Review Med Oncol. 2025 May 16;42(6):213. doi: 10.1007/s12032-025-02760-y.

Epigenetic reprogramming and antitumor immune responses in gliomas: a systematic review

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PMID: 40380049 DOI: 10.1007/s12032-025-02760-y

Abstract

Gliomas, particularly glioblastoma, are among the most aggressive and treatment-resistant brain tumors. Their immunosuppressive tumor microenvironment (TME) and intrinsic molecular heterogeneity hinder effective therapeutic responses. Epigenetic dysregulation in gliomas significantly impacts tumor progression and immune evasion, presenting an opportunity for therapeutic intervention. This systematic review evaluates the role of epigenetic reprogramming in modulating antitumor immune responses in gliomas and explores its potential to enhance treatment outcomes. A comprehensive literature search across major databases, adhering to PRISMA guidelines, identified preclinical and clinical studies examining the effects of epigenetic therapies on glioma-associated immune modulation. Inclusion criteria focused on studies involving DNA methylation inhibitors, histone deacetylase inhibitors, chromatin remodelers, and non-coding RNA-based therapies. Key outcomes included immune activation, tumor progression, survival, and TME modulation. Among 22 included studies, epigenetic therapies demonstrated substantial efficacy in reprogramming the glioma immune landscape. DNA methylation inhibitors such as decitabine enhanced antigen presentation and immune recognition, while histone deacetylase inhibitors improved T-cell-mediated cytotoxicity. Non-coding RNA-targeted interventions disrupted immune suppression and facilitated immune cell infiltration. These strategies showed synergistic potential with immune checkpoint inhibitors, leading to tumor growth inhibition and improved survival in preclinical models. Epigenetic therapies hold promise in overcoming glioma-induced immune resistance by modulating immune escape mechanisms and reprogramming the TME. Their integration with existing treatment modalities, including immunotherapy, represents a transformative avenue for glioma management. Further clinical validation is warranted to optimize their therapeutic potential and safety.

Keywords: DNA methylation; Epigenetic reprogramming; Glioblastoma multiforme; Gliomas; Histone modification.