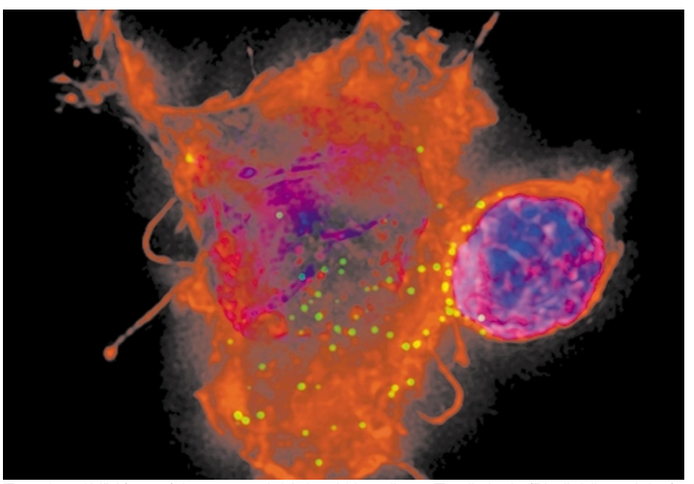
Jennifer Bell

References and links

ORIGINAL RESEARCH PAPER McDonald, D. *et al.* Recruitment of HIV and its receptors to dendritic cell–T-cell junctions. *Science* 1 May 2003 (DOI: 10.1126/science.1084238)

WEB SITE

Thomas Hope's homepage:
http://www.uic.edu/depts/mcmi/faculty/hope.html



Transfer of HIV (green) from a myeloid dendritic cell to a T cell. Actin (Phalloidin staining) is shown in red and DNA (Hoechst staining) is shown in blue. Image is courtesy of D. McDonald and T. Hope, University of Illinois at the Chicago College of Medicine.