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Glioma cells influence the migration of neuralized mouse embryonic stem cells in vivo

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Of the 200,000 brain tumors diagnosed in the United States each year, approximately 23% of them are glioblastomas (Brain Tumor Society 2004). These aggressive tumors spread rapidly and are resistant to standard treatment, and the average survival rate of patients diagnosed with glioblastomas is approximately one year. Current research suggests there is great potential for neural stem cells (NSCs) to be used as a delivery vehicle for therapeutic agents against tumors. Studies have shown NSCs have an innate attraction to tumors and other inflammatory diseases of the brain. This NSC pathotropism is due in part to inflammatory signals, angiogenesis, reactive astrocytosis, and tumor cytokines (M&uumlller, et al. 2006). By harnessing their natural tropism, NSCs engineered with chemotherapeutic properties can be used to track and target tumors for destruction. To demonstrate the therapeutic potential of NSCs as a transplantable, therapeutic delivery system, we are investigating the in vivo migratory behavior and cellular fate of neuralized mouse embryonic stem cells (mESCs) in the presence of glioma cells. In this study, neuralized mESCs and SF767 human glioblastoma cells were injected into opposite hemispheres of the mouse cortex, and frozen sections of the brain tissue were examined to determine the extent of mESC migration and survival. After 3 days in vivo, co-localization of tumor and neuralized mESCs was evident in multiple sections. Previously, we have seen co-localization of neuralized mESCs and tumor cells on organotypic mouse brain slices after approximately one week of migration. NSC migration to tumor cells in vivo lends support to current efforts to use stem cells as a therapeutic deliver system. Furthermore, the neuralized mESCs' proximity to the tumor cells will allow for the specific delivery of chemotherapeutic agents to tumor sites. Expanding our knowledge of fundamental characteristics and behaviors of neural stem cells will facilitate the development of novel and effective stem cell therapies for glioblastomas.