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# MGMT in TMZ-based glioma therapy: Multifaceted insights and clinical trial perspectives

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## Abstract

Temozolomide (TMZ) is the most preferred and approved chemotherapeutic drug for either first- or second-line chemotherapy for glioma patients across the globe. In glioma patients, resistance to treatment with alkylating drugs like TMZ is known to be conferred by exalted levels of MGMT gene expression. On the contrary, epigenetic silencing through MGMT gene promoter methylation leading to subsequent reduction in MGMT transcription and protein expression, is predicted to have a response favoring TMZ treatment. Thus, MGMT protein level in cancer cells is a crucial determining factor in indicating and predicting the choice of alkylating agents in chemotherapy or choosing glioma patients directly for a second line of treatment. Thus, in-depth research is necessary to achieve insights into MGMT gene regulation that has recently enticed a fascinating interest in epigenetic, transcriptional, post-transcriptional, and post-translational levels. Furthermore, MGMT promoter methylation, stability of MGMT protein, and related subsequent adaptive responses are also important contributors to strategic developments in glioma therapy. With applications to its identification as a prognostic biomarker, thus predicting response to advanced glioma therapy, this review aims to concentrate on the mechanistic role and regulation of MGMT gene expression at epigenetic, transcriptional, post-transcriptional, and post-translational levels functioning under the control of multiple signaling dynamics.

**Keywords:** Chemoresistance; Chemotherapy; Glioblastoma multiforme (GBM); O6-methylguanine-DNA methyltransferase (MGMT); Progression-free survival (PFS); Temozolomide (TMZ).