IN BRIEF

TRANSPLANTATION

Visualizing the innate and adaptive immune responses underlying allograft rejection by two-photon microscopy

Celli, S., Albert, M. L. & Bousso, P. *Nature Med.* 15 May 2011 (doi:10.1038/nm.2376)

This study used real-time two-photon intravital microscopy of a new model of ear skin transplantation to investigate the roles of donor and host cells in the direct and indirect pathways of antigen presentation that lead to T cell activation. The findings show that the first wave of antigen-presenting cells that reaches the draining lymph nodes (DLNs) consists of dermal dendritic cells (DCs) of donor origin that migrate from the graft but die rapidly. The graft is then rapidly infiltrated in an antigen-independent manner by host $CD11b^+$ monocytes and inflammatory DCs, which pick up donor antigens before migrating to the DLNs and cross-priming $CD8^+$ T cells. Activated effector T cells were shown to enter the graft through closed-end recipient blood vessels in the skin surrounding the graft and to accumulate first at the dermis–epidermis junction of the graft before widespread dissemination. This spatiotemporal analysis of allograft rejection provides a new system in which to test potential immunotherapies to block the rejection response.

CO-STIMULATION

Trans-endocytosis of CD80 and CD86: a molecular basis for the cell-extrinsic function of CTLA-4

Qureshi, O. S. *et al. Science* **332**, 600–603 (2011)

The T cell inhibitory function of cytotoxic T lymphocyte antigen 4 (CTLA4) could be mediated through various mechanisms. Although CTLA4 has been proposed to mediate a cell-intrinsic inhibitory signal to T cells through its cytoplasmic domain, other studies have shown that CTLA4 also has cell-extrinsic functions. This paper supports the latter model by showing that CTLA4 expressed by T cells can capture its ligands (CD80 and CD86) from the surface of neighbouring cells through a process of trans-endocytosis that is triggered by T cell receptor stimulation. Endocytosis of CD80 and CD86 is followed by lysosomal degradation. The depletion of CD80 and CD86 from antigen-presenting cells (APCs) prevents the co-stimulation of T cells through the stimulatory receptor CD28. Both $CD4^+$ effector and regulatory T cells were shown to deplete CD80 and CD86 from APCs in a similar manner in *in vitro* and *in vivo* models.

VACCINES

Profound early control of highly pathogenic SIV by an effector memory T-cell vaccine

Hansen, S. G. *et al. Nature* 11 May 2011 (doi:10.1038/nature10003)

A vaccine against simian immunodeficiency virus (SIV) that was generated by expressing SIV genes in a rhesus cytomegalovirus (RhCMV) vector was previously shown to induce mucosal effector memory T (T_{EM}) cell responses, in contrast with vaccines containing non-persistent viral vectors that induce systemic central memory T cell responses. Here, the efficacy of the RhCMV–SIV vaccine was evaluated and RhCMV–SIV-immunized rhesus macaques were shown to have SIV-specific $CD8^+$ T cell responses and a persistent T_{EM} cell phenotype following SIV infection. Moreover, 13 out of 24 vaccinated animals exhibited a transient viraemia that was rapidly controlled, and no SIV nucleic acids could be detected in vaccinated animals 52 weeks or longer after SIV infection. Importantly, these animals had no $CD4^+$ T cell loss, so the authors suggest that the use of persistent viral vectors (such as CMV) in vaccines may promote the early control of SIV and HIV.