IN BRIEF

T CELL MEMORY

Identifying memory CD4$^+$ T cell precursors

Two groups have tracked CD4$^+$ T cells in infected mice to determine how memory CD4$^+$ T cell populations arise *in vivo*. Pepper *et al.* identified two CD4$^+$ T cell populations that were present in the early stages of *Listeria monocytogenes* infection and that gave rise to distinct memory subsets. The effector T cells of one population expressed T-bet and differentiated into T helper 1 (T_H1)-type effector memory T cells in an interleukin-2-dependent manner. The other CD4$^+$ T cell population expressed BCL-6 and CXCR5, depended on B cell-delivered signals through ICOS and gave rise to T central memory (T_{CM}) cells. Thus, the precursor T_{CM} cells closely resembled follicular helper T (T_{FH}) cells, which promote B cell antibody responses. However, the T_{CM} cells localized to the T cell areas of lymph nodes and did not retain BCL-6 expression. The authors suggest that CXCR5$^+$ effector T cells that maintain BCL-6 expression may differentiate into T_{FH} cells; the remainder may become T_{CM} cells. Marshall *et al.* studied acute LCMV infection and also described two populations of effector CD4$^+$ T cells with distinct memory potential. The CD4$^+$ T cells of the first population were T-bet^{hi}LY6C^{hi} and resembled terminally differentiated effectors. The second T cell population had a T-bet^{mid}LY6C^{mid} phenotype, was longer-lived and showed increased proliferation in response to secondary viral infection. This latter population showed a gene-expression profile that was remarkably similar to that of mature memory CD4$^+$ T cells, suggesting that the T-bet^{mid}LY6C^{mid}CD4$^+$ T cells are memory cell precursors and gain memory cell attributes rapidly following virus infection.

ORIGINAL RESEARCH PAPERS Pepper, M. *et al.* Opposing signals from the Bcl6 transcription factor and the interleukin-2 receptor generate T helper 1 central and effector memory cells. *Immunity* **35**, 583–595 (2011) | Marshall, H. D. *et al.* Differential expression of Ly6C and T-bet distinguish effector and memory Th1 CD4$^+$ cell properties during viral infection. *Immunity* **35**, 633–646 (2011)

T CELL MEMORY

The ID of memory CD8$^+$ T cells

Two recent studies published in *Nature Immunology* describe the differential expression of the transcriptional regulator ID3 in short-lived effector and long-lived memory CD8$^+$ T cell subsets and its role in memory CD8$^+$ T cell generation. Yang *et al.* identified two distinct CD8$^+$ T cell populations (ID3^{low} and ID3^{hi}) in infected mice. ID3 expression preceded the expression of long-lived memory markers, and ID3^{hi}CD8$^+$ T cells shared the phenotype and cytokine profile of long-lived memory T cells. Moreover, ID3^{hi}CD8$^+$ T cells generated long-lived memory cells following their transfer into infected hosts. Ji *et al.* observed that the transcriptional repressor BLIMP1 (also known as PRDM1) — which is expressed in short-lived effector CD8$^+$ T cells — downregulates ID3 expression. Both groups showed that ID3 is required for the generation of long-lived memory T cells because it promotes T cell survival, and this may be linked to ID3-dependent expression of genes involved in DNA repair (Ji *et al.*). Although both groups reported that ID3 does not influence the expression of ID2, Yang *et al.* found that loss of ID2 expression results in ID3 upregulation. Interleukin-2 (IL-2), IL-12 and IL-21 were shown to upregulate ID2 and downregulate ID3 expression, suggesting that the balance between ID2 and ID3 regulates memory CD8$^+$ T cell generation in response to cytokines.

ORIGINAL RESEARCH PAPERS Ji, Y. *et al.* Repression of the DNA-binding inhibitor Id3 by Blimp-1 limits the formation of memory CD8$^+$ T cells. *Nature Immunol.* 6 Nov 2011 (doi:10.1038/ni.2153) | Yang, C. Y. *et al.* The transcriptional regulators Id2 and Id3 control the formation of distinct memory CD8$^+$ T cell subsets. *Nature Immunol.* 6 Nov 2011 (doi:10.1038/ni.2158)