

In vivo Determination of Effector and Memory CD8 T cell Cytotoxicity

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In this study, we have reevaluated the cytotoxic activity of anti-viral CD8 T cells at both the activated effector and resting memory cell stage of differentiation using an *in vivo* killing assay. In only fifteen minutes, seventy five percent of the adoptively transferred target cells were killed in LCMV infected mice, indicating that CD8 T cells can destroy target cells extremely rapidly *in vivo*. Furthermore, activated effector CD8 T cells were largely dependent on perforin for this rapid cytotoxic activity. Although memory CD8 T cells are considered poorly cytolytic based on *in vitro* ⁵¹Cr release assays, memory CD8 T cells displayed very rapid cytotoxic activity *in vivo*. When peptide-pulsed targets were transferred into LCMV-immune mice up to 200 days post-infection, we could detect antigen-specific killing in approximately one hour. In fact, we were able to directly compare the *in vivo* lytic activity of activated effector and resting memory CD8 T cells by measuring killing by equal numbers of effector and memory cells. Strikingly, after a brief lag phase, memory CD8 T cells killed at approximately the same rate as effector T cells. These data indicate that resting memory CD8 T cells are likely much more efficient killers *in vivo* than previously appreciated.