TIP-1 as one Biomarker of Tumor Progression and Radiation Sensitivity within Malignant Glioma

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Abstract

Malignant glioma is one of the leading causes of death from cancer. Although spatially and temporally controlled radiotherapy can now be delivered precisely to the tumor lesions, tumor control with radiation is still poor due to the intrinsic or adapted radioresistance and the highly invasive capability of the malignant glioma cells. Through in vivo screening of phage-displayed peptides, we have identified one heptapeptide (HVGGSSV) that selectively bound to the tumors responding to ionizing radiation. TIP-1 was identified as the molecular target that mediated the specific binding of the heptapeptide. It was found that IR induced the translocation of the predominantly intracellular TIP-1 protein onto the plasma membrane surface of cancer cells. It was also found that the membrane association of TIP-1 was more dominant within the migrating malignant glioma cells. Tissue array indicated that TIP-1 was overexpressed within some human malignant glioma of advanced stages. To study the roles of TIP-1 in progression and radiation sensitivity of malignant glimas, we have studied multiple malignant glioma cell lines in which TIP-1 expression level was genetically modified. The data indicated that membrane association of TIP-1 regulated directional migration of malignant glioma cells through interacting with b-PIX and modulating Rac1 activation. The intracellular TIP-1 confers radioresistance of glioma cells through regulating p53 protein activation and stabilization. TIP-1 also enhanced tumor-driven angiogenesis and promoted tumor progression within animal models. Taken together, our data suggested that TIP-1 is one biomarker of tumor progression and radiation sensitivity of malignant glioma and can be a novel molecular target in cancer imaging and therapy.