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Immunological challenges and opportunities in glioblastoma multiforme: A comprehensive view from immune system lens

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Abstract

Glioblastoma multiforme (GBM), also known as grade IV astrocytoma, is the most common and deadly brain tumour. It has a poor prognosis and a low survival rate. GBM cells' immunological escape mechanism helps them resist advanced multimodal therapy. In physiological homeostasis, brain astrocytes and microglia suppress infections and clear the potential pathogen from the system. However, in severe pathological conditions like cancer, the immune response fails to eliminate mutated and rapidly over-proliferating GBM cells. The malignant cells' interactions with immune cells and the neoplasm's immunosuppressive environment enable the avoidance and their clearance. Immunotherapy efficiently addresses these difficulties, as shown by sufficient evidence. This review discusses how GBM cells inhibit and elude the immune system. These include MHC molecule expression alteration and PD-L1 and CTLA-4 immune checkpoint overexpression. Without co-stimulation, these changes induce effector T-cell tolerance and anergy. The review also covers how MDSCs, TAMs, Herpes Virus Entry Mediators, and Human cytomegalovirus protein decrease the effector immune response against glioblastoma. The latter part discusses various therapies that are available in the market or under clinical trials which revolves around combating resistance against the available multimodal therapies. The recent trends indicate that there are various monoclonal antibodies and peptide-based vaccines that can be utilized to overcome the immune evasion technique harbored by GBM cells. A strategic development of Immunotherapy considering these hallmarks of immune evasion may help in designing a therapy that may prove to be effective in killing the GBM cells thereby, improving the overall survival of GBM-affected patients.

Keywords: Glioblastoma; Immune checkpoints; Immune evasion; Immunotherapy; Virus; cancer-immunity.