IN BRIEF

IMMUNE RESPONSES

Dendritic cell stimulation by mycobacterial Hsp70 is mediated through CCR5.

Floto, R. A. *et al. Science* 20 Oct 2006 (doi:10.1126/science.1133515)

Activation of an effective host immune response to mycobacterial infection involves activation of dendritic cells (DCs) by mycobacterial heat-shock protein 70 (HSP70). But how do these cells recognize HSP70 and how does this protein induce an effector immune response? This study shows that mycobacterial HSP70 induces calcium signalling in immature DCs through CC-chemokine receptor 5 (CCR5). This recognition and signalling by CCR5 results in DC aggregation, T-cell clustering around the DCs, formation of immunological synapses between the two cell types and the generation of effector immune responses. So, CCR5 is acting as a pattern-recognition receptor for mycobacterial HSP70, an observation that might have implications for the use of HSPs in tumour-directed DC immunotherapy.

REGULATORY T CELLS

Alterations in CD46-mediated Tr1 regulatory T cells in patients with multiple sclerosis.

Astier, A. L. *et al. J. Clin. Invest.* 09 Nov 2006 (doi:10.1172/JCI129251)

Patients with multiple sclerosis (MS) have been shown to have a defect in $CD4^+CD25^+$ regulatory T-cell function. However, the role of other regulatory T-cell subtypes, such as interleukin-10 (IL-10)-producing T_R1 (T regulatory 1) cells, in MS is not known. The complement-regulatory receptor CD46 is a potent co-stimulatory molecule for the development of T_R1 cells. Astier *et al.* showed that co-stimulation of T cells from patients with MS with CD46-specific antibodies results in a striking defect in the induction of T_R1 cells and subsequent IL-10 production compared with T cells from healthy donors. This defect was associated with altered expression of CD46 cytoplasmic isoforms, with an increase in CYT2-isoform expression following activation of T cells from patients with MS through CD46. Therefore, defects in at least two regulatory T-cell subtypes are associated with this autoimmune disease.

T-CELL SIGNALLING

Differential requirement for Lck during primary and memory $CD8^+$ T cell responses.

Tewari, K. *et al. Proc. Natl Acad. Sci. USA* **103**, 16388–16393 (2006)

T-cell receptor (TCR)-dependent signalling has an integral role in the activation and maintenance of T cells. Activation of LCK is one of the first biochemical events that occurs following TCR ligation. But when and with what stringency is LCK required for effective TCR-mediated activation and function? Using mice that express LCK in an inducible T-cell-specific manner, the authors showed an essential requirement for LCK-dependent signalling in the activation and clonal expansion of naive $CD8^+$ T cells. The magnitude of $CD8^+$ T-cell clonal expansion depended on the duration of uninterrupted LCK-dependent TCR signalling. By contrast, maintenance and reactivation of memory $CD8^+$ T cells was normal in LCK-deficient T cells. Therefore, the differentiation of memory $CD8^+$ T cells from naive T cells is associated with a differential requirement of the signalling adaptor LCK.