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Targeting epigenetic mechanisms of resistance to chemotherapy in gliomas

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Abstract

Glioma, an aggressive type of brain tumors of glial origin is highly heterogeneous, posing significant treatment challenges due to its intrinsic resistance to conventional therapeutic schemes. It is characterized by an interplay between epigenetic and genetic alterations in key signaling pathways which further endorse their resistance potential. Aberrant DNA methylation patterns, histone modifications and non-coding RNAs may alter the expression of genes associated with drug response and cell survival, induce gene silencing or deregulate key pathways contributing to glioma resistance. There is evidence that epigenetic plasticity enables glioma cells to adapt dynamically to therapeutic schemes and allow the formation of drug-resistant subpopulations. Furthermore, the tumor microenvironment adds an extra input on epigenetic regulation, increasing the complexity of resistance mechanisms. Herein, we discuss epigenetic changes conferring to drug resistance mechanisms in gliomas in order to delineate novel therapeutic targets and potential approaches that will enable personalized treatment.

Keywords: Drug resistance; Gliomas; HDAC inhibitors; Histone deacetylases; LncRNAs; Lysine demethylases; MiRNAs; TMZ.

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