

Requirements for Memory CD8 T Cell Function and Survival in Non-lymphoid Tissues

Leo Lefrançois

University of Connecticut Health Center, Department of Medicine,
Division of Rheumatology, Farmington, Connecticut

The generation of immunological memory is crucial for the establishment of protection against secondary microbial infections. Many of the rules governing the generation, migration, and maintenance of memory T cells remain to be elucidated. Analysis of primary and memory responses induced by infection with vesicular stomatitis virus or with *Listeria monocytogenes* revealed that antigen-specific CD8 and CD4 T cells were present in many non-lymphoid tissues. Moreover, CD8 memory T cells in non-lymphoid tissues retained effector levels of lytic activity, as opposed to their splenic counterparts with low lytic ability. The requirement for cytokines in controlling lymphoid and non-lymphoid CD8 T cell responses was also examined. IL-7 was essential for survival of naïve CD8 T cells and was important for generation of a normal memory population. Autocrine IL-2 preferentially controlled the magnitude of the primary response in non-lymphoid tissues but had little effect on memory cells. IL-15 was utilized for optimal expansion of primary CD8 T cells and had a further role in maintenance of antigen-specific memory cells. In contrast, IL-15Ra played no role in primary expansion and was only partially responsible for CD8 memory T cell proliferation/survival. Overall, our findings revealed the existence of distinct CD8 memory T cell pools based on function and location and further demonstrated that gC cytokines controlled distinct stages of the CD8 T cell immune response.

Supported by grants from the National Institutes of Health.

References:

Schluns, K.S., Kieper, W.C., Jameson, S.C., Lefrançois, L. 2000. Interleukin-7 mediates the homeostasis of naïve and memory CD8 T cells in vivo. *Nature Immunol.* 1:426-432.

Masopust, D., Jiang, J., Shen, H. and Lefrançois, L. 2001. Direct analysis of the dynamics of the intestinal mucosa CD8 T cell response to systemic virus infection. *J.Immunol.*, 166:2348-2356.

Pope, C., Kim, S.K., Marzo, A., Masopust, D., Williams, K., Jiang, J., Shen, H. and Lefrançois, L. 2001. Organ-specific regulation of the CD8 T cell response to *Listeria monocytogenes* infection. *J.Immunol.*, 166:3402-3409.

Masopust, D., Vezys, V., Marzo, A. and Lefrançois, L. 2001. Preferential localization of effector memory cells in nonlymphoid tissue. *Science* 291:2413-2417.