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DNA damage response and growth factor signaling pathways in gliomagenesis and therapeutic resistance.

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Abstract

The dismal prognosis of glioblastoma multiforme (GBM) is mainly due to the poor response of GBM patients to any therapeutic modalities, which include ionizing radiation and DNA-alkylating agents. In the last few years, the important role of the DNA damage response (DDR) pathway in tumor formation and modulation of therapeutic response has been appreciated. Interestingly, several of the genetic alterations commonly found in GBMs (such as epidermal growth factor receptor amplification and PTEN inactivation) have also recently been shown to regulate the activity of the DNA repair machinery and, consequently, the response to DNA-damaging agents used routinely in the clinic. In this review, we focus on some of these findings that suggest that at least some of the pathways driving GBM formation could be directly responsible for the therapy resistance of this tumor type. Possible therapeutic approaches exist that may either overcome or take advantage of these GBM genetic alterations to improve the response of these tumors to DNA-damaging therapy. *Cancer Res*; 71(18); 5945-9. ©2011 AACR.

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