

Memory CD8 T Cell Subsets: Lineage Relationship and Protective Immunity

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Memory CD8 T cells are an important component of protective immunity. Recent studies have shown that memory T cells can be divided into two subsets; “central” (T_{CM}) and “effector” (T_{EM}) memory cells. However, three important questions remain unanswered. First, what is the lineage relationship between these two memory T cell subsets? Second, which subset has the greater capacity to persist long-term *in vivo*? And, third, which subset is more effective in protective immunity? Our results show that T_{CM} have the greater capacity to persist long-term *in vivo* and are more efficient on a per cell basis than T_{EM} in conferring protective immunity because of their increased proliferative potential. In addition, we show that T_{CM} are derived from T_{EM} and that the duration of this differentiation is programmed within the first week after immunization. Based on these findings we propose that T_{CM} and T_{EM} do not necessarily represent two distinct subsets, but are part of a continuum that culminates in the differentiation of memory CD8 T cells that have finally acquired the two salient properties of memory cells; the “stem cell” like ability to undergo antigen-independent proliferative renewal for long-term maintenance, and the ability to rapidly proliferate and acquire effector functions upon reinfection.