IN BRIEF

APOPTOSIS

TRAIL-expressing T cells induce apoptosis of vascular smooth muscle cells in the atherosclerotic plaque.

Sato, K. *et al. J. Exp. Med.* 17 Jan 2006 (doi:10.1084/jem.20051062)

Rupture of atherosclerotic plaques is a frequent cause of acute coronary syndromes (ACSs), such as myocardial infarction. In this paper, plaque-infiltrating activated $CD4^+$ T cells were shown to contribute to plaque instability. *In vitro*, plaque-derived $CD4^+$ T cells could effectively kill vascular smooth-muscle cells (VSMCs). Killing was mediated through death receptor 5 (DR5) expressed by VSMCs, as incubation with antibodies specific for the DR5 ligand TRAIL inhibited T-cell killing of VSMCs. *In vivo*, adoptive transfer of plaque-derived $CD4^+$ T cells to immunodeficient mice bearing human plaque implants resulted in apoptosis of VSMCs, which was prevented by co-administration of TRAIL-specific antibody. Importantly, patients with ACS have a higher frequency of TRAIL-expressing $CD4^+$ T cells in the blood compared with controls, indicating that these cells might be involved in plaque rupture.

T-CELL SIGNALLING

Direct manipulation of activator protein-1 controls thymocyte proliferation *in vitro*.

Thornton, T. M. *et al. Eur. J. Immunol.* **36**, 160–169 (2006)

While studying the role of BATF (activating transcription factor B) in thymocyte proliferation, Thornton *et al.* unexpectedly observed that certain conditions of T-cell stimulation inhibit the transcription of transgenes under the control of the *Lck* promoter, a system that is widely used in T-cell studies. Consistent with the function of BATF as an inhibitor of activator protein 1 (AP1)-driven transcription, stimulation of *Batf*-transgenic T cells with CD3-specific and CD28-specific antibody or concanavalin A inhibited proliferation. However, when these T cells were stimulated with PMA and ionomycin, proliferation was normal. This was the result of unexpected downregulation of *Lck*-promoter-driven transcription and rapid loss of BATF protein. Nevertheless, the authors went on to show that inhibition of AP1 activity by BATF has a direct and reversible effect on T-cell proliferation *in vitro*.

AUTOIMMUNITY

Human plasmacytoid pre-dendritic cells activate NK cells through glucocorticoid-induced tumor necrosis factor receptor-ligand (GITRL).

Hanabuchi, S. *et al. Blood* 5 Jan 2006 (doi:10.1182/blood-2005-08-3419)

To investigate, at the molecular level, how plasmacytoid dendritic cells (pDCs) regulate immune responses, Hanabuchi *et al.* carried out microarray analyses of unactivated human pDCs and pDCs activated by herpes simplex virus 1 or influenza virus A. Expression of mRNA encoding glucocorticoid-induced TNF-receptor-related protein ligand (GITRL) by pDCs was upregulated following activation by viruses. Consistent with this, GITRL expression was increased on the cell surface of pDCs following activation by viruses or CpG DNA. Natural killer (NK) cells express high levels of the receptor for GITRL and pDCs activated by CpG DNA induced NK-cell cytotoxicity and interferon-γ (IFNγ) production in a GITRL-dependent manner. Such GITRL-mediated co-stimulation of NK cells required the presence of IFNα and provides a new mechanism of NK-cell–pDC crosstalk.

IMMUNE RESPONSES

A single ER protein for multiple processes

Reporting in *Nature Immunology*, Bruce Beutler and colleagues have identified an endoplasmic reticulum (ER)-resident protein that is crucial to both Toll-like receptor (TLR) signalling and antigen presentation.

Unlike other TLRs, which are expressed on the cell surface, TLR3, TLR7 and TLR9 are located mainly in endosomes, and they detect nucleic acids. Using the random germline mutagen *N*-ethyl-*N*-nitrosourea and by screening for mutants with defective TLR signalling, Beutler and colleagues identified a mutant mouse, denoted triple D (3d), that is defective at detecting nucleic acids but not other TLR ligands. The 3d mutant mice had increased susceptibility to infection with mouse cytomegalovirus, resistance to which is known to require TLR3- and TLR9-signalling pathways. Moreover, the robust interleukin-12 response that is normally induced against a mutant strain of *Listeria monocytogenes* that cannot escape endosomes was severely impaired in macrophages from 3d mutant mice.

Surprisingly, in addition to these innate sensing defects, mice that were homozygous for the 3d mutation also had impaired MHC class II antigen presentation and defective cross-presentation of exogen ous antigen by MHC class I molecules.

The authors localized the 3d mutation to the gene Unc93b1, which encodes a protein of unknown function. Transfection of 3d-mutant-bone-marrow-derived dendritic cells with wild-type Unc93b1 corrected the nucleic-acid-sensing defect and correlated with mouse genotype.

As the endosomal–lysosomal compartment is required by both the TLR-signalling and antigen-presentation pathways that are impaired in 3d-mutant mice, the authors were surprised to observe that UNC93B is expressed mainly in the ER and not in endosomes.

Although further studies are required to identify how UNC93B is involved in these two processes, the authors ruled out a role for UNC93B in endosome acidification and in cellular localization of TLRs and MHC molecules.

Lucy Bird

ORIGINAL RESEARCH PAPERS Tabeta, K. *et al.* The *Unc93b1* mutation 3d disrupts exogenous antigen presentation and signaling via Toll-like receptors 3, 7 and 9. *Nature Immunol.* 15 Jan 2006 (doi:10.1038/ni1297)