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### **Recognition and Killing of Brain Tumor Stem-Like Initiating Cells by CD8+ Cytolytic T Cells.**

Brown CE, Starr R, Martinez C, Aguilar B, D'Apuzzo M, Todorov I, Shih CC, Badie B, Hudecek M, Riddell SR, Jensen MC.

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Solid tumors contain a subset of stem-like cells that are resistant to the cytotoxic effects of chemotherapy/radiotherapy, but their susceptibility to cytolytic T lymphocyte (CTL) effector mechanisms has not been well characterized. Using a panel of early-passage human brain tumor stem/initiating cell (BTSC) lines derived from high-grade gliomas, we show that BTSCs are subject to immunologic recognition and elimination by CD8(+) CTLs. Compared with serum-differentiated CD133(low) tumor cells and established glioma cell lines, BTSCs are equivalent with respect to expression levels of HLA class I and ICAM-1, similar in their ability to trigger degranulation and cytokine synthesis by antigen-specific CTLs, and equally susceptible to perforin-dependent CTL-mediated cytolysis. BTSCs are also competent in the processing and presentation of antigens as evidenced by the killing of these cells by CTL when antigen is endogenously expressed. Moreover, we show that CTLs can eliminate all BTSCs with tumor-initiating activity in an antigen-specific manner in vivo. Current models predict that curative therapies for many cancers will require the elimination of the stem/initiating population, and these studies lay the foundation for developing immunotherapeutic approaches to eradicate this tumor population. [Cancer Res 2009;69(23):OF1-8].

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