

## **The Role of SerpinB3 in Glioblastoma Cancer Stem Cell Proliferation**

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GBM is the most common primary malignant brain tumor. Early detection of this tumor type remains challenging and median survival time of those affected remains around 14-16 months. Currently there is no cure for GBM, and radiation, surgery, and chemotherapy are used to try and combat this disease. GBM ranks #1 among all cancers in terms of average years of life lost. This poor prognosis can be partially attributed to the extremely high recurrence rate of the disease. GBM tumor cells are highly infiltrative and include subpopulations of cells with the capacity to self-renew and generate the cellular diversity present in the tumor. The actions of these cells, commonly referred to as Cancer Stem Cells or CSCs, are strongly associated with disease recurrence. This research is focused on improving the understanding of glioblastoma CSCs and developing therapies that specifically target these cells. Junction Adhesion Molecule A or JAM-A was initially identified as a cell junction protein that is responsible for maintaining thin tissue forming the outer layer of a body's surface and lining the alimentary canal and other hollow structures. Studies in the past have demonstrated that JAM-A is able to regulate both pro and anti-tumorigenic processes in cancer, and might be useful as a biomarker of malignant tumors. The majority of these studies provide evidence for JAM-A having an intrinsic, pro-tumorigenic role in regulating the CSC phenotype, cancer cell proliferation, and metastasis for multiple tumor types, in particular GBM. None of these studies, however, have focused specifically on the isolated role of JAM-A or its potential role in a larger signaling network for cancers. SerpinB3 was chosen for functional assessments due to its previously identified role in the tumorigenesis of hepatocellular carcinoma and limited known role in GBM. Endogenous JAM-A binding to SerpinB3 was confirmed through immunoprecipitation of SerpinB3 that demonstrated JAM-A binding. To investigate the CSC-specific role of SerpinB3, SB3 will be knocked down in a human GBM xenograft model (T4121) utilizing two non-overlapping short-hairpin RNA constructs. The GBM CSCs will be orthopedically inserted into the mice via an intracranial injection. This study will have a threefold outcome, provide the identity of a novel binding domain within junctional adhesion molecules; identify an interaction that can be specifically targeted with drugs to fight against an otherwise therapeutically resistant cell population; and clarify the role SB3 plays in GBM CSCs specifically