IN BRIEF

TOLERANCE

Genetic regulation of peripheral tolerance

This study examines the molecular programmes that determine the proliferative defect of self-reactive CD8⁺T cells in response to antigen; this defect is a component of peripheral tolerance. Using a T cell receptor-transgenic mouse model, the authors showed that self-reactive tolerant T cells can respond to immunization with their cognate antigen during homeostatic proliferation in lymphopenic recipients, but that these 'rescued' T cells reacquire tolerance once the hosts are lymphoreplete, even in the absence of the self antigen ('re-tolerized' T cells). Microarray analysis showed that tolerant T cells have a specific gene-expression signature, which was largely replaced by a gene signature similar to that of memory T cells in rescued T cells. Re-tolerized T cells re-established the gene signature of tolerant T cells, and the authors identified microRNA-181a as a possible key regulator of a genetic memory of tolerance. ORIGINAL RESEARCH PAPER Schietinger, A. et al. Rescued tolerant CD8 T cells are preprogrammed to reestablish the tolerant state. Science 335, 723-727 (2012)

TECHNIQUE

Visualizing $\gamma\delta$ T cells in the epidermis

Using a new imaging approach known as intravital dynamicsimmunosignal correlative microscopy — which enables single-cell dynamics to be related to intracellular signalling — the authors studied the *in vivo* interactions of $\gamma\delta$ dendritic epidermal T cells (DETCs). They showed that DETCs have multiple long-lived dendrites, containing clusters of T cell receptors (TCRs) and tyrosine-phosphorylated proteins, that are anchored in the apical epidermis (specifically at squamous keratinocyte tight junctions). Dendrite anchoring correlated with the presence of the V γ 5 TCR, which was shown to be activated independently of the environmental microbiota. Further experiments suggested that $V\gamma 5^+$ DETCs are physiologically activated in the steady state by a self antigen in the epidermis, resulting in TCR clusters on immobilized DETC dendrites that are similar to earlyintermediate immunological synapses. A physiological ligand for $\gamma\delta$ DETCs (rather than a stress-induced ligand) could maintain these cells in a state of pre-activation targeted at the important barrier-forming tight junctions.

ORIGINAL RESEARCH PAPER Chodaczek, G. *et al.* Body-barrier surveillance by epidermal γδTCRs. *Nature Immunol.* 12 Feb 2012 (doi:10.1038/ni.2240)

NATURAL KILLER T CELLS

Defining iNKT cell subpopulations

This study clarifies our view of the heterogeneity of invariant natural killer T (iNKT) cells by defining the development and functional properties of distinct subsets in mice. Interleukin-17 receptor B (IL-17RB)-expressing iNKT cells produce the T helper 2 (T_2)-type cytokines IL-9, IL-10 and IL-13 and the T_17-type cytokines IL-17A and IL-22, whereas IL-17RB- iNKT cells produce mainly the T₁1-type cytokine interferon-γ. IL-17RB⁺ and IL-17RB⁻ iNKT cell subsets were shown to develop independently in the thymus. Further studies showed three distinct iNKT cell subpopulations in the thymus: IL-23-responsive CD4-IL-17RB+ cells that produce T_{μ} 17-type cytokines; IL-25-responsive CD4⁺IL-17RB⁺ cells that produce T_{μ}^{2} - and T_{μ}^{1} 7-type cytokines; and IL-12-responsive CD4⁺ or CD4⁻ IL-17RB⁻ cells that produce T₁₁-type cytokines. These populations also exist as phenotypically and functionally distinct subtypes with different distribution patterns in the periphery, and it will be interesting to determine their differential roles in pathological conditions.

ORIGINAL RESEARCH PAPER Watarai, H. et al. Development and function of invariant natural killer T cells producing T₁₁2- and T₁₁17-cytokines. PLoS Biol. **10**, e1001255 (2012)