S7-2

4-1BB Costimulation Enhances HSV-1-Specific $CD8^+$ T Cell Responses

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Optimal immunological control of cutaneous herpes simplex virus type 1 (HSV-1) infection is dependent upon the presence of functional HSV-1-specific T lymphocytes. 4-1BB was detected on 40% of HSV-1 specific CD8+ T cells (gB/H-2Kb tetramer positive CD8 T cells) in draining lymph node following foot-pads infection with HSV-1 KOS. 4-1BB+ T cells showed enhanced proliferation and survival capacity compared with 4-1BB-T cells. When agonistic 4-1BB mAb was injected into HSV-1 infected mice, HSV-1-specific CD8+ T cells showed; approximately 3-4 fold enhanced expansion compared with control IgG-treated group and showed enhanced in vivo cytotoxicity against gB-peptide pulsed splenocytes. To determine whether dendritic cells were involved in the effect of anti-4-1BB mAb, we observed that dendritic cells in HSV-1 KOS infected mice expressed 4-1BB. Thus, *in vivo* 4-1BB stimulation with an agonistic Ab showed an expansion of $CD8\alpha^+$DC population. Our studies demonstrate that 4-1BB costimulation may prove useful as a strategy to enhance antiviral $CD8^+$ T cell responses.