HIGHLIGHTS

IMMUNE REGULATION

Competitive success

Affinity maturation is a well-understood process by which the affinity of antibodies produced by B cells increases during an immune response. It has recently become evident that T-cell responses can also undergo affinity maturation — repeated exposure to antigen results in the development of an increasingly restricted T-cell repertoire consisting of T cells with greater affinity for antigen. Reporting in *Nature Immunology*, Kedl and colleagues now describe a mechanism for affinity maturation in T cells. High-affinity T cells successfully compete with low-affinity T cells by inducing the loss of peptide–MHC complexes from antigen-presenting cells (APCs), therefore reducing the likelihood of APC interaction with the low-affinity cells.

Competition between T cells was shown *in vivo* using transgenic T cells in adoptive-transfer experiments. T cells with the OT1 T-cell receptor (TCR) specific for an ovalbumin (OVA) peptide were transferred into non-transgenic animals, and the mice were challenged with dendritic cells (DCs) loaded with OVA. OVA–MHC tetramers were used to assess the response of the endogenous T cells — the transferred OT1 T cells almost completely blocked the host T-cell response. The group then evaluated the ability of high- and low-affinity T cells, generated *in vivo*, to modulate host T-cell responses. C57BL/6 mice were challenged with OVA-expressing vaccinia virus and left to rest for 25 days to allow a memory response to develop. Transfer of high-affinity T cells followed by challenge with OVA-pulsed DCs resulted in almost complete inhibition of the host T-cell response, but transfer of low-affinity T cells produced much less inhibition. The competition between cells of the same peptide–MHC specificity was more efficient than competition between T cells with differing specificity.

Next, Kedl and colleagues examined whether removal of MHC–peptide complexes from the APC surface had a role in T-cell competition. DCs from GFP (green fluorescent protein) transgenic mice were pulsed with OVA and transferred intradermally into C57/BL6 mice. A monoclonal antibody was used to measure the amount of OVA–MHC expressed on DCs after transfer in the presence or absence of OT1 T cells. When OT1 T cells were co-transferred, expression of OVA–MHC on the DC surface decreased rapidly and was virtually undetectable after 48 hours.

These results support a model of T-cell competition that ensures the success of high-affinity T cells and improved immune responses. So, although current research emphasises the importance of APCs in controlling immune responses, it seems that the T cells themselves might have an important role.

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References and links

ORIGINAL RESEARCH PAPER Kedl, R. M., Schaefer, B. C., Kappler, J. W. & Marrack, P. T cells down-modulate peptide–MHC complexes on APCs *in vivo*. *Nature Immunol.* **3**, 27–32 (2002)