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CD4 and CD8 T cells differ in their proliferative responses

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Alice Lorenzi,[Aff1]

Aff1 Department of Rheumatology, University of Leeds, UK

Keywords

Proliferation, transgenic, T lymphocyte

Context

Major histocompatibility complex (MHC) class I and II restricted T lymphocytes serve independent but integrated roles in the adaptive immune response to infection - responding to peptide antigens derived from intracytoplasmic and intravesicular cell compartments respectively - thus protecting against different classes of pathogen. The *in vivo* proliferative responses of $CD8^+$ T cells have recently been demonstrated to be independent of both antigen concentration and duration of exposure, resulting in predetermined clonal expansion and differentiation. Less is known about $CD4^+$ T-cell proliferative responses.

Significant findings

This study reports a labeled (5-carboxyfluorescein diacetate succinimidyl ester [CFSE]), adoptive transfer system to quantitate antigen specific (transgenic) $CD4^+$ T-cell responses to recombinant peptide (*Listeria monocytogenes* [LM] expressing ovalbumin [OVA]). Proliferative responses to peptide were assessed by the following the decay of CFSE fluorescence in the OVA specific $CD4^+$ cells by flow cytometry. $CD4^+$ and $CD8^+$ responses (in a similar, viral peptide based model) were demonstrated to be very different. In response to a similar stimulus, $CD8^+$ T cells expanded at least 10-fold more than $CD4^+$ T cells. This was assessed by both CFSE decay and population size at day 8. Additionally, a much smaller percentage of $CD4^+$ cells differentiated to effector Interferon-? production (27% $CD4^+$ versus >85% $CD8^+$). This difference was noted even after prolonged exposure to antigen.

The effect of the specific peptide used in the study (LM), or the efficiency of its presentation by MHC I versus MHC II, on T-cell responses was tested and shown not to affect basic proliferative responses.

Furthermore, the transgenic cells used and the viral vector for OVA peptide were varied without affecting the original findings. Stimulation with anti-CD3 in the presence of IL-2 with and without costimulation from anti-CD28 also resulted in proliferative responses similar to those of the described model.

Comments

This work suggests that an 'intrinsic mechanism' controls proliferative responses to antigen, which is different in $CD4^+$ and $CD8^+$ cells. The point in cell ontogeny at which this mechanism is differentiated remains to be elucidated. The impact of different cytokine environments on the proliferative responses of T-lymphocyte subsets would be interesting to study. Control of lymphocyte proliferation is vital to the maintainance of homeostasis in the immune response. A role for dysregulation of these 'intrinsic' mechanisms of proliferation could be important in the pathogenesis of autoimmune disease.

Methods

Transgenic mice, flow cytometry

References

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