Abstract: Angiogenesis, the formation of new blood vessels, is a complex multi step process that includes proliferation, migration and differentiation of endothelial cells and plays a crucial role in growth and vascularization of primary brain tumors. The progression of glioma angiogenesis is the result of an intricate balance between pro-angiogenic and anti-angiogenic factors as well development of inflammation through secretion of inflammatory molecules by inflammatory cells. T11 target structure (T11TS), a bioactive molecule, has been documented as an anti neoplastic agent in glioma induced rats and also in human glioma in vitro. This novel molecule induces apoptosis of tumor cells by way of immune potentiation and impairs the glioma cell cycle, but its role in glioma angiogenesis has not been worked out in detail. Matrix metalloproteinases (MMPs) are enzymes promoting tumor angiogenesis by enzymatically remodeling the extracellular matrix and altering surface protein expression such as integrin αv and the matrix-bound proteins like TGF-β1. The present study was formulated to assess the efficacy of T11TS in the modulations of MMP-2 and −9 and their endogenous inhibitors (TIMP-1 and TIMP-2) as well as modulations of cell surface receptors like integrin αv and VE-cadhrine, cytoplasmic bound protein Beta Catennin in glioma-induced rats and also on the phenotypic markers of endothelial cells (CD31 and CD34). Apart from these above molecules we have focused also to check whether T11TS also modulates the cytokine expressions (IL-8, IL-6 & TNF-α, TGF-β) and their secretion. The techniques used were Zymography, Western blot, ELISA and Flow cytometric analyses. It was observed that T11TS administration significantly downregulates the expression of matrix metalloproteinase-2 and −9 along with its ligand integrin αv and upregulates TIMP-1 and TIMP-2. In situ immunofluorescence and FACS results revealed that T11TS administration decreased the expression of the phenotypic markers (CD31/PECAM1, CD34), inhibiting the cell grip through down regulation of Integrin αv, VE-cadhrine, CD44 in glioma associated ECs and also downregulating TGF-β1 expression from microglia cells and IL-8, IL-6 & TNF-α in glioma associated endothelial cells. These results suggest that T11TS suppresses the expression of positive angiogenic growth factors and potentiates the expression of negative regulators in glioma-associated endothelial cells (ECs), resulting in an anti-angiogenic effect on glioma induced angiogenesis.

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Manoj Kumar Singhal
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