CTF1

The CTF1 gene (Cardiotrophin-1) encodes a protein that is part of the cytokine family, specifically within the IL-6 family of cytokines. This gene plays a crucial role in various biological processes, including inflammation, cell differentiation, cardiac hypertrophy, and neuronal regeneration.

Key Functions of the CTF1 Gene: Cardioprotection:

CTF1 protein promotes cardiomyocyte survival and plays a role in the adaptive hypertrophy of the heart, helping the heart respond to stress or injury. Neuronal Regeneration:

It is involved in the regeneration and survival of neurons, making it relevant in neuroprotective pathways. Inflammatory Response:

Like other IL-6 family cytokines, CTF1 contributes to the immune response by regulating inflammation and cellular signaling pathways. Role in Development:

CTF1 is critical for embryonic development and has been implicated in the development of certain tissues, such as the heart and nervous system. Mechanism of Action: CTF1 binds to a receptor complex that includes the leukemia inhibitory factor receptor (LIFR) and gp130, triggering intracellular signaling pathways such as:

JAK/STAT pathway MAPK pathway These pathways mediate its effects on cell survival, differentiation, and growth.

Clinical Relevance: Heart Disease: CTF1 is being studied for its role in cardiac remodeling and its potential as a therapeutic target for heart failure. Neurodegenerative Disorders: Its role in neuronal survival makes it a candidate for research into conditions like Alzheimer's and Parkinson's disease. Cancer: Aberrant expression of CTF1 has been linked to certain cancers, where it may influence tumor growth and survival.

CTF1 expression in glioma

It has been investigated for its role in various cancers, including glioma. Gliomas are aggressive primary brain tumors, and understanding the molecular mechanisms underlying their progression is critical for developing effective therapies.

CTF1 Expression in Glioma Elevated Expression:

Studies have found that CTF1 expression is elevated in glioma tissues compared to normal brain tissue. This overexpression is often associated with tumor progression and poor prognosis. Role in Tumor Progression:

CTF1 promotes cell proliferation, invasion, and survival in gliomas. It activates downstream signaling pathways such as: JAK/STAT3 pathway: This pathway is crucial in promoting oncogenic processes like proliferation, resistance to apoptosis, and immune evasion. PI3K/AKT pathway: This pathway is linked to cell survival and resistance to chemotherapy. These pathways contribute to the aggressive behavior of glioma cells. Impact on the Tumor Microenvironment:

CTF1 can modulate the glioma microenvironment, promoting angiogenesis (formation of new blood vessels), which is vital for tumor growth. It might also influence immune cell infiltration and create an immunosuppressive environment favorable for tumor progression. Prognostic Marker:

Elevated levels of CTF1 expression have been correlated with shorter overall survival in glioma patients, particularly in high-grade gliomas like glioblastoma. Therapeutic Implications:

Targeting CTF1 or its downstream pathways (e.g., STAT3 inhibitors) offers a potential therapeutic approach for gliomas. Combining such targeted therapies with conventional treatments like radiotherapy and temozolomide (TMZ) may improve patient outcomes. Key Research Directions Biomarker Development: CTF1 could be developed as a diagnostic or prognostic biomarker, helping to stratify patients based on their likelihood of progression or response to therapy. Therapeutic Targeting: Further research is required to design small-molecule inhibitors or neutralizing antibodies targeting CTF1 or its signaling pathways. Preclinical and Clinical Studies: Testing the efficacy of CTF1-targeted therapies in preclinical glioma models and clinical trials is crucial to validate their potential.

A study aimed to evaluate CTF1 expression in glioma, its relationship to glioma prognosis and the tumor immune microenvironment, and effects on glioma phenotypes to identify a new target for glioma treatment.

Cai et al. initially assessed the expression of CTF1, a member of the IL-6 family, in glioma, using bioinformatics tools and publicly available databases. Furthermore, they examined the correlation between CTF1 expression and tumor prognosis, DNA methylation patterns, m6A-related genes, potential biological functions, the immune microenvironment, and genes associated with immune checkpoints. They also explored potential associations with drug sensitivity. To assess the impact on glioma cell proliferation and apoptosis, they employed various assays, including the Cell Counting Kit-8, colony formation assay, and flow cytometry.

CTF1 gene and protein expression were significantly elevated in glioma tissues, and correlated with malignancy and poor prognosis. CTF1 was an independent prognostic factor and negatively associated with DNA methylation. The involvement of CTF1 in m6A modifications contributed to glioma progression. Enrichment analysis revealed immune response pathways linked with CTF1 in glioma, including natural killer cell cytotoxicity, NOD-like receptor signaling, Toll-like receptor signaling, antigen processing, chemokine signaling, and cytokine receptor interactions. CTF1 expression correlated positively with pathways related to apoptosis, inflammation, proliferation, and epithelial-mesenchymal transition, and PI3K-AKT-mTOR signaling. Additionally, CTF1 expression was positively associated with macrophage, eosinophil, and neutrophil contents and immune checkpoint-related genes, but negatively associated with sensitivity to 14 drugs. In vitro experiments confirmed that CTF1 knockdown inhibited glioma cell proliferation and promoted apoptosis.

This study identifies CTF1 as a significant independent prognostic factor that is closely associated with the tumor immune microenvironment in glioma. Additionally, reduced expression of CTF1 suppresses the proliferation and induces apoptosis of glioma cells in vitro. Consequently, CTF1 is a potentially promising novel therapeutic target for glioma treatment [1)].

This study by Cai et al. makes a significant contribution to understanding glioma biology, particularly the role of CTF1 in tumor progression and its association with the immune microenvironment. While the findings are promising, particularly for prognosis and therapy development, there is a need for

further experimental and clinical validation. Addressing the limitations highlighted will be crucial to advancing CTF1 as a therapeutic target and realizing its potential in glioma treatment.

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Cai H, Tian S, Liu A, Xie G, Zhang H, Wu X, Wan J, Li S. Relationship between CTF1 gene expression and prognosis and tumor immune microenvironment in glioma. Eur J Med Res. 2025 Jan 9;30(1):17. doi: 10.1186/s40001-024-02192-w. PMID: 39780198.