Interfering with Glioblastoma Multiforme (GBM) Metabolism to Complement the Therapeutic Effects of Temozolomide

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Glioblastoma multiforme (GBM), a serious form of brain cancer, has an average life expectancy of approximately 1.2 years. The current standard of care is treatment with a drug known as Temozolomide (TMZ) which has been proposed to cause cell cycle checkpoint arrest and apoptotic death by DNA damage. However, some cells overcome TMZ treatment by over-expression of DNA repair enzymes. Cells that make up GBM use available glucose at a very high rate (high rate glycolysis), and exhibit a plasticity in substrate selection for energy production (ATP) via mitochondrial oxidative phosphorylation. These metabolic differences suggest that metabolic intermediates may provide new therapeutic targets. The advantages of targeting GBM metabolism include: (1) GBM can no longer use an efficient strategy for energy production, and (2) metabolic disruption results in stresses that can alter the cell surface and lead to recognition of the potential danger by immune cells from the tumor micro-environment. The purpose of this project is to test the hypothesis that by interfering with tumor-selective energy strategies, including the use of fatty acids (fatty acid oxidation) and amino acid oxidation, in combination with TMZ will result in increased tumor cell death.

Awards Won: