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The function of chaperones in the radioresistance of glioblastoma: a new insight into the current knowledge

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Abstract

Radiotherapy remains a cornerstone of brain tumor treatment; however, its effectiveness is frequently undermined by the development of radioresistance. This review highlights the pivotal role of molecular chaperones in promoting radioresistance and explores the potential to increase radioresistance in brain cancers, particularly glioblastoma (GBM). Among chaperones, heat shock proteins (HSPs), such as HSP70 and HSP90, have been identified as key contributors to radioresistance, acting through mechanisms that include the maintenance of protein homeostasis, enhancement of DNA repair processes, and protection of cancer stem cells. Specifically, HSP70 and HSP90 are crucial in stabilizing oncogenic proteins and preventing apoptosis, thus enabling tumor survival during radiotherapy. Also, HSP27 and GRP78 are involved in the radioresistance of brain tumors mainly by suppressing cell death and enhancing tumor stem cell propagation. Emerging evidence also suggests that targeting these chaperones, in combination with radiotherapy, can enhance tumor radiosensitivity, offering promising therapeutic strategies. Recent studies have revealed novel aspects of chaperone-mediated autophagy and interaction with non-coding RNAs, providing deeper insights into the molecular mechanisms underlying radioresistance. This review also addresses the potential of combining chaperone-targeted therapies, such as HSP90 inhibitors, with radiotherapy to overcome resistance. Ultimately, understanding these mechanisms may pave the way for innovative clinical applications and personalized therapeutic approaches in brain tumor treatment.

Keywords: Brain tumors; Chaperone; Glioblastoma; Heat shock proteins; Radioresistance.