

Etomoxir for glioblastoma

The importance of [fatty acid oxidation](#) (FAO) in the bioenergetics of [glioblastoma](#) (GBM) is being realized. [Etomoxir](#) (ETO), a [carnitine](#) palmitoyltransferase 1 ([CPT1](#)) inhibitor exerts [cytotoxic](#) effects in GBM, which involve interrupting the FAO pathway.

Shim et al. from [Seoul](#) hypothesized that FAO inhibition could affect the outcomes of current standard [temozolomide](#) (TMZ) [chemotherapy](#) against GBM.

The FAO-related gene expression was compared between GBM and the tumor-free cortex. Using four different GBM [tumorspheres](#) (TSs), the effects of ETO and/or TMZ were analyzed on [cell viability](#), [Citric acid cycle](#) intermediates, and [adenosine triphosphate](#) (ATP) production to assess metabolic changes. Alterations in tumor stemness, invasiveness, and associated [transcriptional](#) changes were also measured. A [mouse orthotopic xenograft](#) model was used to elucidate the combinatory effect of TMZ and ETO.

GBM tissues exhibited overexpression of FAO-related genes, especially [CPT1A](#), compared to the tumor-free cortex. The combined use of ETO and TMZ further inhibited the [Citric acid cycle](#) and [ATP](#) production more than single uses. This combination treatment showed superior suppression effects compared to treatment with individual agents on the [viability](#), [stemness](#), and [invasiveness](#) of GBM TSs, as well as better [downregulation](#) of FAO-related [gene expression](#). The results of the [in vivo](#) study showed prolonged [survival](#) outcomes in the combination treatment group.

ETO, an FAO inhibitor, causes a lethal [energy](#) reduction in the GBM TSs. When used in combination with TMZ, ETO effectively reduces GBM cell [stemness](#) and [invasiveness](#) and further improves survival. These results suggest a potential novel treatment option for GBM ¹⁾.

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