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PTOP Expression Correlates with Telomerase Activity and Grades of Malignancy in Human Glioma Tissues

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Abstract : Glioblastoma multiforme (GBM) is the most aggressive form of brain tumors, with an extremely poor prognosis. Telomeres lenght is associated with tumor progression in several type of human cancers and telomere elongation is a common molecular feature of advanced malignancies. Among the telomeric shelterin proteins PTOP is required for telomeric protein complex assembly, telomerase recruitment and activity, and telomere length regulation through a PTOP-telomerase interaction. Previous studies suggest that PTOP upregulation is involved in radioresistance and telomere lengthening in colorectal cancer cells. Moreover, in human osteosarcoma cells PTOP deletion led to telomere shortening, increased apoptosis and radiation sensitivity enhancement. However, to date, little is known about the role of PTOP in progression of glioma cancers. In light of this background aim of the study is to investigate the expression of PTOP in different grades of human glioma and its correlation with the pathological grade of gliomas, grades of malignancy, proliferative activity and apoptosis. Fifteen Low Grade Astrocytomas (LGA), 18 Anaplastic Astrocytomas (AA) and 26 Glioblastoma Multiforme (GBM) samples were analyzed. Three samples of normal brain tissue (NBT) were used as controls. The expression levels of PTOP, h-TERT, BIRC1 and cyclin D1 were determined by real time PCR and/or western blot. Results obtained shows that PTOP expression in glioma tissues is tightly correlated with clinical grade ($p < 0.01$). No correlation was found between PTOP expression and other clinicopathologic parameters. The expression of PTOP was positively correlated with the expression of hTERT and TERF1. Furthermore PTOP positively correlates with cyclin D1 and negatively correlates with the expression of BIRC1. Our findings indicate that PTOP might play key role in the progression of glioma regulating telomerase activity and likely through regulation of cell cycle and apoptosis. In conclusion results obtained prompted us to speculate that PTOP might represents a potential molecular bio marker and a therapeutic target for the treatment of glioblastoma tumors.

Keywords : glioblastoma, PTOP, telomere, brain tumors
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