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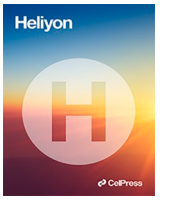

Review article

Expression of lncRNAs in glioma: A lighthouse for patients with glioma

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ABSTRACT

Glioma is the most common malignant tumour in the central nervous system, accounting for approximately 30 % of the primary tumours of this system. The World Health Organization grades for glioma include: Grade I (pilocytic astrocytoma), Grade II (astrocytoma, oligodastoma, etc.), Grade III (anaplastic astrocytoma, anaplastic oligodastoma, etc.) and Grade IV (glioblastoma). With grade increases, the proliferation, invasion and other malignant biological properties of the glioma are enhanced, and the treatment results are less satisfactory. The overall survival of patients with glioblastoma is less than 15 months. Recent research has focused on the roles of long non-coding RNAs, previously regarded as "transcriptional noise", in diseases, leading to a new understanding of these roles. Therefore, we conducted this review to explore the progress of research regarding the expression and mechanism of long non-coding RNAs in glioma.

1. Introduction/background

Glioma is the most common form of primary malignant brain tumour with characteristics of heterogeneity on tumour-related genes and tumour susceptibility [1,2]. Therapeutic approaches for glioma include surgery, radiotherapy and chemotherapy; however, the overall prognosis of patients is not optimistic. In particular, the median survival time of patients with glioblastoma (GBM) is 14.6 months [2–4]. We discovered that the treatment options for glioma are less selective than those of other tumour types, and the overall treatment efficacy is poor. For this review, we conducted a literature search using Pubmed. We found that long-coding RNA (lncRNA) has an important role in the development and manifestation of different tumours. Abnormal expression of lncRNA is reported to be associated with the occurrence, development, recurrence, metastasis, and chemotherapy resistance of tumours. Therefore, elucidating the role of lncRNA could assist in diagnosis, prognosis, and targeted treatment. Furthermore, some tumours have entered the clinical validation stage. Postoperative treatment for patients with glioma is mainly based on chemotherapy and radiotherapy; other treatment options are significantly limited. Therefore, studying the molecular mechanisms of proliferation and invasion in glioma is important [5]. Recently, many studies have focused on the mechanisms of lncRNAs in affecting the growth of glioma [6,7]. LncRNAs belong to a large class of noncoding RNAs with a length greater than 200 nucleotides. These RNAs are involved in numerous biological processes, including cancer cell proliferation and invasion [6]. Studies have shown that lncRNAs have an important role in dosage compensation effect, epigenetic regulation, cell cycle control and regulation of cell differentiation [8]. In general, lncRNAs are divided into the following five groups according to their positions within the coding genes: (1) sense lncRNAs overlap with the sense chain of the

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Table 1
High expression of lncRNA in glioma and different mechanisms of regulation.

LncRNA	Funtional mechanism	Biological functions	Refs.
ADAMTS9-AS2	┤MDM2 mediated FUS K48-ubiquitination → FUS	↑ TMZ-resistance	31
AGAP2-AS1	→ EZH2/LSD1 ┤TFPI2	↑ Proliferation,invasion ↓ Apoptosis	32
CASC2c	┤miR-101┤CPEB1 ceRNA, Histone modification DNA methylation	↑ Maligant characteristic	33
CCAT2	↑ VEGF,Bcl-2 ↓ Bax,caspase-3	↑Migration,proliferation angiogenesis	115
	┤miR-424┤PI3K/AKT/VEGFA ceRNA	↑Angiogenesis,proliferation, migration	116
CRNDE	┤miR-384┤PIWIL4→STAT3 ceRNA	↑ Proliferation,invasion, migration ↓ Apoptosis	27
	Histone acylation→CRNDE →mTOR→P70S6K	↑ Proliferation,invasion, migration ↓ Apoptosis	28
	┤miR-136-5p┤Bcl2/Wnt2 →PI3K/AKT/mTOR , ceRNA	↑ Proliferation,invasion, migration ↓ Apoptosis	29
	↑EGFR,Bcl2 ↓Bax	↑ Proliferation	30
ECONEXIN	┤miR-411-5p┤TOP2A , ceRNA	↑ Proliferation	34
FOXD1-AS1	↑ Protein eIF5a	↑ Proliferation	35
H19	┤miR-29a┤VASH2,ceRNA	↑ Proliferation, angiogenesis	11
	┤miR-675┤CDK6,ceRNA	↑ Proliferation,migration	12
	CD133+	↑ Stemness of glioblastoma	13
	↓miR-152	↑ Proliferation,invasion	14
HOTAIR	┤miR-326┤FGF1→PI3K/AKT/ MEK1/2, ceRNA	↑ Proliferation,invasion, migration ↓ Apoptosis	15
	↑ EZH2/PRC2	↑ Proliferation	16
	┤miR-148b-3p┤USF1→ZO-1/ occludin/claudin-5	↓BTB permeability	17
	The serum-derived exosomes	Prognostic biomarker	18
	DNA methylation, co-expression with HOXA9	Independent prognostic marker	19
LINC00152	miR4435-2HG is a homolog of LNC	↑Invasion	20
	┤miR-103a-3p┤FEZF1→CDC25A →PI3K/AKT, ceRNA	↑ Proliferation,invasion, migration ↓ Apoptosis	21
LINC01116	┤miR-31-5p┤VEGFA,ceRNA	↑ Proliferation,invasion, migration ↓ Apoptosis	36
LINC01140	┤miR-199a-3p┤ZHX1,ceRNA	↑ Proliferation,invasion, migration ↓ Apoptosis	37
MANTIS	↑BRG1/BAF155/RNA Pol II →SOX18,SMAD6,COUP-TFII	↑ Angiogenesis	38
MATN1-AS1	┤miR-200b/c/429┤CHD1,ceRNA	↑ Proliferation↓ Apoptosis	39

LncRNA	Funtional mechanism	Biological functions	Refs.
MCM3AP-AS1	┤miR-211┤KLF5/AGGF1→PI3K/AKT/ERK1/2,ceRNA	↑ Angiogenesis,proliferation, migration	40
MIAT	—	↑ Proliferation.Biomarker	41
MIR22HG	┤miR-22-3p→SFRP2┤Wnt/ß-catenin ┤miR-22-5p→PCDH15┤Wnt/ß-catenin CeRNA	↑ Proliferation,invasion	117
MIR155HG	┤miR-155-3p→PCDH7┤Wnt/ß-catenin ┤miR-155-5p→PCDH9┤Wnt/ß-catenin CeRNA	↑ Proliferation,invasion migration↓ Apoptosis	118
NEAT1	EGFR→NEAT1→EZH2→Wnt/ß-catenin	↑ Proliferation,invasion	22
	┤miR-132┤SOX2,ceRNA	↑ Proliferation,invasion migration ↓ Apoptosis	23
	COX2/mPGES-1/CYP4A→NEAT1 ┤miR-194-5p┤AKT→VEGF/FGF-2/TGF-ß ceRNA	↑ Angiogenesis	119
PAXIP1-AS1	→ETS1→KIF14	↑ Proliferation,invasion migration,angiogenesis	120
PCED1B	┤miR-194-5p┤PCED1B,ceRNA	↑ Proliferation↓ Apoptosis	121
PVT1	┤miR-26b ┤CTGF,ceRNA	↑ Angiogenesis	122
	┤miR-488-3p┤MEF2C,ceRNA	↑ Proliferation,invasion	123
	┤miR-186┤Atg7/Beclin1,ceRNA	↑ Proliferation,invasion	124
SBF2-AS1	ZEB1→SBF2-AS1┤miR-211-5p┤XRCC4→DNA DSB repair, ceRNA	↑ TMZ-resistance	125
SNHG15	┤miR-153┤VEGFA/Cdc42,ceRNA	↑ Angiogenesis	126
SOX2OT	SOX2OT┤miR-194-5p/miR-122 ↑ ⊥ ~~SOX~~/TDGF-1→JAK/STAT Positive feedback loop, ceRNA	↑ Proliferation,invasion migration↓ Apoptosis	127
TALC	┤miR-20b-3p ┤c-MET→AKT/MAPK/STAT3→MGMT	↑ TMZ-resistance	128
TALNEC2	—	Radiation-resistance	129
XIST	↓miR-152	↑ Proliferation,invasion migration↓ Apoptosis	24
	┤miR-137┤FOXC1/ZO-2 C~~ker~~R7	↓ BTB permeability, angiogenesis	25
	↓miR-429	↑ Angiogenesis,proliferation, Invasion,migration	26
GATA6-AS	↓TUG1	↑ Proliferation↓ Apoptosis	102
linc00645	┤miR-205-3p┤ZEB1→TGF-β ↑EMT	↑ Invasion,migration	130

┤Inhibitory modification →Stimulatory modification

↑ Promote/Up-regulate ↓Suppress/Down-regulate

protein coding sequence; (2) antisense lncRNAs overlap with the antisense chain of the protein coding sequence; (3) bidirectional lncRNAs sequences are located on the antisense chain more than 1000 nucleotides away from the starting point of protein transcription, and transcriptional directions between the sequences are opposite; (4) intronic lncRNAs originate from introns of protein-coding genes which are completely located in the intron of another transcript; and (5) intergenic lncRNAs originate from DNA sequences between two protein-coding genes and are not adjacent to any protein-coding gene. Research has shown that multiple lncRNAs are expressed in glioma and normal brain tissues and these RNAs are significantly different [5,6]. LncRNA expression is related to the clinical classification and prognosis of malignant glioma [9,10]. Hundreds of lncRNAs are differentially expressed in different diseases, and a growing number have been proven to be crucial in glioma pathogenesis. This article aims to outline and summarise the research regarding the expression and mechanism of action of lncRNAs on the tumour characteristics of glioma.

2. The role of lncRNA in tumour development

LncRNA exhibits various biological functions in cancer, including epigenetic regulation, DNA damage and cell cycle regulation, regulation of microRNA (miRNA), involvement in signal transduction pathways, and mediating hormone-induced cancer.

Epigenetics refers to heritable changes in genetic phenotype and gene expression, without involving changes in the DNA sequence. It mainly includes modifications such as DNA methylation, histone modification, and chromatin remodeling. Recently, research has shown that lncRNAs play a crucial role in mediating cancer through epigenetic regulation. LncRNAs can regulate gene expression through epigenetic, transcriptional and post transcriptional regulation, thus participating in various biological processes such as cell proliferation, differentiation and apoptosis in cancer. During cancer development, lncRNAs are involved in regulating various epigenetic complexes, thereby inhibiting or activating gene expression. In addition, lncRNAs can participate in gene transcription processes mediated by DNA methylation, acetylation, and other pathways to regulate tumour development. Further, lncRNAs are widely involved in regulating the occurrence and development of tumours through physiological or pathological processes such as DNA damage repair and cell cycle regulation. DNA damage repair and appropriate cell cycle checkpoint regulation are crucial for maintaining cell integrity. In cancer, lncRNAs act as regulatory molecules to regulate the P53 gene and cell cycle, thereby enhancing the transcription of various downstream genes and causing cell cycle arrest, apoptosis, or aging, maintaining the integrity of the cell genome and clearing damaged cells. Recent research has been conducted on the interaction between lncRNA and miRNA. MiRNA is associated with the occurrence and development of many cancers and can complement and pair with target RNAs, resulting in restricted gene expression and protein synthesis. LncRNAs can directly or indirectly interact with miRNAs, leading to a loss of regulatory function. The competitive endogenous RNA (ceRNA) hypothesis is a novel gene expression regulation model, in which lncRNA transcripts compete with miRNA response elements to bind to the same miRNA to regulate their respective expression levels, thereby affecting cell function. The abnormal activation of lncRNAs in signaling pathways, which in turn promotes the occurrence and development of cancer, has also been extensively studied. Therefore, research on lncRNAs is expected to lead to the development of therapeutic drugs for treating cancer.

3. Expression of lncRNAs in glioma

3.1. High expression of lncRNAs in glioma and different mechanisms of regulation

Some lncRNAs are significantly up-regulated in glioma and act as oncogenes (Table 1). Several studies have shown that lncRNAs, such as lncRNA H19, promote glioma-induced endothelial cell proliferation, migration and tube formation in vitro by down-regulating miR-29a, which may modulate the onset of glioma by affecting the biological behaviours of glioma vascular endothelial cells [11]. Other research on the mechanism of lncRNA H19's influence on glioma shows that H19 may promote glioma cell proliferation and migration by up-regulating CDK6. This influence may predict poor prognosis of patients as a result of ceRNA competing with miRNA-675 [12]. H19 is significantly overexpressed in CD133+ glioblastoma cells and increases neurosphere formation of these cells [13]. Knocking down H19 will suppress glioma cell proliferation and invasion by up-regulating miR-152 [14], providing evidence for the potential application of H19 as a therapy target for glioma. HOTAIR is another important lncRNA overexpressed in glioma, which can promote malignant behaviour through the PI3K/AKT and MEK 1/2 signaling pathways by down-regulating miR-326 [15]. Polycomb repressive complex2 (PRC2) has been found to modulate glioma cell cycle progression by binding HOTAIR's 5'domain to the PRC2 complex [16]. HOTAIR also reduces the permeability of the blood tumour barrier (BTB), resulting in decreased absorption/dose of medications such as those used in chemotherapy [17]. Importantly, HOTAIR is highly expressed in serum exosomes of patients with GBM and can be used as a peripheral tumour marker [18,19]. LINC00152 acts as an oncogene through a 3′-hairpin structure [20] and the miR-103a-3p/FEZF1/CDC25A axis [21]. Regulated by EGFR, NEAT1 is critical for glioma cell growth and invasion by binding to EZH2 and increasing the WNT/β-catenin signaling pathway [22]. It also participates in the action of ceRNA against miR-132 to regulate the expression of SOX2, thereby promoting angiogenic Akt- FGF-2/TGF-β/VEGF signaling through miR-194-5p by the same function [23]. Some researchers have testified that knocking down lncRNA XIST exerts tumour-suppressive functions and anti-angiogenesis ability in human glioma, which increases the BTB permeability by regulating multiple miRNAs [24–26]. Growing evidence [27–30] shows that many lncRNAs, such as CRNDE, ADAMTS9-AS2 [31], AGAP2-AS1 [32], CASC2c [33], ECONEXIN [34], FoxD1-AS1 [35], LINC01116 [36], LINC01140 [37], MANTIS [38], MATN1-AS1 [39], MCM3AP-AS1 [40], and MIAT [41] can contribute to glioma progression. Many other lncRNAs are highly expressed in glioma cells and can promote malignancy.

Table 2
Low expression of lncRNA in glioma and different mechanisms of regulation.

LncRNA	Funtional mechanism	Biological functions	Refs.
ADAMTS9-AS2	↑ADAMTS9	↓Migration	80
CASC2	↓miR-21	↓Proliferation,invasion migration ↑ Apoptosis	76
	┤miR-181a┤PTEN┤AKT,ceRNA	↑TMZ sensitivity↓ Proliferation	77
	↓Wnt/ß-catenin,cyclin D1, c-Myc	↓Proliferation,migration	78
	┤miR-193a-5p┤mTOR┤Autophagy, ceRNA	↑TMZ sensitivity	79
ENST00462717	↓MDM2/MAPK	↓Proliferation,migration	81
GAS5	GAS5┤miR-196a-5p┤FOXO1 MMP/PTD1 Positive feedback loop, ceRNA	↓Proliferation,invasion migration ↑ Apoptosis	42
	┤miR-222┤Plexin C1/bmf→Bax ⊥ ⊥ cofilin Bcl-2	↓Proliferation,migration migration ↑ Apoptosis	43
	↓miR-18a-5p ,ceRNA	↓Proliferation,invasion migration ↑ Apoptosis	44
	↓GSTM3	↓Proliferation,migration migration ↑ Apoptosis	47
	→mTOR┤Autophagy	↑Cisplatin sensitivity	48
	Transcriptional factor TFAP2A	—	49
	→EZH2→PRC2→miR-424┤AKT3 C-Myc/cyclinD1/Bcl-2 ⊥ Bax	↓Proliferation,invasion migration ↑ Apoptosis	45
	┤miR-10b→Sirtuin1┤PTEN┤PI3K/AKT MEK/ERK	↓Proliferation,invasion migration ↑ Apoptosis	46
	—	Prognostic predictor	50,51,52 53,54,55
GSA5-AS1	┤miR-106b-5p┤TUSC2,ceRNA	↓Proliferation,invasion, migration	83
HOTTIP	┤BRE┤p53 CDK2/Cyclin A	↓Proliferation	84
Linc00320	↓ Wnt/ß-catenin	↓Proliferation	85
MEG3	┤miR-6088┤SMARCB1,ceRNA	↓Proliferation,migration	56
	↓ Wnt/ß-catenin	↓Proliferation	59
	→Sirt7 ┤PI3K/AKT/mTOR ↑LC3-II/I,Beclin-1,Bax,caspases ↓P62,Bcl-2	↓Proliferation,migration	61
	MiR-377→MEG3→PTEN	↓ Migration,invasion	63

LncRNA	Funtional mechanism	Biological functions	Refs.
	—	↑Cisplatin sensitivity	65
	┤miR-93→PI3K/AKT,ceRNA	↓Proliferation	62
	┤miR-19a┤PTEN, ceRNA	↓Proliferation,migration, invasion	66
	┤miR-96-5p┤MTSS1	↓Proliferation	58
	TUN→MEG3┤Wnt/ß-catenin	↓Proliferation,invasion	60
	PIWIL1→MEG3┤miR-330-5p┤RUNX3 ↓ZO-1,occludin,claudin-5	↑BTB permeability	57
SLC26A4	→NFKB1→NPTX1┤VEGFA	↓Angiogenesis	86
TSLC1-AS1	↑TSLC1	↓Proliferation,migration, invasion	87
TUSC7	↓miR-23b	↓Proliferation,migration, Invasion	73
	┤miR-10a →MAR1	↑TMZ sensitivity	74
	—	Prognostic biomarker	75

3.2. Low expression of lncRNAs in glioma and different mechanisms of regulation

The down-regulated lncRNAs have anticancer effects and inhibit cell cycle and proliferation (Table 2). Dysregulation of tumour suppressors is common in all types of cancer. LncRNA GAS5 is widely studied in glioma. LncRNA GAS5 suppresses the malignancy of human glioma stem cells via a miR-196a-5p/FOXO1 positive feedback loop [42]. This research provides evidence of a ceRNA regulatory network in which GAS5 and miR-222 [43], miR-18a-5p [44], miR-424 [45] and miR-10b [46] form a reciprocal repression feedback loop to inhibit tumour proliferation. In addition, GAS5 can act directly on target genes or related signaling pathways to play a role in tumour inhibition [47–55]. MEG3, another lncRNA extensively studied in glioma, has anti-tumour mechanisms that are more complex than those of other lncRNAs. MEG3 modulates different targets such as the miR-6088/SMARCB1 [56], miR-330-5p/RUNX3 [57], and miR-96 -5p/MTSS1 axes [58]. In addition, MEG3 regulates the WNT/β-catenin [59,60] and PI3K/AKT/mTOR signaling pathways [61,62], and PTEN [63], VEGF/VEGFR [64] and other target genes [65–72] to inhibit glioma cell proliferation, invasion and migration. LncRNA TUSC7 has an anti-tumour role in modulating miR-23b [73] and improving the sensitivity of glioma cells to temozolomide [74,75]. With deepening research, more tumour suppressor genes have been discovered, such as CASC2 [76–79], ADAMTS9-AS2 [80], ENST00462717 [81], RPL34-AS1 [82], GAS5-AS1 [83], HOTTIP [84], Linc00320 [85], SLC26A4-AS1 [86], and TSLC1-AS1 [87]. Increasing evidence indicates that these lncRNAs may become therapeutic targets for inhibiting the malignant behaviour of glioma.

3.3. Dual expression of lncRNA in glioma and different mechanisms of regulation

Our literature review netted research which revealed the dual expression of two lncRNAs in glioma (Table 3). LncRNA MALAT1 is one of the most conserved lncRNAs in terms of its primary sequence [88–90] and was first recognized as a biomarker to predict metastasis and survival in early-stage non-small cell lung cancer [91]. Research has shown that MALAT1 increases the activity of FBXW7 [92] by inhibiting the expression of miR-155 and the MMP2/ERK/MAPK signaling pathway [93], thereby having antitumour effects. In addition, MALAT1 promotes the proliferation of glioma through various ways [94–97] by reducing the sensitivity of glioma cells to temozolomide [98,99]. Similarly, LncRNA TUG1 has an antitumour role in the upregulation of PTEN by sponging miR-26a [100]. Further, the combination of lncRNA TUG and lncRNA GATA6-AS[101,102] has antitumour effects. Other studies showed that TUG1 promotes tumour vascular endothelial cell proliferation by modulating miR-299 [103], miR-6321 [104], and miR-144 [105] and the Notch pathway [106,107], thus improving the malignant biological behaviour of glioma cells. Further research is required to explore the dual expression of lncRNAs.

Table 3
Dual expression of lncRNA in glioma and different mechanisms of regulation.

LncRNA	Funtional mechanism	Biological functions	Refs.
MALAT1↑	↑MDR/ZEB1	↑ TMZ-resistance	98,99
	┤miR-199a┤ZHX1,ceRNA ↑Bax ↓Bcl-2	↑ Proliferation	94
	┤miR-129 ┤S0X2,ceRNA	↑ Proliferation	95
	┤miR-101┤Rap1B,ceRNA	↑ Proliferation ↓ Apoptosis	96
	→ERK/MAPK ↑ Nestin,SOX2	↑ Proliferation	97
MALAT1↓	┤miR-155┤FBXW7,ceRNA	↓Proliferation	92
	↓ERK/MAPK,MMP2	↓Proliferation,invasion	93
TUG1↑	┤miR-299 ┤VEGF,ceRNA	↑ Angiogenesis	103
	Notch→TUG1┤miR-145	↑Stemness of GSCs	106,107
	┤miR-6321┤ATF2/VEGF/SDF-1 ┤PAX1	↑ Angiogenesis	104
	┤miR-144┤HSF2,ceRNA ↑ZO-1,occludin,claudin-5	↓ BTB permeability	105
TUG1↓	↑caspase-3,caspase-9 ↓Bcl-2	↑Apoptosis	101
	┤miR-26a┤PTEN,ceRNA	↑Apoptosis	100

4. Conclusions and perspectives

Glioma is the most common malignant tumour in the central nervous system, accounting for approximately 30 % of primary brain tumours [1]. Glioma is broadly invasive and tends to transition from a low-grade to a high-grade tumour [108]. The 10-year survival rate for low-grade glioma is less than 50 %, and the prognosis for high-grade glioma is worse [109]. At present, the treatment is mainly surgery and adjuvant chemoradiotherapy; however, the curative effects are not optimal [2,3]. To improve the effectiveness of therapies, the pathogenesis of glioma at the genetic and molecular levels must be studied to discover new biomarkers and therapeutic targets. Specifically, breakthrough therapies incorporating lncRNAs could potentially significantly affect prognosis. Historically, due to the lack of related knowledge and research, lncRNAs have been regarded as "transcriptional noise" and transcription by-products of RNA polymerase II on lncRNAs, and therefore have not been considered to have biological effects on glioma [110–112]. Due to the extensive application of lncRNA deep sequencing and gene chip technology, many lncRNAs differentially expressed in glioma have been found. Recently, the research of lncRNA effects on tumours has shown geometric growth; the abnormal expression of lncRNAs found in glioma is now known to have an important role in tumourigenesis, proliferation, angiogenesis, invasion, metastasis, etc. Rynkeviciene et al. showed that lncRNA affects both transcriptional and posttranscriptional factors with complex mechanisms [111], many of which remain unclear. Many studies have found that lncRNAs are associated with glioma tissue types; this association may have an important role in the basic pathological processes of glioma [113,114]. However, further research is needed to discover the specific lncRNAs which are vital in glioma development. Enhanced diagnostic strategies and targeted therapies using lncRNAs may improve prompt diagnosis and offer new treatment options for patients with glioma.

Research on lncRNA has shown that some factors can lead to differences in lncRNA expression or lower expression abundance. One such factor is gene copy number variation (deletion or amplification). This variation occurs at the DNA level. We are aware that lncRNA needs to be transcribed. A missing or amplified corresponding gene of lncRNA on the plasmid can lead to abnormal transcription templates. In addition, transcription factors, histone modifications, and DNA methylation are influencing factors. Further research is needed on these and other factors.

LncRNA can affect various biological processes such as tumour cell apoptosis, drug resistance, and tumour metastasis, playing an important role in revealing the occurrence and development of tumours. However, research on lncRNA is still in its initial stages, and

the identified functional lncRNAs are based on biological evidence. To date, the number of lncRNAs speculated by bioinformatics methods represents only a small proportion. The need for in-depth research on the mechanism of lncRNA action and its clinical application remains. Some lncRNAs related to the development of human tumours have little tissue specificity. In addition, the experimental methods for studying lncRNA are limited. Finally, the question of whether known functional lncRNAs can be applied in clinical practice to safely and effectively treat tumours remains unanswered. However, we believe that in the future, a combination of molecular biology, proteomics, and animal experiments can be used to delve into the regulatory roles that specific lncRNAs have in tumour occurrence and development. Furthermore, elucidating the signal transduction pathways that specific lncRNAs participate in during the regulation of promoters and the identification of effective targets may contribute to improving the diagnosis and treatment of tumours.

LncRNA is closely related to the occurrence and development of tumours, and new drug research and development targeting lncRNA has made certain progress. Small molecule inhibitors, nucleic acid drugs, and related regulators of lncRNA have been discovered. With the continuous discovery of lncRNA structural information and functional motifs, designing or discovering small molecule inhibitors with related targets has become a reality. Methylation inhibitor 5-azapurine-2 ′- deoxycytidine (5-aza-dC) can inhibit methylation in the imprinting control region of the H19 gene and downregulate H19 gene expression. The latest research on nucleic acid drug small interfering RNA (siRNA) has also been significant in contributing to the potential development of targeted lncRNA drugs. Research on drugs related to siRNA as a regulator to inhibit lncRNA targets is underway. The indirect regulator of lncRNA is also a new direction for drug research and development. For example, estradiol can induce the increased expression of the antisense transcript lncRNA of HOTAIR by regulating the estrogen receptor, and the overexpression of HOTAIR promotes the development of breast cancer. Therefore, using estrogen receptor inhibitors or estradiol antagonists can indirectly regulate the expression of lncRNA HOTAIR, thereby achieving anticancer effects. These studies indicate that epigenetics-based modulators have the potential to become novel drugs that will exert anti-tumour effects by regulating lncRNA expression and related pathways.

In conclusion, lncRNAs are expected to be tools for targeted treatment combined with traditional or new therapeutic approaches and may compensate for the deficiencies of other treatment methods. We believe that future investigations will lead to affluent clinical translations of glioma-associated lncRNAs and translate into novel therapeutic paradigms, thereby producing improved anti-tumour benefits for patients with glioma.

Data availability statement

No data was used for the research described in the article.

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Ethics approval

Review and/or approval by an ethics committee was not needed for this study because the study did not directly involve patients or patient care.

Informed consent

Informed consent was not required for this study because of the nature of the article.

CRediT authorship contribution statement

Xiaolin Lu: Writing – original draft. **Dongzhi Zhang:** Writing – review & editing, Resources, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] M. Weller, W. Wick, K. Aldape, et al., Glioma, Nat. Rev. Dis. Prim. (2015) 15017, https://doi.org/10.1038/nrdp. Jul 16;1:15017 1.
[2] N. Sanai, M.S. Berger, Surgical oncology for gliomas: the state of the art, Nat. Rev. Clin. Oncol. 15 (2) (2018) 112–125.
[3] L.H.M. Geraldo, et al., Glioblastoma therapy in the age of molecular medicine, Trends Cancer 5 (1) (2019) 46–65.
[4] I.Y. Eyüpoglu, et al., Surgical resection of malignant gliomas-role in optimizing patient outcome, Nat. Rev. Neurol. 9 (3) (2013) 141–151.
[5] K.M. Kiang, et al., Long non-coding RNAs: the key players in glioma pathogenesis, Cancers 7 (3) (2015) 1406–1424.
[6] A. Bhan, et al., Long noncoding RNA and cancer: a new paradigm, Cancer Res. 77 (15) (2017) 3965–3981.
[7] W.X. Peng, et al., LncRNA-mediated regulation of cell signaling in cancer, Oncogene 36 (41) (2017) 5661–5667.
[8] L. Nair, et al., Regulation of long non-coding RNAs and genome dynamics by the RNA surveillance machinery, Nat. Rev. Mol. Cell Biol. 21 (3) (2020) 123–136.
[9] R. Rynkeviciene, et al., Non-coding RNAs in glioma, Cancers 11 (1) (2018).
[10] M. Wang, et al., The functional roles of exosomal long non-coding RNAs in cancer, Cell. Mol. Life Sci. 76 (11) (2019) 2059–2076, https://doi.org/10.1007/s00018-019-03018-3.
[11] P. Jia, et al., Long non-coding RNA H19 regulates glioma angiogenesis and the biological behavior of glioma-associated endothelial cells by inhibiting microRNA-29a, Cancer Lett. 381 (2) (2016) 359–369.
[12] C. Li, et al., H19 derived microRNA-675 regulates cell proliferation and migration through CDK6 in glioma, Am J Transl Res 7 (10) (2015) 1747–1764.
[13] X. Jiang, et al., Increased level of H19 long noncoding RNA promotes invasion, angiogenesis, and stemness of glioblastoma cells, J Neurol Surg 124 (1) (2016) 129–136.
[14] L. Chen, et al., Long noncoding RNA H19 promotes proliferation and invasion in human glioma cells by downregulating miR-152, Oncol. Res. 26 (9) (2018) 1419–1428.
[15] J. Ke, et al., Knockdown of long non-coding RNA HOTAIR inhibits malignant biological behaviors of human glioma cells via modulation of miR-326, OOncotarget. Oncotarget 6 (26) (2015) 21934–21949.
[16] K. Zhang, et al., Long non-coding RNA HOTAIR promotes glioblastoma cell cycle progression in an EZH2 dependent manner, Oncotarget 6 (1) (2015) 537–546.
[17] L. Sa, et al., The role of HOTAIR/miR-148b-3p/USF1 on regulating the permeability of BTB, Front. Mol. Neurosci. 10 (2017) 194.
[18] S.K. Tan, et al., Serum long noncoding RNA HOTAIR as a novel diagnostic and prognostic biomarker in glioblastoma multiforme, Mol. Cancer 17 (1) (2018) 74.
[19] A. Xavier-Magalhães, C.S. Gonçalves, A. Fogli, et al., The long non-coding RNA HOTAIR is transcriptionally activated by HOXA9 and is an independent prognostic marker in patients with malignant glioma, Oncotarget 9 (21) (2018) 15740–15756, https://doi.org/10.18632/oncotarget.24597, 2018.
[20] B.J. Reon, et al., LINC00152 promotes invasion through a 3′-hairpin structure and associates with prognosis in glioblastoma, Mol. Cancer Res. 16 (10) (2018) 1470–1482.
[21] M. Yu, et al., Linc00152 promotes malignant progression of glioma stem cells by regulating miR-103a-3p/FEZF1/CDC25A pathway, Mol. Cancer 16 (1) (2017) 110.
[22] Q. Chen, et al., Long noncoding RNA NEAT1, regulated by the EGFR pathway, contributes to glioblastoma progression through the WNT/beta-catenin pathway by scaffolding EZH2, Clin. Cancer Res. 24 (3) (2018) 684–695.
[23] K. Zhou, et al., Knockdown of long non-coding RNA NEAT1 inhibits glioma cell migration and invasion via modulation of SOX2 targeted by miR-132, Mol. Cancer 17 (1) (2018) 105.
[24] Y. Yao, et al., Knockdown of long non-coding RNA XIST exerts tumor-suppressive functions in human glioblastoma stem cells by up-regulating miR-152, Cancer Lett. 359 (1) (2015) 75–86.
[25] H. Yu, et al., Knockdown of long non-coding RNA XIST increases blood-tumor barrier permeability and inhibits glioma angiogenesis by targeting miR-137, Oncogenesis 6 (3) (2017) e303.
[26] Z. Cheng, et al., Long non-coding RNA XIST promotes glioma tumorigenicity and angiogenesis by acting as a molecular sponge of miR-429, J. Cancer 8 (19) (2017) 4106–4116.
[27] J. Zheng, et al., CRNDE promotes malignant progression of glioma by attenuating miR-384/PIWIL4/STAT3 axis, Mol. Ther. 24 (7) (2016) 1199–1215.
[28] Y. Wang, et al., CRNDE, a long-noncoding RNA, promotes glioma cell growth and invasion through mTOR signaling, Cancer Lett. 367 (2) (2015) 122–128.
[29] D.X. Li, X.R. Fei, Y.F. Dong, et al., The long non-coding RNA CRNDE acts as a ceRNA and promotes glioma malignancy by preventing miR-136-5p-mediated downregulation of Bcl-2 and Wnt2, Oncotarget 8 (50) (2017) 88163–88178, https://doi.org/10.18632/oncotarget.21513, 2017.
[30] K.M. Kiang, et al., CRNDE expression positively correlates with EGFR activation and modulates glioma cell growth, Targeted Oncol. 12 (3) (2017) 353–363.
[31] Y. Yan, et al., Novel function of lncRNA ADAMTS9-AS2 in promoting temozolomide resistance in glioblastoma via upregulating the FUS/MDM2 ubiquitination axis, Front. Cell Dev. Biol. 7 (2019) 217.
[32] W.Z. Luo, X.Y. Li, Z.Y. Song, et al., Long non-coding RNA AGAP2-AS1 exerts oncogenic properties in glioblastoma by epigenetically silencing TFPI2 through EZH2 and LSD1. Jun 11;11(11):3811-3823, Aging (Albany NY) 11 (11) (2019) 3811–3823, https://doi.org/10.18632/aging.102018, 2019.
[33] C. Liu, et al., CASC2c as an unfavorable prognosis factor interacts with miR-101 to mediate astrocytoma tumorigenesis, Cell Death Dis. 8 (3) (2017) e2639.
[34] S. Deguchi, et al., Oncogenic effects of evolutionarily conserved noncoding RNA ECONEXIN on gliomagenesis, Oncogene 36 (32) (2017) 4629–4640.
[35] Y.F. Gao, et al., LncRNA FOXD1-AS1 acts as a potential oncogenic biomarker in glioma, CNS Neurosci. Ther. 26 (1) (2020) 66–75.
[36] J. Ye, et al., A novel lncRNA-LINC01116 regulates tumorigenesis of glioma by targeting VEGFA, Int. J. Cancer 146 (1) (2020) 248–261.
[37] Y. Xin, et al., LncRNA LINC01140 inhibits glioma cell migration and invasion via modulation of miR-199a-3p/ZHX1 axis, OncoTargets Ther. 13 (2020) 1833–1844.
[38] M.S. Leisegang, et al., Long noncoding RNA MANTIS facilitates endothelial angiogenic function, Circulation 136 (1) (2017) 65–79.
[39] J. Zhu, et al., MATN1-AS1 promotes glioma progression by functioning as ceRNA of miR-200b/c/429 to regulate CHD1 expression, Cell Prolif. 53 (1) (2020) e12700.
[40] C. Yang, et al., The effect of MCM3AP-AS1/miR-211/KLF5/AGGF1 axis regulating glioblastoma angiogenesis, Front. Mol. Neurosci. 10 (2017) 437.
[41] A. Bountali, et al., RNA sequencing reveals a key role for the long non-coding RNA MIAT in regulating neuroblastoma and glioblastoma cell fate, Int. J. Biol. Macromol. 130 (2019) 878–891.
[42] X. Zhao, et al., GAS5 suppresses malignancy of human glioma stem cells via a miR-196a-5p/FOXO1 feedback loop, Biochim. Biophys. Acta Mol. Cell Res. 1864 (10) (2017) 1605–1617.
[43] X. Zhao, et al., Gas5 exerts tumor-suppressive functions in human glioma cells by targeting miR-222, Mol. Ther. 23 (12) (2015) 1899–1911.
[44] Q. Liu, et al., Long noncoding RNA GAS5 regulates the proliferation, migration, and invasion of glioma cells by negatively regulating miR-18a-5p, J. Cell. Physiol. 234 (1) (2018) 757–768.
[45] C. Jin, J. Zhao, Z.P. Zhang, et al., Long non-coding RNA GAS5, by up-regulating PRC2 and targeting the promoter methylation of miR-424, suppresses multiple malignant phenotypes of glioma, J. Neuro Oncol. 148 (3) (2020) 529–543, https://doi.org/10.1007/s11060-020-03544-2.
[46] Y. Ding, et al., Long noncoding RNA-GAS5 attenuates progression of glioma by eliminating microRNA-10b and sirtuin 1 in U251 and A172 cells, Biofactors 46 (3) (2020) 487–496.
[47] G. Li, et al., LncRNA GAS5 regulates the proliferation, migration, invasion and apoptosis of brain glioma cells through targeting GSTM3 expression. The effect of LncRNA GAS5 on glioma cells, J. Neuro Oncol. 143 (3) (2019) 525–536.
[48] J. Huo, X.B. Chen, Long noncoding RNA growth arrest-specific 5 facilitates glioma cell sensitivity to cisplatin by suppressing excessive autophagy in an mTOR-dependent manner, J. Cell. Biochem. 2018 (2018) 1–10.
[49] J. Yuan, et al., LncRNA GAS5 indel genetic polymorphism contributes to glioma risk through interfering binding of transcriptional factor TFAP2A, DNA Cell Biol. 37 (9) (2018) 750–757.
[50] J. Shen, et al., Serum HOTAIR and GAS5 levels as predictors of survival in patients with glioblastoma, Mol. Carcinog. 57 (1) (2018) 137–141.

[51] E.A. Toraih, et al., Dual biomarkers long non-coding RNA GAS5 and microRNA-34a co-expression signature in common solid tumors, PLoS One 13 (10) (2018) e0198231.
[52] A. García-Claver, et al., Gene expression changes associated with erlotinib response in glioma cell lines, Eur. J. Cancer 49 (7) (2013) 1641–1653.
[53] Q. Liu, et al., Altered expression of long non-coding RNAs during genotoxic stress-induced cell death in human glioma cells, J. Neuro Oncol. 122 (2) (2015) 283–292.
[54] M. Norouzi, et al., Doxorubicin-loaded iron oxide nanoparticles for glioblastoma therapy: a combinational approach for enhanced delivery of nanoparticles, Sci. Rep. 10 (1) (2020) 11292, https://doi.org/10.1038/s41598-020-68017-y.
[55] X.R. Xia, et al., Effects of small nucleolar RNA SNORD44 on the proliferation, apoptosis and invasion of glioma cells, Histochem. Cell Biol. 153 (4) (2020) 257–269.
[56] X. Gong, M.Y. Huang, Tumor-suppressive function of lncRNA-MEG3 in glioma cells by regulating miR-6088/SMARCB1 axis, BioMed Res. Int. 2020 (2020) 4309161.
[57] S. Shen, et al., PIWIL1/piRNA-DQ593109 regulates the permeability of the blood-tumor barrier via the MEG3/miR-330-5p/RUNX3 axis, Mol. Ther. Nucleic Acids 10 (2018) 412–425.
[58] S. Zhang, et al., Long non-coding RNA MEG3 suppresses the growth of glioma cells by regulating the miR-96-5p/MTSS1 signaling pathway, Mol. Med. Rep. 20 (5) (2019) 4215–4225.
[59] X. Gong, M. Huang, Long non-coding RNA MEG3 promotes the proliferation of glioma cells through targeting Wnt/beta-catenin signal pathway, Cancer Gene Ther. 24 (9) (2017) 381–385.
[60] X. Li, et al., Tunicamycin inhibits progression of glioma cells through downregulation of the MEG-3-regulated wnt/beta-catenin signaling pathway, Oncol. Lett. 15 (6) (2018) 8470–8476.
[61] D.H. Xu, G.N. Chi, C.H. Zhao, D.Y. Li, Long noncoding RNA MEG3 inhibits proliferation and migration but induces autophagy by regulation of Sirt7 and PI3K/AKT/mTOR pathway in glioma cells, J. Cell. Biochem. 120 (5) (2018) 7516–7526, https://doi.org/10.1002/jcb.28026.
[62] L. Zhang, et al., Long non-coding RNA MEG3 inhibits cell growth of gliomas by targeting miR-93 and inactivating PI3K/AKT pathway, Oncol. Rep. 38 (4) (2017) 2408–2416.
[63] D. Wang, et al., Participation of tumor suppressors long non-coding RNA MEG3, microRNA-377 and PTEN in glioma cell invasion and migration, Pathol. Res. Pract. 215 (10) (2019) 152558.
[64] W. Ruan, et al., Knockdown of long noncoding RNA MEG3 impairs VEGF-stimulated endothelial sprouting angiogenesis via modulating VEGFR2 expression in human umbilical vein endothelial cells, Gene 649 (2018) 32–39.
[65] B. Ma, et al., Long non-coding RNA MEG3 contributes to cisplatin-induced apoptosis via inhibition of autophagy in human glioma cells, Mol. Med. Rep. 16 (3) (2017) 2946–2952.
[66] N. Qin, et al., Long noncoding RNA MEG3 suppresses glioma cell proliferation, migration, and invasion by acting as a competing endogenous RNA of miR-19a, Oncol. Res. 25 (9) (2017) 1471–1478.
[67] X. Li, et al., Tunicamycin inhibits progression of glioma cells through downregulation of the MEG-3-regulated wnt/beta-catenin signaling pathway, Oncol. Lett. 15 (6) (2018) 8470–8476.
[68] H. Zhao, et al., Long non-coding RNA MEG3 regulates proliferation, apoptosis, and autophagy and is associated with prognosis in glioma, J. Neuro Oncol. 140 (2) (2018) 281–288.
[69] P. Wang, et al., Overexpression of the long non-coding RNA MEG3 impairs in vitro glioma cell proliferation, J. Cell. Biochem. 113 (6) (2012) 1868–1874.
[70] X. Zhang, et al., A pituitary-derived MEG3 isoform functions as a growth suppressor in tumor cells, J. Clin. Endocrinol. Metab. 88 (11) (2003) 5119–5126.
[71] Z. Yang, et al., Meg3 induces EMT and invasion of glioma cells via autophagy, OncoTargets Ther. 13 (2020) 989–1000.
[72] K.M. Kiang, et al., Long non-coding RNAs: the key players in glioma pathogenesis, Cancers 7 (3) (2015) 1406–1424.
[73] C. Shang, et al., Long non-coding RNA TUSC7, a target of miR-23b, plays tumor-suppressing roles in human gliomas, Front. Cell. Neurosci. 10 (2016) 235.
[74] C. Shang, et al., Long non-coding RNA TUSC7 inhibits temozolomide resistance by targeting miR-10a in glioblastoma, Cancer Chemother. Pharmacol. 81 (4) (2018) 671–678.
[75] X.L. Ma, et al., Long non-coding RNA TUSC7 expression is independently predictive of outcome in glioma, Eur. Rev. Med. Pharmacol. Sci. 21 (16) (2017) 3605–3610.
[76] P. Wang, et al., Long non-coding RNA CASC2 suppresses malignancy in human gliomas by miR-21, Cell. Signal. 27 (2) (2015) 275–282.
[77] Y. Liao, et al., LncRNA CASC2 interacts with miR-181a to modulate glioma growth and resistance to TMZ through PTEN pathway, J. Cell. Biochem. 118 (7) (2017) 1889–1899.
[78] R. Wang, et al., Long noncoding RNA CASC2 predicts the prognosis of glioma patients and functions as a suppressor for gliomas by suppressing Wnt/beta-catenin signaling pathway, Neuropsychiatric Dis. Treat. 13 (2017) 1805–1813.
[79] C. Jiang, et al., Upregulation of CASC2 sensitized glioma to temozolomide cytotoxicity through autophagy inhibition by sponging miR-193a-5p and regulating mTOR expression, Biomed. Pharmacother. 97 (2018) 844–850.
[80] J. Yao, et al., A new tumor suppressor LncRNA ADAMTS9-AS2 is regulated by DNMT1 and inhibits migration of glioma cells, Tumour Biol 35 (8) (2014) 7935–7944.
[81] A. Wang, et al., Long non-coding RNA ENST00462717 suppresses the proliferation, survival, and migration by inhibiting MDM2/MAPK pathway in glioma, Biochem. Biophys. Res. Commun. 485 (2) (2017) 513–521.
[82] J. Zhao, et al., Long non-coding RNA Linc00152 is involved in cell cycle arrest, apoptosis, epithelial to mesenchymal transition, cell migration and invasion in gastric cancer, Cell Cycle 14 (19) (2015) 3112–3123.
[83] W. Huang, et al., LncRNA GAS5-AS1 inhibits glioma proliferation, migration, and invasion via miR-106b-5p/TUSC2 axis, Hum. Cell 33 (2) (2020) 416–426.
[84] L.M. Xu, et al., Over-expression of the long non-coding RNA HOTTIP inhibits glioma cell growth by BRE, J. Exp. Clin. Cancer Res. 35 (1) (2016) 162.
[85] S. Tian, et al., Long non-coding RNA Linc00320 inhibits glioma cell proliferation through restraining Wnt/beta-catenin signaling, Biochem. Biophys. Res. Commun. 508 (2) (2019) 458–464.
[86] Y. Yu, et al., Long non-coding RNA SLC26A4-AS1 exerts antiangiogenic effects in human glioma by upregulating NPTX1 *via* NF-kB1 transcriptional factor, FEBS J. 288 (1) (2021) 212–228.
[87] X. Qin, et al., LncRNA TSLC1-AS1 is a novel tumor suppressor in glioma, Int. J. Clin. Exp. Pathol. 7 (6) (2014) 3065–3072.
[88] B. Zhang, et al., The lncRNA Malat1 is dispensable for mouse development but its transcription plays a cis-regulatory role in the adult, Cell Rep. 2 (1) (2012) 111–123.
[89] J.E. Wilusz, et al., 3′ end processing of a long nuclear-retained noncoding RNA yields a tRNA-like cytoplasmic RNA, Cell 135 (5) (2008) 919–932.
[90] J.N. Hutchinson, et al., A screen for nuclear transcripts identifies two linked noncoding RNAs associated with SC35 splicing domains, BMC Genom. 8 (2007) 39.
[91] P. Ji, et al., MALAT-1, a novel noncoding RNA, and thymosin beta4 predict metastasis and survival in early-stage non-small cell lung cancer, Oncogene 22 (39) (2003) 8031–8041.
[92] S. Cao, et al., Tumor-suppressive function of long noncoding RNA MALAT1 in glioma cells by suppressing miR-155 expression and activating FBXW7 function, Am. J. Cancer Res. 6 (11) (2016) 2561–2574.
[93] Y. Han, et al., Tumor-suppressive function of long noncoding RNA MALAT1 in glioma cells by downregulation of MMP2 and inactivation of ERK/MAPK signaling, Cell Death Dis. 7 (3) (2016) e2123.
[94] K. Liao, et al., Blocking lncRNA MALAT1/miR-199a/ZHX1 axis inhibits glioblastoma proliferation and progression, Mol. Ther. Nucleic Acids 18 (2019) 388–399.
[95] Z. Xiong, et al., LncRNA MALAT1/miR-129 axis promotes glioma tumorigenesis by targeting SOX2, J. Cell Mol. Med. 22 (8) (2018) 3929–3940.

[96] Z. Li, et al., Long non-coding RNA MALAT1 promotes proliferation and suppresses apoptosis of glioma cells through derepressing Rap1B by sponging miR-101, J. Neuro Oncol. 134 (1) (2017) 19–28.
[97] Y. Han, et al., Downregulation of lncRNA-MALAT1 affects proliferation and the expression of stemness markers in glioma stem cell line SHG139S, Cell. Mol. Neurobiol. 36 (7) (2016) 1097–1107.
[98] H. Li, et al., Long non-coding RNA MALAT1 decreases the sensitivity of resistant glioblastoma cell lines to temozolomide, Cell. Physiol. Biochem. 42 (3) (2017) 1192–1201.
[99] S.S. Kim, et al., Targeted nanocomplex carrying siRNA against MALAT1 sensitizes glioblastoma to temozolomide, Nucleic Acids Res. 46 (3) (2018) 1424–1440.
[100] J. Li, et al., Long non-coding RNA TUG1 acts as a miR-26a sponge in human glioma cells, Biochem. Biophys. Res. Commun. 477 (4) (2016) 743–748.
[101] J. Li, et al., LncRNA TUG1 acts as a tumor suppressor in human glioma by promoting cell apoptosis, Exp Biol Med. 241 (6) (2016) 644–649.
[102] Y. Liao, et al., LncRNA GATA6-AS promotes cancer cell proliferation and inhibits apoptosis in glioma by downregulating lncRNA TUG1, Cancer Biother Radiopharm. 34 (10) (2019) 660–665.
[103] H. Cai, et al., Long non-coding RNA taurine upregulated 1 enhances tumor-induced angiogenesis through inhibiting microRNA-299 in human glioblastoma, Oncogene 36 (3) (2017) 318–331.
[104] G. Yu, et al., LncRNA TUG1 functions as a ceRNA for miR-6321 to promote endothelial progenitor cell migration and differentiation, Exp. Cell Res. 388 (1) (2020) 111839.
[105] H. Cai, et al., The long noncoding RNA TUG1 regulates blood-tumor barrier permeability by targeting miR-144, Oncotarget 6 (23) (2015) 19759–19779.
[106] K. Katsushima, et al., Targeting the Notch-regulated non-coding RNA TUG1 for glioma treatment, Nat. Commun. 7 (2016) 13616.
[107] Z. Zhao, et al., Downregulation of the long non-coding RNA taurine-upregulated gene 1 inhibits glioma cell proliferation and invasion and promotes apoptosis, Oncol. Lett. 15 (3) (2018) 4026–4032.
[108] R. Chen, et al., Glioma subclassifications and their clinical significance, Neurotherapeutics 14 (2) (2017) 284–297.
[109] D.T.W. Jones, et al., Pediatric low-grade gliomas: next biologically driven steps, Neuro Oncol. 20 (2) (2018) 160–173.
[110] L. Liu, et al., "The roles of long noncoding RNAs in breast cancer metastasis" Cell Death, Dis 11 (9) (2020) 749.
[111] R. Rynkeviciene, et al., Non-coding RNAs in glioma, Cancers 11 (1) (2018).
[112] K. Struhl, Transcriptional noise and the fidelity of initiation by RNA polymerase II, Nat. Struct. Mol. Biol. 14 (2) (2007) 103–105.
[113] C. Jones, et al., Pediatric high-grade glioma: biologically and clinically in need of new thinking, Neuro Oncol. 19 (2) (2017) 153–161.
[114] Z. Peng, et al., New insights into long noncoding RNAs and their roles in glioma, Mol. Cancer 17 (1) (2018) 61.