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Molecular mechanisms of anti-angiogenic potential of the novel bio-molecule T11 target structure (T11TS) in malignant glioma abrogation: A preclinical study

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The crucial role of angiogenesis in malignant glioma progression makes it a potential target of therapeutic intervention in glioma. T11 target structure (T11TS), a novel bioactive molecule has been documented by us as an anti-neoplastic agent in glioma induced rats and also in human glioma in vitro. The present preclinical study deciphers the anti-angiogenic potential of T11TS and the underlying molecular mechanisms in malignant glioma. Glioma associated brain endothelial cells (GABEC) were isolated and characterized with phenotypic markers of endothelial cells (CD31 and CD34), whose level diminished with T11TS administration, inhibiting the cell grip. T11TS administration significantly down-regulates the expression of integrin α v and Matrix metalloproteinases (MMP-2 and -9) which enzymatically remodel the ECM and up-regulate the inhibitors TIMP-1 and TIMP-2. In GABEC T11TS administration disrupt initiation of glioma angiogenesis by significantly down-regulating VEGF/VEGFR-2 expression and pro-survival PI3K/Akt/eNOS proteins along with eNOS phosphorylation and NO production, but significantly up-regulates PTEN expression. T11TS therapy remarkably inhibits endothelial angiotensin-1/Tie-2 signaling associated with vessel maturation and stabilization. It simultaneously antagonizes EGFR activation and components of Raf/MEK/ERK pathway, which are essential for angiogenesis induction and proliferation. T11TS dampens pro-inflammatory cytokines which are indispensable for tumor growth and metastatic propagation but up-regulates anti-inflammatory cytokines resulting complete abrogation of glioma inflammation and angiogenesis. T11TS triggers apoptosis in GABEC via activation of intrinsic pathway as well extrinsic pathway. Taken together our findings suggest that T11TS can be introduced as an effective angiogenesis inhibitor in human glioma as T11TS targets multiple levels of angiogenic signaling cascade impeding glioma neo-vascularization.

Biography

Swapna Chaudhuri is an alumnus of University of Calcutta. She has joined School of Tropical Medicine in 2008 as Professor. Her research areas are in the fields of Cancer Immunology and Immunotherapy, Respiratory and Infectious Immunology and Immunotherapy. She taught at both Post-graduate and undergraduate levels and has published sixty papers in high impact factor journals and also reviews, monographs, book chapters. She has won many Academic laurels and Fellowships, affiliated to twelve Academic Societies, Editorial Committee Member of many national and international journals and reviewer of seventeen high impact factor journals. She is also a Principal Investigator of twenty one projects and supervised 21 PhD, MD and DM students.

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