Temozolomide resistance

- Neuroepithelial tumors of the central nervous system with EWSR1::PATZ1 fusion: a case report and literature review
- Integrated Workflow for Drug Repurposing in Glioblastoma: Computational Prediction and Preclinical Validation of Therapeutic Candidates
- MiR 329/449 Suppresses Cell Proliferation, Migration and Synergistically Sensitizes GBM to TMZ by Inhibiting Src/FAK, NF-kB, and Cyclin D1 Activity
- Epigenetic Alterations in Glioblastoma Multiforme as Novel Therapeutic Targets: A Scoping Review
- Nanoparticles of silver and titanium can increase temozolomide sensitivity against human glioblastoma: an in vitro study on apoptosis and inflammation
- An In Vivo Model of Recurrent Glioblastoma
- Exosomal circular RNAs as drivers of temozolomide resistance in glioblastoma: Mechanisms and implications
- Unlocking glioblastoma: breakthroughs in molecular mechanisms and next-generation therapies

see Temozolomide resistance in glioblastoma.

Understanding the mechanistic basis for glioma temozolomide resistance is an important obstacle in developing an effective form of chemotherapy. Glycogenolysis is known to play an essential role in cell proliferation and potassium homeostasis and involves the glycogen phosphorylase isoenzyme BB (GPBB). Plasma GPBB was correlated with TMZ-resistance. Elevated plasma GPBB concentrations were found to be more frequent in a TMZ-resistant cohort of patients with poor survival rates. TMZ inhibits cell proliferation and induces TMZ resistance by upregulating the expression of O(6)-methylguanine-DNA methyltransferase (MGMT). This process requires glycogenolysis, which was confirmed herein by treatment with 1,4-dideoxy-1,4-imino-D-arabinitol hydrochloride, a glycogenolysis inhibitor and a special GPBB inhibitor. Acute TMZ treatment leads to upregulation of [Ca2+]i, extracellular-regulated kinase (ERK)1/2 phosphorylation, and chronic TMZ treatment leads to upregulation of the expression of Na,K-ATPase, ERK1/2, and MGMT protein. Upregulation was abolished for each of these by inhibitors of transient receptor potential channel 1 and the inositol trisphosphate receptor. L-channel [Ca2+]i inhibitors and RyR antagonists had no such effect. These results demonstrate that [Ca2+]i-dependent glycogenolysis participates in acquired glioma TMZ-resistance by upregulating MGMT via a Na,K-ATPase/ERK1/2 signaling pathway. GPBB and glycogenolysis may therefore represent novel therapeutic targets for overcoming TMZ-resistant gliomas [1)]

1)
Xu J, Zhang Y, Guo X, Sun T. Glycogenolysis in Acquired Glioma Resistance to Temozolomide: A Role for the [Ca2+]i-dependent Activation of Na,K-ATPase/ERK1/2 Signaling. Front Pharmacol. 2018 Aug 7;9:873. doi: 10.3389/fphar.2018.00873. PMID: 30131700; PMCID: PMC6090282.