

ABSTRACT

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Temozolomide Resistance: A Multifarious Review on Mechanisms Beyond
O-6-Methylguanine-DNA Methyltransferase.

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BACKGROUND: Chemotherapy with the oral alkylating agent temozolomide still
prevails as a linchpin in the therapeutic regimen of glioblastoma alongside
radiotherapy. In view of the impoverished prognosis and sparse chemotherapeutic
medicaments associated with glioblastoma, the burgeoning resistance to
temozolomide has made the whole condition almost irremediable.

OBJECTIVE: The present review highlights the possible mechanisms of drug
resistance following chemotherapy with temozolomide.

METHOD: The review summarizes the recent developments, as published in articles
from Scopus, PubMed, and Web of Science search engines.

DESCRIPTION: One of the prime resistance mediators, O-6-methylguanine-DNA
methyltransferase, upon activation, removes temozolomide-induced methyl adducts
bound to DNA and reinstates genomic integrity. In the bargain, neoteric advances
in the conception of temozolomide resistance have opened the door to explore
several potential mediators like indirect DNA repair systems, efflux mechanisms,
epigenetic modulation, microenvironmental influences, and autophagy-apoptosis
processes which constantly lead to failure of chemotherapy.

CONCLUSION: This very review throws light on recent discoveries, proposed
theories, and clinical developments in the field of temozolomide resistance to
summarize the complex and intriguing involvement of onco-biological pathways.

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