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Understanding the origins of gliomas and developing novel therapies: cerebrospinal fluid and subventricular zone interplay.

[Glantz M](#), [Kesari S](#), [Recht L](#), [Fleischhack G](#), [Van Horn A](#).

Department of Neurosurgery, Penn State Hershey Medical Center, Hershey, PA 17033-0859, USA. mjg@massmed.org

Glioblastoma multiforme (GBM), the most common malignant primary brain tumor in adults, carries a poor prognosis, with median survival generally less than 1 year. Although initial therapy often eradicates the bulk of the tumor, disease recurrence, usually within 2 cm of the original tumor, is almost inevitable. This may be due to a failure of current therapies to eradicate viable chemotherapy- and radiotherapy-resistant neoplastic progenitor cells, which may then repopulate tumors. An increasing body of preclinical data suggests that these cells may correspond to stem cells derived from the subventricular zone (SVZ), which migrate to tumor sites and contribute to glioma growth and recurrence. Therapeutic targeting of SVZ stem cell populations via cerebrospinal fluid (CSF)-directed therapy may provide a means for limiting tumor recurrence. This approach has proved successful in the treatment of medulloblastoma, another brain tumor thought to be derived from stem cells. We discuss the rationale and design considerations for a clinical trial to evaluate the efficacy of CSF-directed therapy for preventing GBM recurrence.

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