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# The Ketogenic Diet Reverses Gene Expression Patterns and Reduces Reactive Oxygen Species Levels When Used as an Adjuvant Therapy for Glioma.

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### Abstract

ABSTRACT:

**BACKGROUND:** Malignant brain tumors affect people of all ages and are the second leading cause of cancer deaths in children. While current treatments are effective and improve survival, there remains a substantial need for more efficacious therapeutic modalities. The ketogenic diet (KD) - a high-fat, low-carbohydrate treatment for medically refractory epilepsy - has been suggested as an alternative strategy to inhibit tumor growth by altering intrinsic metabolism, especially by inducing glycopenia.

**METHODS:** Here, we examined the effects of an experimental KD on a mouse model of glioma, and compared patterns of gene expression in tumors vs. normal brain from animals fed either a KD or a standard diet.

**RESULTS:** Animals received intracranial injections of bioluminescent GL261-luc cells and tumor growth was followed in vivo. KD treatment significantly reduced the rate of tumor growth and prolonged survival. Further, the KD reduced reactive oxygen species (ROS) production in tumor cells. Gene expression profiling demonstrated that the KD induces an overall reversion to expression patterns seen in non-tumor specimens. Notably, genes involved in modulating ROS levels and oxidative stress were altered, including those encoding cyclooxygenase 2, glutathione peroxidases 3 and 7, and periredoxin 4.

**CONCLUSIONS:** Our data demonstrate that the KD improves survivability in our mouse model of glioma, and suggests that the mechanisms accounting for this protective effect likely involve complex alterations in cellular metabolism beyond simply a reduction in glucose.

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