Long non-coding RNA in glioma

- LINC01783 Promotes Glioma Tumorigenesis by Enhancing GATA3 Expression Through CBP-Mediated H3K27 Acetylation to Suppress PTEN Expression
- Delivery of LOXL1-AS1-siRNAs using targeting peptide-engineered extracellular vesicles with focused ultrasound to suppress medulloblastoma metastasis
- LINC00601 promotes the progression of glioma via the p-STAT3 signaling pathway
- A novel approach to enhance glioblastoma multiforme treatment efficacy: non-coding RNA targeted therapy and adjuvant approaches
- Identification of an immunomodulatory lncRNA signature associated with immune cell reprogramming in high-grade glioma
- Radio-chemotherapy and metformin selectively modulate the heterogeneous landscape of glioma with ribosome biogenesis, long non coding RNA and immune-escape markers as major player
- An overview of lncRNA GAPLINC's role in human cancer growth and metastasis
- NF-YB-driven expression of long non-coding RNA linc01811 inhibiting glioma tumorigenesis by regulating miR-4635/NF-YB axis: A positive feedback loop

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In glioma cells, there are problems with certain pathways or signals in the body. Think of these pathways like roads in a city. They control how cells grow and behave. LncRNAs can mess up these pathways, making the cancer cells resistant to drugs and causing them to grow and spread more.

Specifically, lncRNAs mess with two important pathways called “Wnt/β-catenin” and “PI3K/Akt.” These pathways are like traffic signs for the cells, telling them what to do. When lncRNAs interfere with these pathways, they make the glioma cells do bad things like grow too much, move around the brain, and resist treatment.

A review article by Li et al. looks at all the research that has been done on glioma and how these lncRNAs mess with these pathways. The goal is to understand this better so that doctors and scientists can find new ways to treat glioblastoma and help patients live longer and better lives [1)].

The biological functions of Long non-coding RNAs (lncRNAs) in the glioma have gained much attention in research. However, the deep-going mechanism by which lncRNA regulates the gliomagenesis is still ambiguous.

They participate extensively in biological processes of various cancers. The majority of these transcripts are uniquely expressed in differentiated tissues or specific cancer types [2)].

It has been found that lncRNAs (long non-coding RNA) play a key role in angiogenesis, tumor growth, infiltration, and metastasis of glioma. Since specific lncRNAs have an aberrant expression in brain tissue, cerebrospinal fluid as well as peripheral circulation of glioma patients, they are considered to be potential biomarkers. A review focuses on the biological characteristics of lncRNA and its value as a biomarker for glioma diagnosis and prognosis. Moreover, in view of the role of lncRNAs in glioma proliferation and chemoradiotherapy resistance, they discussed the feasibility of lncRNAs as therapeutic targets. Finally, the persisting deficiencies and future prospects of using lncRNAs as clinical biomarkers and therapeutic targets were concluded [3)].

They are associated with tumor size, WHO grade, and prognosis in glioma patients. lncRNAs could function as potential molecular biomarkers of the clinicopathology and prognosis of glioma [4)].

Univariate Cox regression analysis revealed 19 lncRNAs with survival time dependency. These nine lncRNAs were used to construct our survival model via multivariate Cox regression analysis: TP73-AS1, AC078883.3, RP11-944L7.4, HAR1B, RP4-635E18.7, HOTAIR, SAPCD1-AS1, AC104653.1, and RP5-1172N10.2. The nine lncRNAs associated with them were inputted into the DAVID database for gene ontology and KEGG function enrichment analysis. The result showed these genes were enriched with ion binding, transport, cell-cell signaling, plasma membrane parts, and more, and they were mainly related to neuroactive ligand-receptor interaction pathway, calcium signaling pathway, and the mitogen-activated protein kinase signaling pathway.

The nine lncRNAs were a set of biomarkers for the prognosis of patients with Glioblastoma, enabling a more accurate prediction of survival and revealing more biological functions [5)].

In an article, Li et al. from Nanjing provided an overview of how lncRNAs regulate cellular processes in glioma, enumerated the lncRNAs that may act as glioma biomarkers, and showed their potential clinical implications [6)].

MALAT1

HOTAIR

Evidence has suggested that retinal noncoding RNA3 (RNCR3) is a Glioblastoma-associated noncoding RNA and is under-expressed in Glioblastoma. However, the function and mechanism of RNCR3 on Glioblastoma cell growth and apoptosis are still uncertain.

In a study, Zhang et al., found that the level of RNCR3 is decreased in U87, U251, U373, and A172 Glioblastoma cell lines when compared with the normal human astrocytes. Elevating Long non-coding RNA RNCR3 expression markedly inhibits U87 and U251 cell survival and proliferation. Further studies indicated that RNCR3 overexpression promotes U87 and U251 cell apoptosis and activity caspase-3/7. Moreover, we found that RNCR3 overexpression promotes Krüppel-like factor 16 (KLF16) expression through inhibiting the level of miR-185-5p. We demonstrated that KLF16 is a direct target of miR-185-5p. An increased miR-185-5p level by a miR-185-5p mimic or decreased KLF16 by KLF16 small interfering RNA both reversed the function of RNCR3 overexpression on Glioblastoma cell growth and apoptosis. In summary, this study focuses on investigating the key molecular mechanisms of RNCR3 involved in Glioblastoma cell growth and apoptosis. Our data indicated that RNCR3 overexpression inhibits cell growth and induces its apoptosis through the miR-185-5p/KLF16 axis [7)].

Previous findings have indicated that lncRNA-maternally expressed gene 3 (MEG3) is involved in tumorigenesis of several cancers, including glioma [8].

In addition, the interaction of Long non-coding RNA (lncRNAs) with signaling pathways in gliomas with EZH2 [9].

The long non-coding RNA Hox transcript antisense intergenic RNA (HOTAIR) is a cell cycle-related lncRNA in human glioma, and its expression is closely associated with glioma staging and poor prognosis. Although lysine specific demethylase 1 (LSD1) and polycomb repressive complex 2 (PRC2) have been demonstrated to be functional targets of HOTAIR, how HOTAIR regulates glioma cell cycle progression remains largely unknown.

EZH2 (predominant PRC2 complex component) inhibition blocked cell cycle progression in glioma cells, consistent with the effects elicited by HOTAIR siRNA. However, the inhibition of LSD1 did not affect cell cycle progression in glioma cells. These results suggest that HOTAIR might regulate cell cycle progression through EZH2.

A intracranial mice model also revealed delayed tumor growth in HOTAIR siRNA- and EZH2 inhibitor-treated groups. Moreover, in HOTAIR knock-down cell lines, the expression of the PRC2-binding domain of HOTAIR (5' domain) but not of the LSD1-binding domain of HOTAIR (3' domain) resulted in accelerated cell cycle progression. In conclusion, HOTAIR promotes cell cycle progression in glioma as a result of the binding of its 5' domain to the PRC2 complex [10] Wang et al., screened four-lncRNA signature (AGAP2-AS1, TPT1-AS1, LINC01198 and MIR155HG) from the lncRNA expression profile from the GSE16011, CGGA and REMBRANDT datasets. The patients in low risk group had longer overall survival than high risk group (median OS 2208.25 vs. 591.30 days; $P < 0.0001$). Moreover, patients in the low risk group showed similar overall survival to Grade II patients ($P = 0.1669$), while the high risk group showed significant different to Grade IV ($P = 0.0005$) with similar trend. So based on the four-lncRNA, the anaplastic gliomas could be divided into grade II-like and grade IV-like groups. On the multivariate analysis, it showed the signature was an independent prognostic factor ($P = 0.000$). The expression of four lncRNAs in different grades showed that AGAP2-AS1, LINC01198 and MIR155HG were increased with tumor grade, while TPT1-AS1 was decreased. Knockdown of AGAP2-AS1 can inhibit the cell proliferation, migration and invasion, while increase the apoptosis cell rates in vitro. In conclusion, our results showed that the four-lncRNA signature has prognostic value for anaplastic glioma. Moreover, clinicians should conduct corresponding therapies to achieve best treatment with less side effects for two groups patients [11].

Test and Answers

Question 1: What is the role of lncRNAs in glioma cells?

a) They facilitate cell growth and behavior. b) They have no impact on glioma cells. c) They interfere with cellular pathways, making glioma cells resistant to treatment. d) They promote normal cell growth.

Question 2: Which two cellular pathways do lncRNAs mess with in glioma cells?

a) Traffic pathways and communication pathways. b) Wnt/β-catenin and PI3K/Akt pathways. c) Cell division and cell adhesion pathways. d) Metabolism and immune response pathways.

Question 3: What is the main goal of the review article by Li et al.?

a) To explain how lncRNAs work in normal cells. b) To describe the history of glioma research. c) To explore the potential clinical applications of lncRNAs in glioma treatment. d) To discuss unrelated topics in cancer research.

Question 4: According to the text, what do lncRNAs have in common with glioma?

a) They are absent in glioma cells. b) They do not affect glioma progression. c) They have unique expressions in glioma cells. d) They are involved in liver cancer, not glioma.

Question 5: What is the potential value of lncRNAs in diagnosing and treating glioma?

a) They have no value in glioma diagnosis or treatment. b) They can be used as potential biomarkers and therapeutic targets. c) They are only useful in diagnosing other types of cancer. d) They have value in predicting heart disease, not glioma.

Question 6: Which of the following lncRNAs is NOT mentioned as being involved in glioma in the text?

a) MALAT1 b) HOTAIR c) RNCR3 d) DNA

Question 7: What is the function of the lncRNA RNCR3 in glioblastoma cells?

a) It promotes cell growth and inhibits apoptosis. b) It has no effect on glioblastoma cells. c) It inhibits cell growth and promotes apoptosis. d) It is only found in normal brain cells.

Question 8: How does HOTAIR affect the cell cycle in glioma cells?

a) It doesn't affect the cell cycle. b) It accelerates cell cycle progression by binding to LSD1. c) It slows down cell cycle progression by binding to PRC2. d) It has no impact on the cell cycle.

Question 9: What was the result of the study conducted by Wang et al. regarding a four-lncRNA signature?

a) It had no impact on glioma prognosis. b) It was only useful in diagnosing grade IV gliomas. c) It identified two groups of glioma patients with different survival outcomes. d) It had no independent prognostic value.

Question 10: According to the text, what is the importance of identifying the two groups of glioma patients using the four-lncRNA signature?

a) It helps identify patients with other types of cancer. b) It guides clinicians to choose the best treatment strategies for different patient groups. c) It has no clinical implications. d) It improves the overall survival of glioma patients.

Answers:

c) They interfere with cellular pathways, making glioma cells resistant to treatment. b) Wnt/β-catenin and PI3K/Akt pathways. c) To explore the potential clinical applications of lncRNAs in glioma treatment. c) They have unique expressions in glioma cells. b) They can be used as potential biomarkers and therapeutic targets. d) DNA c) It inhibits cell growth and promotes apoptosis. b) It accelerates cell cycle progression by binding to LSD1. c) It identified two groups of glioma patients with different survival outcomes. b) It guides clinicians to choose the best treatment strategies for

different patient groups.

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