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Key methylation modifications in glioma stem cells

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Abstract

Glioblastoma (GBM), the most aggressive primary brain tumor in adults, is characterized by a poor prognosis with a median survival of approximately 15 months despite multimodal therapies. Its hallmark heterogeneity and cellular plasticity, driven by glioma stem cells (GSCs), which contribute to therapeutic resistance and tumor recurrence. GSCs, identified by markers such as CD133, CD15, and Nestin, exhibit self-renewal capacity, multilineage differentiation potential, and tumor-initiating ability. These cells demonstrate intrinsic resistance to radiation and chemotherapy, enhanced invasiveness, and the ability to remodel the tumor microenvironment through immune modulation and angiogenesis. Metabolic reprogramming in GSCs supports their aggressive phenotype by meeting bioenergetic demands. It also generates metabolites that drive epigenetic remodeling. Among epigenetic mechanisms, methylation of DNA, RNA, and proteins plays a critical role in regulating GSC plasticity, gene expression, and signaling pathways. This review explores the dynamics of methylation in GSCs, encompassing the latest research on DNA, RNA, and protein methylation within the field of GSCs. This review further provides insights for future research by proposing a hierarchical regulatory network of methylation in GSCs to deepen understanding of their unique characteristics. Furthermore, this review highlights the potential for developing additional methylation-related clinical markers to enhance diagnostic approaches.

Keywords: Biomarkers; Epigenetic regulation; Glioma stem cell; Methylation.

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