Molecular mechanisms of temozolomide resistance in glioblastoma multiforme.

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Abstract
Glioblastoma multiforme (GBM; WHO astrocytoma grade IV) is considered incurable owing to its inherently profound resistance towards current standards of therapy. Considerable effort is being devoted to identifying the molecular basis of temozolomide resistance in GBMs and exploring novel therapeutic regimens that may improve overall survival. Several independent DNA repair mechanisms that normally safeguard genome integrity can facilitate drug resistance and cancer cell survival by removing chemotherapy-induced DNA adducts. Furthermore, subpopulations of cancer stem-like cells have been implicated in the treatment resistance of several malignancies including GBMs. Thus, a growing number of molecular mechanisms contributing to temozolomide resistance are being uncovered in preclinical studies and, consequently, we are being presented with a broad range of potentially novel targets for therapy. A substantial future challenge is to successfully exploit the increasing molecular knowledge contributing to temozolomide resistance in robust clinical trials and to ultimately improve overall survival for GBM patients.

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