IN BRIEF

HIV

HIV-1 envelope protein binds to and signals through integrin $\alpha_4\beta_7$, the gut mucosal homing receptor for peripheral T cells.

Arthos, J. *et al. Nature Immunol.* 10 February 2008 (doi:10.1038/ni1566)

The gut is the main site of HIV-1 replication and $CD4^+$ T-cell loss. But how is preference for the gut achieved? Arthos *et al.* show that this is achieved by the binding of HIV-1 envelope protein gp120 to activated $\alpha_4\beta_7$-integrin, which is specifically induced on $CD4^+$ T cells exposed to retinoic acid in the gut. The interaction is mediated by a conserved tripeptide sequence in gp120 that mimics the binding motif in the host $\alpha_4\beta_7$-integrin ligands. Mutation of this sequence in naturally occurring HIV-1 variants reduced their replicative capacity in the gut. Binding of gp120 to $\alpha_4\beta_7$-integrin also led to the rapid activation of lymphocyte function-associated antigen 1 (LFA1; $\alpha_4\beta_2$-integrin), which is involved in stabilizing cell–cell adhesions, and therefore this may promote viral spread through virological synapses.

IMMUNE RESPONSES

Macrophage and T cell dynamics during the development and disintegration of mycobacterial granulomas.

Egen, J. G. *et al. Immunity* 6 February 2008 (doi:10.1016/j.immuni.2007.12.010)

Organized inflammatory lesions known as granulomas are crucial for a protective response to mycobacterial pathogens. Egen *et al.* use intravital imaging to show for the first time the dynamic nature of granulomas. Granulomas form in the liver ~2 weeks after infection of mice with *Mycobacterium bovis* Bacillus Calmette–Guérin, which is rapidly cleared from the blood by liver-resident macrophages (Kupffer cells). Infected Kupffer cells persist in the liver and initiate granuloma formation by attracting uninfected Kupffer cells and blood monocytes. Activated $CD4^+$ T cells are then recruited in response to tumour-necrosis factor (TNF), which is also required for maintenance of the granuloma structure. In comparison to the relatively static myeloid network, the T cells displayed rapid motility within the confines of the granuloma, making intimate contacts with the myeloid network for the induction of protective immune responses.

REGULATORY T CELLS

Human regulatory T cells inhibit polarization of T helper cells toward antigen-presenting cells via a TGF-β-dependent mechanism.

Esquerré, M. *et al. Proc. Natl Acad. Sci. USA* **105**, 2550–2555 (2008)

The mechanisms used by regulatory T (T_{Reg}) cells to suppress the early activation of T helper (T_H) cells are not fully understood. Early T_H-cell activation by antigen-presenting cells (APCs) requires productive T-cell receptor (TCR) engagement and polarization of the secretory machinery towards the APC. By visualizing the activation of human T_H cells by APCs that were simultaneously interacting with human T_{Reg} cells using confocal microscopy, Esquerré *et al.* showed that functional TCR engagement was not affected by T_{Reg} cells. However, polarization of the secretory machinery in T_H cells to the point of APC contact was reduced in the presence of T_{Reg} cells. This effect was mediated by transforming growth factor-β (TGFβ) produced by the T_{Reg} cells. So, by interfering with polarization of the secretory machinery, T_{Reg} cells can regulate T_H-cell activation.