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### **Recruitment and function of bystander CD8 T cells following viral CNS infection**

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Bystander activation of heterologous memory T cells is a well documented event during the immune response to many viral infections. The activation of these non-specific viral T cells may lead to autoimmune diseases and also contribute to the sustainability of immunological memory. Although the central nervous system (CNS) is generally protected from immune cell infiltration by the blood brain barrier, activated T cells can gain access and potentially contribute to immune pathology during inflammation. Recruitment and retention of heterologous CD8 T cells was therefore analyzed following CNS infection with a neurotropic mouse hepatitis virus (MHV). BALB/c mice mount a dominant L<sup>d</sup>-restricted CD8 T cell response specific for a peptide in the MHV nucleocapsid protein (pN), which accounts for up to 40% of CD8 T cells within the CNS. To monitor a distinct heterologous CD8 T cell subset, mice were immunized with recombinant vaccinia virus expressing a D<sup>d</sup>-restricted peptide derived from HIV-1 IIIB gp160, designated p18, 4-5 weeks prior to MHV challenge. Based on intracellular cytokine staining and flow cytometry, the results show that p18-specific memory T were recruited to the CNS prior to recruitment of pN-specific CD8 T cells. However, during progression of the infection, there was an increase in pN-specific cells and a gradual decrease in p18-specific CD8 T cells. Following control of MHV viral replication, pN-specific CD8 T cells were retained within the CNS at ~30 %, whereas p18-specific cells had decreased to barely detectable levels, indicating that antigen presentation was crucial in maintaining recruited CD8 T cell subsets. *Ex vivo* cytolytic (CTL) activity of CNS mononuclear cells specific for p18 and pN peptide was compared to determine the ability of homologous or heterologous virus-specific CD8 T cells to exert effector function. Lysis was only observed on target cells presenting pN peptide, not p18 peptide, even when differences in numbers of antigen specific T cells were accounted for. These results suggest chemokine/activation induced bystander recruitment of CD8 T cells into the CNS; however, local retention and effector function appears strictly antigen dependent.

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