TM-08. DIFFERENTIAL VASCULAR PATTERN OF GLIOMA STEM CELLS
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Treatment of the glioblastoma (GBM) tumors with anti-angiogenic therapies has not significantly improved patients’ survival. The lack of clear response is partly due to the heterogeneous nature of GBMs. Such heterogeneity is evident in different molecular subtypes, in tumor microenvironment including hypoxia and tumor metabolic profiles and also at the level of tumor vascularity, such as microvascular density (MVD) and permeability. While heterogeneity in vasculature results in heterogeneous metabolic profile of the tumor cells, no data is available explaining the effect of metabolic status on tumor vasculature. Deciphering the underlying mechanism of tumor vascular heterogeneity is needed, as it can improve design of targeted therapies.

We aimed to establish the differential pattern of tumor vascularity in GBM xenografts of different glioma stem cells (GSCs). Furthermore, we investigated whether GSC tumor vasculature is regulated by changes in glucose metabolism. GSCs were isolated from operative GBM samples and their in-vitro angiogenic profile established using angiogenic arrays and western blot analysis. Glucose metabolism was altered by generating HK2 knockdown of each GSC line and used to generate intracranial xenografts. Tumor growth parameters, overall survival and the in-vivo vascular properties were determined using MRI characteristics and histological analysis. Our results showed that survival rate of the mice and tumor growth pattern varied between different GSCs. MVD and expression of angiogenic factors were different amongst different GSCs and in their matched xenografts. Furthermore, reduced glucose metabolism resulted in reduced MVD and increased animal survival, in GSCs with high MVD. GSC cell lines demonstrate significant variability in their vascular profile. Effective therapeutic strategies would require individual tumor vascular and metabolic status to be taken into account, prior to any therapeutic intervention.