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Tumor niches: perspectives for targeted therapies in glioblastoma

Rashmi Srivastava [1 2], Meghana Dodda [1 3], Han Zou [1 4], Xuejun Li [5 6], Baoli Hu [1 7 8]

Affiliations

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Abstract

Significance: Glioblastoma (GBM), the most common and lethal primary brain tumor with a median survival rate of only 15 months and a five-year survival rate of only 6.8 %, remains largely incurable despite intensive multimodal treatment of surgical resection and radio-chemotherapy. Developing effective new therapies is an unmet need for patients with GBM.

Recent advances: Targeted therapies, such as anti-angiogenesis therapy and immunotherapy, show great promise in treating GBM based upon increasing knowledge about brain tumor biology. Single-cell transcriptomics reveals the plasticity, heterogeneity, and dynamics of tumor cells during GBM development and progression.

Critical issues: While anti-angiogenesis therapy and immunotherapy have been highly effective in some types of cancer, the disappointing results from clinical trials represent continued challenges in applying these treatments to GBM. Molecular and cellular heterogeneity of GBM is developed temporally and spatially, which profoundly contributes to therapeutic resistance and tumor recurrence.

Future directions: Deciphering mechanisms of tumor heterogeneity and mapping tumor niche trajectories and functions will provide a foundation for the development of more effective therapies for GBM patients. In this review, we will discuss five different tumor niches and the intercellular and intracellular communications among these niches, including the perivascular, hypoxic, invasive, immunosuppressive, and glioma-stem cell niches. We will also highlight the cellular and molecular biology of these niches and discuss potential strategies to target these tumor niches for GBM therapy.