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Immunopathology of Glioblastoma

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Abstract

Glioblastoma (GBM), the most frequent and malignant primary brain tumor, is characterized by a highly diverse and profoundly immunosuppressive tumor microenvironment (TME) that provides an unconstrained environment for tumor progression and significantly complicates therapeutic interventions. Despite advances in immunotherapeutic approaches, such as chimeric antigen receptor T cell and immune checkpoint inhibitors, efficacy remains limited due to the complexity of the GBM TME and robust immune evasion mechanisms. In this review, we elucidate the intricate interplay among cellular components within the TME that lead to this immunosuppressive state, including tumor-associated macrophages/microglia, myeloid-derived suppressor cells, regulatory T cells, and glioma stem cells, as well as other critical elements that contribute to TME complexity, such as the severe hypoxia associated with central necrosis, the blood-brain barrier, and the extracellular matrix. This review also highlights mechanisms of immune evasion and recent immunotherapeutic approaches along with their biologic rationale, underscoring the need for integrated therapeutic strategies that both target immunosuppressive elements and enhance immune activation.

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