ABSTRACT

World Neurosurg. 2021 Oct;154:228-231. doi: 10.1016/j.wneu.2021.06.127. Epub 2021 Sep 24.

Perspectives on Microglia-Based Immune Therapies Against Glioblastoma.

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Glioblastoma (GBM) is the most aggressive primary tumor of the central nervous system. Despite aggressive multimodal therapy, it has a dismal prognosis. Over the last 20 years, the approach to GBM research and therapy has involved viewing the pathologic condition as a complex organ system with multiple nonneoplastic cells supporting tumor growth directly or through enhancement of the tumor microenvironment. Understanding the immune system effects on glioma growth, invasion, tumor survival, immune suppression, and angiogenesis is critical in immunotherapy target development. In this review, we discuss how the immune system generates a favorable microenvironment, and clinical trials currently underway targeting immune system pathways. Tumor-associated macrophages, particularly the M2 phenotype, are important residents of the tumor microenvironment, promoting tumor growth through paracrine and direct signaling. Clinical trials targeting PD-L-1, CTLA-4, and colony stimulating factor-1 receptor in GBM are currently under investigation. Additionally, several phase I/II clinical trials are underway using vaccines, oncolytic viruses, antibodies, and chimeric antigen receptor T cells targeting glioma cells. Co-opting the immune system as a therapeutic partner against GBM is in early stages of investigation, and the potential use of such approaches as treatment adjuncts is indispensable for combating this highly heterogeneous disease.

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DOI: 10.1016/j.wneu.2021.06.127
PMID: 34583500