Treating GBM BTSCs through Growth Factor Stimulation and Drug-Polymer Conjugate Therapy

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Glioblastoma (GBM) is the most common malignancy of the central nervous system in adults. Despite medical advancements, long-term patient survival (>5 years) remains bleak (<15%). GBMs contain brain tumor stem cells (BTSCs). GBM BTSCs are thought to have key roles in tumor recurrence, metastasis, and drug resistance. In this study, a novel treatment model for GBM BTSCs through a synergistic growth factor and drug combination was developed. Epidermal Growth Factor (EGF) plays a key role in maintaining the stem-cell niche and promoting proliferation of these cells in vitro. Early stage tumors, tumor cells that are in a state of division are more susceptible to chemotherapy than later-stage tumors. Exogenous EGF was used in conjunction with Temozolomide (TMZ), an anti-neoplastic agent that alkylates DNA, to increase drug efficacy; cells were forced into a mitotic state to sensitize them to DNA-targeting treatment. As EGF stimulated GBM BTSC proliferation, synergistic therapy was 150% more effective than TMZ alone. Additionally, this synergistic model overcame acquired resistance among TMZ-resistant cell lines. A novel 3-dimensional tumor model was used to better simulate the intricate architecture of the tumor in vitro. Further, a co-polymer system to encapsulate drug was utilized to offer a more targeted treatment model. This seemingly paradoxical approach has shown very profound efficacy against 2D and 3D models of GBM, and may also be effective against dormant tumor populations. This methodology can be easily translated to the clinic and potentially allow for increased long-term survival rates by overcoming phenomena such as drug-resistance and dormant cell populations.

Awards Won:
Third Award of $1,000