

Regulating Production and Homeostasis of Naïve and Memory T Cells

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Homeostatic mechanisms regulate the overall size and composition of naïve and memory T cell pools. The primary factors responsible for controlling homeostasis of naïve CD4⁺ and CD8⁺ cells appear to be the self-MHC/peptide ligands expressed on APC and the cytokine, IL-7, presumably produced by non-lymphoid cells. The overall size of the naïve T cell pool thus appears to reflect the basal level of IL-7 produced in the body. In support of this idea, transgenic mice over-expressing IL-7 possess enormously elevated numbers (10-20x the norm) of mature T cells. Strikingly, whereas the majority of CD4⁺ cells in IL-7 transgenic mice is naïve phenotype, most of the CD8⁺ cells are memory (CD44^{hi} CD122^{hi}) phenotype. The survival of CD44^{hi} CD8⁺ cells in IL-7 transgenic mice is IL-15-independent, indicating a role for IL-7 in supporting homeostasis of memory CD8⁺ cells. In support of this idea, wild-type CD44^{hi} CD8⁺ cells underwent efficient homeostatic proliferation in T cell-depleted IL-15⁻ mice, whereas no proliferation was observed when mice were depleted of both IL-7 and IL-15. In addition, competition experiments involving co-injection of large numbers of purified bystander T cells support the idea that an overlapping component, presumably IL-7, regulates both homeostasis of naïve cells and memory CD8⁺ cells. These experiments also indicate that homeostasis of memory CD4⁺ cells is regulated independently of other subsets of T cells.

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