CPEB4

Cytoplasmic polyadenylation element binding protein 4 (CPEB4) is a regulator of gene expression at transcriptional level and has been reported to be associated with biological malignancy in cancers.

It is considered to be a novel therapeutical target for glioblastoma.

In a study, Peng et al., transduced DCs with CPEB4 to explore the immune response in vivo. They found that DCs transduced with recombinant adenovirus encoding CPEB4 could induce specific cytotoxic T lymphocytes (CTLs) to lyse glioma cells and augment the number of IFN-γ secreting T-cells in mice. In addition, the modified DCs could effectively protect mice from lethal challenges against glioma cells, reduce tumor growth and increase the mice life span. These results suggest that the DC transduced with CPEB4 may induce anti-tumor immunity against glioma cells and might be used as an efficient tumor vaccine in clinical applications [1)].

Immunohistochemistry (IHC) was performed to examine the dynamics of CPEB4 expression in glioma and nonneoplastic brain tissues, and the expression of CPEB4 in cell lines and freshly prepared tissue samples was measured using Western blotting and real-time PCR.CPEB4 was highly expressed at the mRNA and protein levels in 4 glioma cell lines and in 4 freshly prepared glioma tissues. Immunohistochemical analysis demonstrated that CPEB4 expression in glioma tissue was higher than that in corresponding nonneoplastic brain tissue ($P<0.01$). This high expression level was further increased in high-grade gliomas, and the CPEB4 expression level correlated with the WHO classification ($r=0.774$, $P<0.01$). Moreover, the overall survival of glioma patients displaying high CPEB4 protein expression ($P<0.01$) was clearly lower than that of those displaying low CPEB4 expression, and the high CPEB4 expression indicated a poorer survival in high-grade glioma patients ($P<0.01$).Our study suggests that CPEB4 is significantly expressed in human glioma and that the upregulation of CPEB4 protein is significantly associated with advanced WHO grade. CPEB4 may serve as a highly sensitive prognostic indicator for glioma patients [2)].

Wang et al., determined the expression of CPEB4 protein using immunohistochemistry in tissue microarrays containing 278 glioma patients (including 98 primary glioblastomas) and evaluated its association with pathological grades and clinical outcome by univariate and multivariate analyses. And then, lentiviral-mediated RNAi targeting CPEB4 was utilized to study the role of CPEB4 in glioblastoma cell proliferation.

CPEB4 expression was positively related to glioma pathological grade ($p < 0.01$) and elevated in glioblastoma ($p < 0.01$). High expression of CPEB4 was associated with significantly poor prognosis, and could be identified as an independent risk factor for overall survival (OS) and progression-free survival (PFS) of glioblastoma patients (hazard ratio (HR) = 1.730, $p = 0.014$ and HR = 1.877, $p = 0.004$, respectively). In vitro studies further showed that downregulation of CPEB4 significantly reduced the growth rate of T98G and U251 cells comparing with the controls.

The study indicated that increased expression of CPEB4 in primary glioblastoma is a novel biomarker for predicting poor outcome of patients and suppression of CPEB4 inhibit tumor cell proliferation, suggesting a potential therapeutic target for glioblastoma [3)].

1)
Peng W, Nan Z, Liu Y, Shen H, Lin C, Lin L, Yuan B. Dendritic cells transduced with CPEB4 induced antitumor immune response. Exp Mol Pathol. 2014 Oct;97(2):273-8. doi: 10.1016/j.yexmp.2014.06.001. Epub 2014 Jun 10. PubMed PMID: 24927871.
2)
Hu W, Yang Y, Xi S, Sai K, Su D, Zhang X, Lin S, Zeng J. Expression of CPEB4 in Human Glioma and Its Correlations With Prognosis. Medicine (Baltimore). 2015 Jul;94(27):e979. doi: 10.1097/MD.0000000000000979. PubMed PMID: 26166131; PubMed Central PMCID: PMC4504610.
3)
Wang HX, Qin R, Mao J, Huang QL, Hong F, Li F, Gong ZY, Xu T, Yan Y, Chao SH, Zhang SK, Chen JX. CPEB4 regulates glioblastoma cell proliferation and predicts poor outcome of patients. Clin Neurol Neurosurg. 2018 Apr 3;169:92-97. doi: 10.1016/j.clineuro.2018.04.008. [Epub ahead of print] PubMed PMID: 29642043.