Title: DNA repair mechanisms and their clinical impact in glioblastoma

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<DOCHEAD>REVIEW

<AT>DNA repair mechanisms and their clinical impact in glioblastoma
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<ABS-HEAD>Abstract

<ABS-P>Despite surgical resection and genotoxic treatment with ionizing radiation and the DNA alkylating agent temozolomide, glioblastoma remains one of the most lethal cancers, due in great part to the action of DNA repair mechanisms that drive resistance and tumor relapse. Understanding the molecular details of these mechanisms and identifying potential pharmacological targets have emerged as vital tasks to improve treatment. In this review, we introduce the various cellular systems and animal models that are used in studies of DNA repair in glioblastoma. We summarize recent progress in our knowledge of the pathways and factors involved in the removal of DNA lesions induced by ionizing radiation and temozolomide. We introduce the therapeutic strategies relying on DNA repair inhibitors that are currently being tested in vitro or in clinical trials, and present the challenges raised by drug delivery across the blood brain barrier as well as new opportunities in this field. Finally, we review the genetic and epigenetic alterations that help shape the DNA repair makeup of glioblastoma cells, and discuss their potential therapeutic impact and implications for personalized therapy.

<KWD>Keywords: Glioblastoma; DNA repair; chemoresistance; temozolomide; ionizing radiation; therapeutic strategies.

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