TROAP

Trophinin-associated protein (TROAP) mediates embryonic transfer, regulates microtubules, and is associated with the biological behavior of various cancers. However, there is limited information on the role of TROAP in glioma.

Methods and results: We obtained clinical information on 1948 patients with glioma from The Cancer Genome Atlas, Gene Expression Omnibus and the Chinese Glioma Genome Atlas. Basal assays were used to measure changes in TROAP expression levels in high-grade glioma cell lines and in normal human astrocytes. Quantitative reverse transcription polymerase chain reaction assays showed that TROAP expression was higher in glioma cell lines than in normal astrocytes. The expression level of TROAP in 749 glioma was significantly higher than that in 228 normal brain tissues using Student's t test. The expression of TROAP has a positive relationship with the clinical characteristics of poor prognosis, such as WHO grade, age and has negatively correlated with the indicators of beneficial prognosis, such as IDH mutation and 1p19q co-deletion. Kaplan-Meier survival curves, single multifactor analysis were used to analyze correlations between TROAP and clinical features and prognosis of gliomas. In addition, TROAP overexpression was an independent risk factor for glioma and was associated with reduced overall survival of patients with glioma particularly in patients with WHO grade III and grade IV glioma. Gene set enrichment analysis showed that homologous recombination, cell cycle, and p53 signaling pathways were enriched in samples overexpressing TROAP.

Conclusion: TROAP is a potential risk factor associated with poor prognosis in patients with glioma and may act as a highly specific biomarker, offering the possibility of individualized glioma treatment [1)].

Experimental evidence demonstrated a crucial role of TROAP (Trophinin-associated protein) in regulating the cell proliferation of multiple tumors, while TROAP expression and function were largely unknown in glioma.

Four gene expression databases (GEO, TCGA, GTEx and CCLE) were enrolled in a study and used for TROAP expression and survival analysis. TROAP expression was quantified by qRT-PCR, western blot and immunohistochemistry assays in glioma tissues and cell lines. TROAP knockdown and overexpression vector were constructed and transfected into glioma cells. CCK-8, colony formation, transwell, and wound healing assays were used to evaluate cell viability, migration and invasion, flow cytometry to determine cell cycle arrest. Gene set enrichment analysis (GSEA) was conducted to screen the pathway involved in TROAP-high phenotype. The expression of cell cycle and Wnt/β-Catenin signaling proteins were analyzed by immunofluorescence and western blot.

Based on the bioinformatic analysis and a series of functional assays, Zhao et al. found the TROAP was enriched in glioma tissues and cell lines, its overexpression was correlated with the clinicopathologic characteristics and poor prognosis. TROAP knockdown inhibited cell proliferation, migration, invasion, and G1/S cell cycle arrest compared with control group in glioma. Mechanism analysis revealed that TROAP activated Wnt/beta-Catenin pathway and upregulated its downstream targets expression, while silencing β-Catenin or Axin2 could reverse the tumor-promoting effects caused by TROAP, confirming that TROAP-induced malignant phenotype and tumorigenesis via Wnt/β-Catenin signaling pathway.

The present study found that TROAP accelerated the progression of gliomagenesis through Wnt/β-

Catenin pathway, and TROAP might be considered as a novel target for glioma therapy [2].

1)
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2)
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