ABSTRACT

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# Gliomas: Genetic alterations, mechanisms of metastasis, recurrence, drug resistance, and recent trends in molecular therapeutic options.

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Glioma is the most common intracranial tumor with poor treatment outcomes and has high morbidity and mortality. Various studies on genomic analyses of glioma found a variety of deregulated genes with somatic mutations including TERT, TP53, IDH1, ATRX, TTN, etc. The genetic alterations in the key genes have been demonstrated to play a crucial role in gliomagenesis by modulating important signaling pathways that alter the fundamental intracellular functions such as DNA damage and repair, cell proliferation, metabolism, growth, wound healing, motility, etc. The SPRK1, MMP2, MMP9, AKT, mTOR, etc., genes, and noncoding RNAs (miRNAs, lncRNAs, circRNAs, etc.) were shown mostly to be implicated in the metastases of glioma. Despite advances in the current treatment strategies, a low-grade glioma is a uniformly fatal disease with overall median survival of ~ 5-7 years while the patients bearing high-grade tumors display poorer median survival of ~ 9-10 months mainly due to aggressive metastasis and therapeutic resistance. This review discusses the spectrum of deregulated genes, molecular and cellular mechanisms of metastasis, recurrence, and its management, the plausible causes for the development of therapy resistance, current treatment options, and the recent trends in malignant gliomas. Understanding the pathogenic mechanisms and advances in molecular genetics would aid in the novel diagnosis, prognosis, and translation of pathogenesis-based treatment opportunities which could pave the way for precision medicine in glioma.



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