The brain tumor microenvironment.

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Abstract
High-grade brain tumors are heterogeneous with respect to the composition of bona fide tumor cells and with respect to a range of intermingling parenchymal cells. Glioblastomas harbor multiple cell types, some with increased tumorigenicity and stem cell-like capacity. The stem-like cells may be the cells of origin for tumor relapse. However, the tumor-associated parenchymal cells such as vascular cells, microglia, peripheral immune cells, and neural precursor cells also play a vital role in controlling the course of pathology. In this review, we describe the multiple interactions of bulk glioma cells and glioma stem cells with parenchymal cell populations and highlight the pathological impact as well as signaling pathways known for these types of cell-cell communication. The tumor-vasculature not only nourishes glioblastomas, but also provides a specialized niche for these stem-like cells. In addition, microglial cells, which can contribute up to 30% of a brain tumor mass, play a role in glioblastoma cell invasion. Moreover, non-neoplastic astrocytes can be converted into a reactive phenotype by the glioma microenvironment and can then secrete a number of factors which influence tumor biology. The young brain may have the capacity to inhibit gliomagenesis by the endogenous neural precursor cells, which secrete tumor suppressive factors. The factors, pathways, and interactions described in this review provide a new prospective on the cell biology of primary brain tumors, which may ultimately generate new treatment modalities. However, our picture of the multiple interactions between parenchymal and tumor cells is still incomplete.

PMID: 22379614 [PubMed - in process]