IN BRIEF

T CELLS

CD8$^+$ T lymphocyte mobilization to virus-infected tissue requires CD4$^+$ T-cell help

Nakanishi, Y. *et al. Nature* **462**, 510–514 (2009)

Effective priming and maintenance of CD8$^+$ T cell responses are known to require 'help' from CD4$^+$ T cells, but is help also required during the effector stage? Now, it is shown that effector cytotoxic T lymphocytes (CTLs) do indeed need CD4$^+$ T cell help to enter virally infected tissue. Virus-specific CTLs that were primed in the presence of CD4$^+$ T cell help and then transferred to mice that lacked CD4$^+$ T cells failed to migrate to the site of herpes simplex virus infection in the vaginal mucosa. CTL recruitment was shown to depend on interferon-γ (IFNγ) production by CD4$^+$ T cells that entered the vagina 2 days earlier. The IFNγ did not act directly on the CTLs but induced the secretion of CXC-chemokine ligand 9 (CXCL9) and CXCL10 by vaginal tissue cells. These chemokines bind to CXC-chemokine receptor 3 expressed by the CTLs, guiding them to the site of infection.

INNATE IMMUNITY

Tuberculous granuloma induction via interaction of a bacterial secreted protein with host epithelium

Volkman, H. E. *et al. Science* 10 Dec 2009 (doi:10.1126/science.1179663)

The immune cell aggregates (granulomas) that form after infection with *Mycobacterium* spp. were originally thought to be protective by containing the infection; we now know that mycobacteria can direct the formation of granulomas as sites for bacterial proliferation and infection of new cells. Ramakrishnan and colleagues show that *Mycobacterium marinum* achieves this in zebrafish by inducing the host protein matrix metalloproteinase 9 (MMP9). The secreted *M. marinum* virulence factor ESAT-6 induces the production of MMP9 by epidermal cells adjacent to the granuloma; in turn, MMP9 recruits additional macrophages to the granuloma. MMP9 activity, the kinetics of granuloma formation and bacterial proliferation were found to be linked. This study provides a mechanistic explanation for the correlation between MMP9 activity and susceptibility to tuberculosis in humans and indicates that MMP9 might be a therapeutic target.

REGULATORY T CELLS

T cell receptor CDR3 sequence but not recognition characteristics distinguish autoreactive effector and Foxp3$^+$ regulatory T cells

Liu, X. *et al. Immunity* 10 Dec 2009 (doi:101.1016/j.immuni.2009.09.023)

This study examined the relationship between effector T cells and regulatory T (T_{Reg}) cells during an autoimmune response to determine whether T_{Reg} cells arise from the conversion of effector T cells or the recruitment of a distinct population. In a T cell receptor-α (TCRα)-transgenic model of experimental autoimmune encephalomyelitis (EAE), the effector T cells and T_{Reg} cells isolated from the central nervous system (CNS) of mice with EAE could be fully distinguished by an acidic versus aliphatic residue at position 4 of the TCRβ complementarity-determining region 3 (CDR3), which shows that they arise from different population reservoirs and argues against their interconversion. In support of conversion being limited, the frequency of shared CDR3 sequences between effector T cells and T_{Reg} cells was similar in pre-immune splenocytes, post-immune splenocytes and CNS-infiltrating cells.