Transforming growth factor Beta

Transforming growth factor-βs (TGF-βs) are a group of multifunctional proteins that have neuroprotective roles in various experimental models.

Transforming growth factor beta (TGFβ) signalling cascade has been implicated in enhancing neuronal excitability and excitatory synaptogenesis following blood brain barrier (BBB) damage and inflammation.

Importance

Transforming growth factor Beta (TGFβ) is upregulated in Marfan's syndrome and some human cancers, and play crucial roles in tissue regeneration, cell differentiation, embryonic development, and regulation of the immune system, promotes the growth of glioma cells, and correlate with the degree of malignancy of gliomas. However, the molecular mechanisms involved in the malignant function of TGF-β are not fully elucidated.

Isoforms of transforming growth factor-beta (TGF-β1) are also thought to be involved in the pathogenesis of pre-eclampsia.

see Transforming growth factor beta receptor

see Transforming growth factor beta signaling pathway

Intrathecal injections of TGF-β1 significantly inhibit neuropathy-induced thermal hyperalgesia, spinal microglia and astrocyte activation, as well as upregulation of tumor necrosis factor-α. However, additional cellular mechanisms for the antinociceptive effects of TGF-β1, such as the mitogen activated protein kinase (MAPK) pathway, have not been elucidated. During persistent pain, activation of MAPKs, especially p38 and extracellular signal-regulated kinase (ERK), have crucial roles in the induction and maintenance of pain hypersensitivity, via both nontranscriptional and transcriptional regulation.

TGF-β-induced epithelial-mesenchymal transition (EMT) plays an important role in tumor progression.

Ling et al., assessed whether the TGF-β-induced EMT contributed to vasculogenic mimicry (VM) formation in glioma, they established an SHG44 cell line stably transfected with TGF-β cDNA loaded lentivirus. SB203580 was employed to inhibit the TGF-β-induced EMT. The results showed that the VM forming ability of cells could be improved by TGF-β over-expression. The migration and invasion capabilities of cells were also enhanced due to EMT. SB203580 was able to weaken cell migration, invasion and VM forming abilities via blocking p38/MAPK signaling pathways, but it had tiny influence on MMP/LAMC2 chain. Consequently, we concluded that EMT inhibition via p38/MAPK signaling pathways would partly impair TGF-β-induced VM formation in glioma [1)].

Types

Transforming growth factor beta 1

TGFβ2

Transforming growth factor beta 3

Guo et al. showed that TGF-β induced the downregulation of MST1 expression in U87 and U251 glioma cells. Treatment of glioma cells with the DNA methylation inhibitor 5-aza-2'-deoxycytidine (5-AzadC) prevented the loss of MST1 expression. Addition of 5-AzadC also reduced the TGF-β-stimulated proliferation, migration and invasiveness of glioma cells. Furthermore, Knockdown of DNMT1 upregulated MST1 expression in gliomas cells. In addition, the inhibition of DNMT1 blocked TGF-β-induced proliferation, migration and invasiveness in glioma cells. These results suggest that TGF-β promotes glioma malignancy through DNMT1-mediated loss of MST1 expression [2].

1)
Ling G, Ji Q, Ye W, Ma D, Wang Y. Epithelial-mesenchymal transition regulated by p38/MAPK signaling pathways participates in vasculogenic mimicry formation in SHG44 cells transfected with TGF-β cDNA loaded lentivirus in vitro and in vivo. Int J Oncol. 2016 Oct 7. doi: 10.3892/ijo.2016.3724. PubMed PMID: 27748800.

2)
Guo Z, Li G, Bian E, Ma CC, Wan J, Zhao B. TGF-β-mediated repression of MST1 by DNMT1 promotes glioma malignancy. Biomed Pharmacother. 2017 Aug 9;94:774-780. doi: 10.1016/j.biopha.2017.07.081. [Epub ahead of print] PubMed PMID: 28802229.