

Stephen C. Jameson

Lymphocyte Homeostasis

Steve Jameson

University of Minnesota, Center for Immunology.

Lymphocyte maintenance is achieved, in part, by homeostatic mechanisms acting on mature cells which increase or decrease the size of specific lymphoid subsets in the absence of foreign antigen stimulation. Persistence of lymphocyte numbers can be achieved by their simple survival, or by active expansion (often called homeostatic proliferation) to compensate for lymphocyte deficiency. Recent studies have shown that the lymphocyte's cytokine and antigen receptors can play an essential role in both types of homeostasis.

Homeostatic mechanisms have been intensely studied in T cells. Naïve T cell survival and homeostatic proliferation are conditioned by available cytokines (including IL-7 and IL-12) and by engagement of the TCR with self peptide/MHC complexes. Cytokine requirements for maintenance of memory T cells are different, with IL-7 and IL-15 both playing a role in CD8 memory persistence but neither cytokine being required for CD4 memory homeostasis.

Here we extend these studies to the NK subset. NK cells are a critical arm of the innate immune system, responding to infected, transformed and generally stressed cells. It is currently unclear whether homeostatic mechanisms are involved in maintaining the NK pool. Here we show that mature NK cells can be induced to proliferate in response to NK deficiency, in a manner analogous to T cell homeostatic proliferation. NK functional properties and most phenotypic markers are maintained throughout this process. Furthermore, we show that NK cell survival requires IL-15. Thus, NK cells exposed to an IL-15 deficient environment rapidly die. Interestingly, rapid loss of NK cells is also observed when these cells are exposed to an IL-15R α deficient environment, suggesting that IL-15 sensitivity of bystander cells is critical for NK cell persistence.

The requirements for homeostasis of different lymphocyte subsets will be discussed, as will be the impact on homeostasis of competition between lymphoid populations for limiting resources (such as cytokines and specific peptide/MHC ligands).

References:

1. **Jameson S.C.** (2002) Maintaining the norm: T-Cell homeostasis. *Nature Reviews: Immunology*. **2**:547-556.
2. Kieper, W. C., M. Prlic, C. S. Schmidt, M.F. Mescher and **S.C. Jameson**. (2001) IL-12 enhances CD8 T cell homeostatic expansion. *J. Immunol.* **166**:5515-5521
3. Prlic, M., B. R. Blazar, A. Khoruts, T. Zell and **S.C. Jameson**. (2001) Homeostatic expansion occurs independently of costimulatory signals *J.Immunol.* **167**:5664-5668
4. Prlic M., B. R. Blazar, M. A. Farrar, and **S. C. Jameson**. In vivo survival and homeostatic proliferation of NK cells. (submitted)