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Chemoresistance of glioblastoma cancer stem cells - much more complex than expected.

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Abstract

ABSTRACT: Glioblastomas (GBM) are a paradigm for the investigation of cancer stem cells (CSC) in solid malignancies. The susceptibility of GBM CSC to standard chemotherapeutic drugs is controversial as the existing literature presents conflicting experimental data. Here, we summarize the experimental evidence on the resistance of GBM CSC to alkylating chemotherapeutic agents, with a special focus on temozolomide (TMZ). The data suggests that CSC are neither resistant nor susceptible to chemotherapy per se. Detoxifying proteins such as O6-methylguanine-DNA-methyltransferase (MGMT) confer a strong intrinsic resistance to CSC in all studies. Extrinsic factors may also contribute to the resistance of CSC to TMZ. These may include TMZ concentrations in the brain parenchyma, TMZ dosing schemes, hypoxic microenvironments, niche factors and the re-acquisition of stem cell properties by non-stem cells. Thus, the interaction of CSC and chemotherapy is more complex than may be expected and it is necessary to consider these factors in order to overcome chemoresistance in the patient.

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