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# Anti-tumor activity and trafficking of self, tumor-specific T cells against tumors located in the brain


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**Abstract** It is commonly believed that T cells have difficulty reaching tumors located in the brain due to the presumed "immune privilege" of the central nervous system (CNS). Therefore, we studied the biodistribution and anti-tumor activity of adoptively transferred T cells specific for an endogenous tumor-associated antigen (TAA), gp100, expressed by tumors implanted in the brain. Mice with pre-established intracranial (i.c.) tumors underwent total body irradiation (TBI) to induce transient lymphopenia, followed by the adoptive transfer of $gp100_{25–33}$-specific $CD8^+$ T cells (Pmel-1). Pmel-1 cells were transduced to express the bioluminescent imaging (BLI) gene luciferase. Following adoptive transfer, recipient mice were vaccinated with $hgp100_{25–33}$ peptide-pulsed dendritic cells ($hgp100_{25–33}$/DC) and systemic interleukin 2 (IL-2). This treatment regimen resulted in significant reduction in tumor size and extended survival. Imaging of T cell trafficking demonstrated early accumulation of transduced T

cells in lymph nodes draining the hgp100$_{25–33}$/DC vaccination sites, the spleen and the cervical lymph nodes draining the CNS tumor. Subsequently, transduced T cells accumulated in the bone marrow and brain tumor. BLI could also detect significant differences in the expansion of gp100-specific CD8$^{+}$ T cells in the treatment group compared with mice that did not receive either DC vaccination or IL-2. These differences in BLI correlated with the differences seen both in survival and tumor infiltrating lymphocytes (TIL). These studies demonstrate that peripheral tolerance to endogenous TAA can be overcome to treat tumors in the brain and suggest a novel trafficking paradigm for the homing of tumor-specific T cells that target CNS tumors.

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**Keywords** Brain tumor - Immunotherapy - T cell trafficking - Dendritic cells

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References secured to subscribers.