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Unraveling the mechanisms of glioblastoma's resistance: investigating the influence of tumor suppressor p53 and non-coding RNAs

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Abstract

Glioblastoma (GB) is one of the most fatal CNS malignancies, and its high resistance to therapy and poor outcomes have made it one of the primary challenges in oncology. Resistance to standard therapy, i.e., radio-chemotherapy with temozolomide, is one of the principal causes of the poor prognostic outcomes of GB. Finding the molecular basis of GB resistance to therapy is key to creating effective solution approaches. The general problem of GB resistance is supervised by cancer suppressive protein, p53, and has become a very special interest in molecular research in recent decades. The principal aim of this manuscript is to perform a comprehensive survey on the complex network of interactions developed by p53 with non-coding RNAs (ncRNA) in the context of GB resistance. The present article details the functional aspects of p53 as a cellular stress response protein, including its roles in apoptosis, cell cycle regulation, and DNA repair in glioblastoma (GB), along with the disruption of p53 and its involvement in chemoresistance (CR). It also highlights several classes of ncRNAs, namely microRNAs, long ncRNAs, and circular RNAs, that manipulate p53 signaling in GB-CR. The article likewise explains how disruption in the expression of these ncRNAs can promote GB-CR and how it interacts with essential cellular functions, such as proliferation, apoptosis, and DNA repair. The manuscript also describes the potential of targeting p53 and ncRNAs with their diagnostic and prognostic potential as novel promising therapeutics for GB. Nevertheless, ncRNA-based biomarkers still present challenges for their suitability in GB resistance. However, modern research continues to discover novel prediction targets, potentially enhancing patient outcomes and therapeutic options. Therefore, the neutralization of this intricate regulatory network of GB resistance might have a primary clinical effect in fighting GB resistance therapy and thus might lead to a substantial increase in patient survival and quality of life.

Keywords: Chemoresistance; DNA repair; Glioblastoma resistance; NcRNAs; P53.

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