T-CELL MEMORY

Memory T cells count their ancestors

Although it is well established that there are two memory T-cell populations — central memory T (T_{CM}) cells and effector memory T (T_{EM}) cells — which can be identified by distinct homing characteristics and effector functions, it is not clear whether these are distinct lineages or whether the development of one subset depends on the other. New data published in *Nature Immunology* now indicate that the naive T-cell precursor frequency determines which of these developmental schemes occurs.

T_{CM} cells express CC-chemokine receptor 7 (CCR7) and CD62L, and are found in lymphoid organs. By contrast, T_{EM} cells do not express either CCR7 or CD62L, and they reside in non-lymphoid tissues and mediate effector functions immediately after activation. Previous studies have led to the emergence of three models of memory T-cell differentiation: first, that T_{CM} cells are a continual source of T_{EM} cells; second, that T_{CM} and T_{EM} cells are distinct lineages; and third, that, over time, T_{EM} cells convert to T_{CM} cells. To further investigate the relationship between T_{CM} and T_{EM} cells, Marzo *et al.* assessed the phenotypic stability of T_{CM} and T_{EM} cells (defined as $CD62L^{hi}$ and $CD62L^{low}$, respectively) after transferring the cells to separate naive recipients. When the transferred memory T-cell subsets were isolated from mice that were infected with ovalbumin-expressing vesicular stomatitis virus (VSV-OVA) and that had previously been recipients of naive $CD8^+$ T cells expressing the OT-I T-cell receptor (OT-I TCR; which is specific for a peptide derived from OVA), the T_{CM} cells remained $CD62L^{hi}$, whereas almost half of the T_{EM} cells converted to T_{CM} cells. By contrast, when polyclonal OVA-specific $CD8^+$ memory T-cell subsets were isolated from wild-type mice infected with VSV-OVA, both T_{CM} and T_{EM} cells maintained their original phenotype. Consistent with a role for naive T-cell precursor frequency in determining $CD8^+$ memory T-cell phenotype, if the number of naive $CD8^+$OT-I TCR^+ T cells transferred to mice that were subsequently infected with VSV-OVA was markedly decreased, then OVA-specific T_{EM} cells did not convert to T_{CM} cells when transferred to secondary recipients.

These data have led the authors to suggest that memory T-cell differentiation fits different models depending on the initial frequency of naive precursors: a high initial frequency of naive precursors leads to the development of T_{CM} cells, T_{EM} cells and a population of $CD62L^{low}$ cells (that is, cells that are phenotypically T_{EM} cells) that can convert to T_{CM} cells, whereas a low initial frequency of naive precursors, such as occurs physiologically, leads to the development of T_{CM} cells and T_{EM} cells as distinct lineages.

Karen Honey

References and links

ORIGINAL RESEARCH PAPER Marzo, A. L. *et al.* Initial T cell frequency dictates memory $CD8^+$ T cell lineage commitment. *Nature Immunol.* **6**, 793–799 (2005)