ANTIGEN PRESENTATION

γδ T cells turn professional

Human γδ T cells can now join dendritic cells (DCs) in the professional antigen-presenting cell (APC) club — a paper recently published in *Science* reports that human γδ T cells that have been activated *in vitro* display typical cell-surface markers of APCs and can stimulate the proliferation and differentiation of αβ T cells.

γδ T cells differ from αβ T cells in many ways. Human γδ T cells can recognize small non-peptidic antigens that are derived from microorganisms or necrotic host cells and that do not require antigen processing, and this recognition does not depend on classical MHC class I or class II molecules. In addition, their effector functions include both innate and adaptive immune functions (that is, secretion of chemokines and cytokines, as well as the ability to provide B-cell help and to develop memory function).

In human peripheral blood, most γδ T cells express the Vγ2Vδ2$^+$ T-cell receptor (TCR) and are referred to as Vδ2$^+$ T cells. Following TCR triggering, these cells transiently upregulate the lymph-node homing receptor CC-chemokine receptor 7 (CCR7) and can be observed in the lymph nodes that drain mucosal tissues. In this study, tonsillar γδ T cells were shown to express CD69, a cell-surface marker that is associated with *in vitro*-stimulated cells, as well as MHC class II molecules and a range of co-stimulatory and adhesion molecules. Similarly, peripheral-blood Vδ2$^+$ T cells stimulated with isopentenyl pyrophosphate (IPP), the prototypical ligand for these cells, expressed various cell-surface markers that are associated with professional APCs, and these markers were almost identical to those expressed by monocyte-derived DCs stimulated with lipopolysaccharide (LPS).

The ability to migrate to lymph nodes and the expression of inducible markers of APCs prompted the authors to examine a potential role for Vδ2$^+$ T cells in antigen presentation to αβ T cells. First, they measured the ability of IPP-stimulated Vδ2$^+$ T cells to stimulate CD4$^+$ αβ T cells in a mixed lymphocyte reaction and in primary responses to superantigen. The proliferation of CD4$^+$ T cells and their differentiation into T-helper cells occurred to a similar extent to that elicited by LPS-matured DCs.

Next, the ability of Vδ2$^+$ T cells to process antigen for presentation to αβ T cells was examined. The authors used two model antigens — tetanus toxoid (TT) and the complex mixture of proteins in *Mycobacterium tuberculosis* protein derivative (PPD) — and they observed proliferation of CD4$^+$ and CD8$^+$ αβ T cells in response to activated Vδ2$^+$ T cells presenting either TT or PPD. Presentation was dependent on intracellular processing, because blockade of protein degradation and peptide loading onto MHC class II molecules, using chloroquine, was shown to inhibit proliferation.

These results show a new role for γδ T cells, in the initiation of adaptive immune responses. Although it will be important to examine the physiological relevance of this function, it seems that Vδ2$^+$ T cells could have a role as APCs in initiating immune responses in inflammatory and/or infectious situations.

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References and links

ORIGINAL RESEARCH PAPER Brandes, M., Willimann, K. & Moser, B. Professional antigen-presentation function by human γδ T cells. *Science* 2 Jun 2005 (doi:10.1126/science.1110267)