TARGETING LONG NON-CODING RNAs IN GLIOBLASTOMA: A NEW FRONTIER IN CANCER THERAPY

by

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A critical review submitted in partial fulfillment
of the requirements for a degree of
Master of Science in Chemical Sciences

The Faculty of Graduate Studies
Laurentian University
Sudbury, Ontario, Canada

CRITICAL REVIEW ESSAY DEFENCE COMMITTEE/COMITÉ DE SOUTENANCE DE LA REVUE CRITIQUE
Laurentian Université/Université Laurentienne
Faculty of Graduate Studies/Faculté des études supérieures

Title of Essay Titre de l'essai	ARGETING LONG NON-CODING RNAs IN GLIOBLASTOMA: A NEW FRONTIER IN CANCER THERAPY	
Name of Candidate Nom du candidat	Limbachiya , Vishva V.	
Degree Diplôme	Master of	
Program Programme	Chemical Sciences	Date of Defence Date de la soutenance August 12, 2025

APPROVED/APPROUVÉ

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Approuvé pour la Faculté des études supérieures
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Laurentian University / Université Laurentienne

Abstract

Glioblastoma (GBM) is the most aggressive primary brain tumor observed in adults. It progresses quickly, it has a poor prognosis and is resistant to common treatments like temozolomide (TMZ). This study critically examines the function that long non-coding RNAs (lncRNAs) play in the pathological processes of GBM, highlighting their roles in tumor heterogeneity, therapeutic resistance, and dysregulated signaling. A systematic search of 679 papers using PRISMA guidelines resulted 389 studies that were chosen for a comprehensive review. The review addresses at how lncRNAs regulate important pathways like PI3K/AKT, p53, NF-κB, Wnt/β-catenin, and JAK/STAT. It also categorizes lncRNAs according to their genetic origin, subcellular location, and functional roles. The article also emphasizes how lncRNAs affect glioma stemness and immune evasion, as well as their dual oncogenic and tumor-suppressive roles. Overall, this work identifies lncRNAs as promising biomarkers and therapeutic targets, supporting their potential integration into precision medicine for GBM.

Key words

Glioblastoma (GBM), long non-coding RNA (lncRNA), Glioma stem cell (GSC), brain tumor, astrocytoma, oncogene, tumor-suppressive, therapy resistance

Acknowledgements

I would like to express my sincere gratitude to my supervisor, Dr. Sujeenthar Tharmalingam, for his continuous guidance, encouragement, and insightful feedback throughout the course of this review. I consider myself truly fortunate to have had the opportunity to work under his supervision. His unwavering support and academic mentorship were instrumental in shaping the direction and depth of my research, and for that, I am deeply thankful.

I am also grateful to Laurentian University for providing a supportive and stimulating academic environment. The faculty and staff of the Department of Chemistry and Biochemistry played an essential role in fostering my learning and professional growth. Special thanks go to Dr. Vasu Appanna for serving on the supervisory committee, reviewing this work, and offering valuable feedback that contributed meaningfully to its improvement. I would like to extend my appreciation to the library staff and research support services at NOSM University, whose assistance with access to essential literature greatly facilitated my study.

Lastly, I am profoundly thankful to my family and friends for their constant support, patience, and encouragement throughout this academic journey. Your belief in me has been a source of strength and motivation during challenging times.

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List of Abbreviations

GBM	Glioblastoma
lncRNA	Long Non-Coding RNA
mRNA	Messenger RNA
miRNA	Micro RNA
ceRNA	Competing Endogenous RNA
GSC	Glioma Stem Cell
TMZ	Temozolomide
PI3K	Phosphoinositide 3-Kinase
EGFR	Epidermal Growth Factor Receptor
TP53	Tumor Protein 53
IDH	Isocitrate Dehydrogenase
MAPK	Mitogen-Activated Protein Kinase
NF-κB	Nuclear Factor Kappa-light-chain-enhancer of Activated B Cells
EMT	Epithelial-Mesenchymal Transition
TGF-β	Transforming Growth Factor Beta
PRC2	Polycomb Repressive Complex 2
MGMT	O6-Methylguanine-DNA Methyltransferase
qRT-PCR	Quantitative Reverse Transcription Polymerase Chain Reaction
IFN-β	Interferon Beta
BBB	Blood Brain Barrier
NEAT1	Nuclear Paraspeckle Assembly Transcript 1
circRNA	Circular RNA
siRNA	Small Interfering RNA
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats

Chapter 1: Introduction

1.1 Brief overview and history of glioblastoma

1.1.1 Importance of molecular research in GBM

The most common and dangerous type of primary brain tumor in adults is GBM, which makes about 15% of all intracranial neoplasms [1]**.** Despite aggressive multimodal treatment, which includes concomitant radiotherapy, temozolomide (TMZ) chemotherapy, and maximal safe surgical resection, the prognosis is still poor, with a median survival of only 12 to 15 months [2]. GBM is one of the worst malignancies to treat because of its high risk of recurrence, significant resistance to treatment, and highly infiltrative nature. Due to the poor efficacy of standard therapy, the focus has switched to comprehending the molecular and genetic pathways that underlie the genesis and progression of GBM. The understanding of GBM has changed during the last 20 years due to molecular research, which has shown complex structures of tumor heterogeneity, epigenetic regulation, and oncogenic signaling [3]. Molecular research has become a key component of contemporary GBM management and drug development because of these insights, which have given rise to a framework for biomarker discovery, patient classification, and the creation of targeted medicines. Molecular research in GBM has improved prognostic evaluation and diagnostic accuracy while also highlighting the underlying mechanisms of tumour heterogeneity and therapy resistance, which are key barriers to effective treatment. For instance, genetic studies into tumor hierarchy and cell plasticity have led to the discovery of glioma stem-like cells (GSCs), which could self-renew and repopulate tumors following treatment [4]. Treating these GSCs directly is necessary because they have unique gene expression patterns and are frequently more resistant to chemotherapy and radiation. Additionally, the use of single-cell transcriptomic and spatial omics technologies has shown significant spatial and transcriptional heterogeneity in GBM tumors, demonstrating how various subpopulations may thrive in the same tumor microenvironment and react differentially to treatment. These insights have changed therapeutic practices, resulting in more individualized, flexible interventions rather than standardized therapy methods [5]. Numerous new therapeutic platforms, including RNA-based treatments, oncolytic viruses, and CAR-T cell therapies, are presently being studied in clinical trials because of molecular research. Overall, further molecular research is essential for both understanding the biology of GBM and converting molecular discoveries into clinically useful treatments. **Figure 1** illustrates the invasion of tumour growth and local recurrence in GSC which can lead to therapy resistance. For treating that, such conventional techniques are available, however long non-coding RNAs (lncRNAs) can control cell survival and resistance.

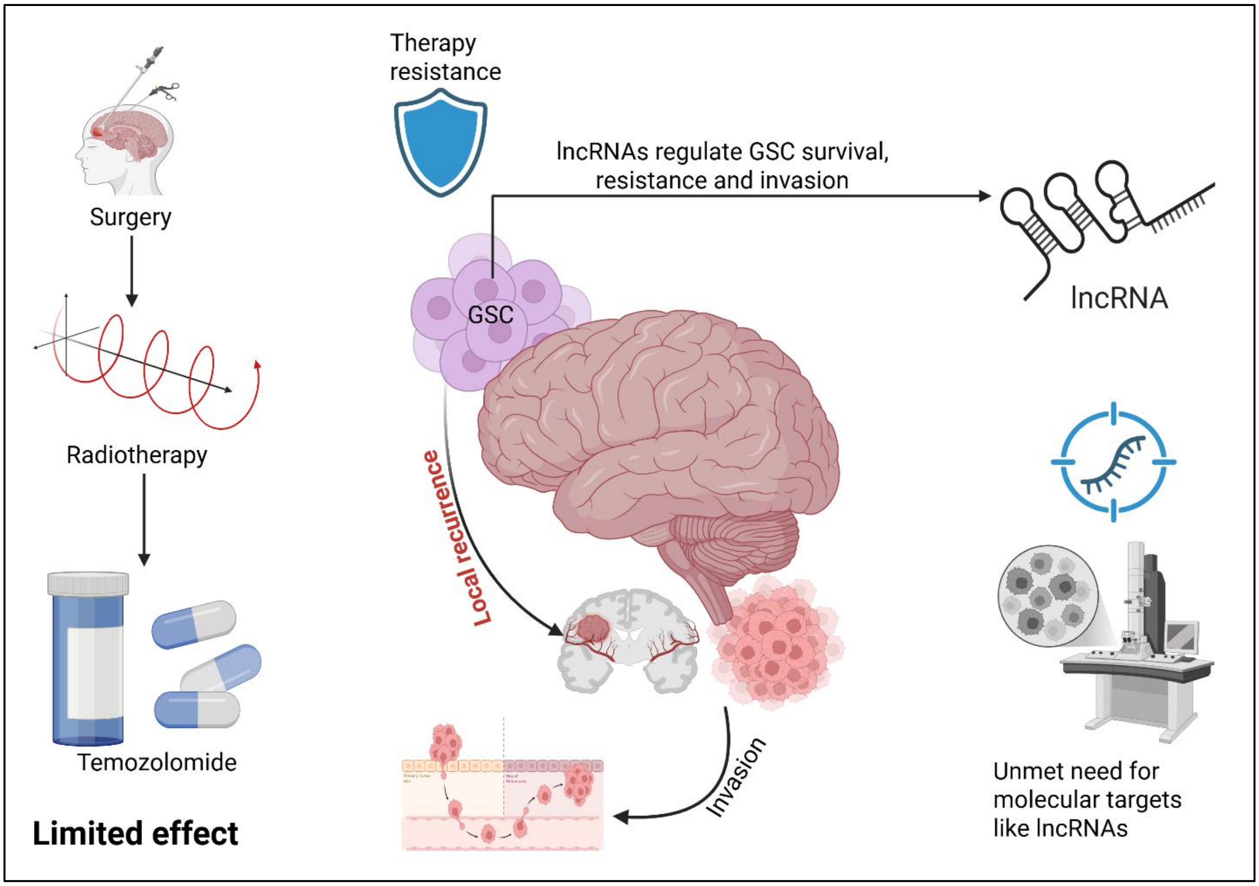


Figure 1 Overview of GBM pathogenesis and clinical challenges.

This figure outlines the complex pathogenesis of GBM, including genetic mutations, molecular subtypes, resistance mechanisms, and therapeutic limitations. It visually integrates the challenges in clinical treatment and highlights the role of lncRNAs in modulating key oncogenic pathways.

1.1.2 Genetic and molecular characteristics of GBM

GBM is characterized by extremely aggressive behavior, poor clinical outcomes, and resistance to treatment due to its considerable genetic and molecular heterogeneity. Mutations in the tumor protein p53 (TP53) gene, activating mutations in the telomerase reverse transcriptase (TERT) promoter, loss or mutation of phosphatase and tensin homolog (PTEN) [6], and amplification and mutation of the epidermal growth factor receptor (EGFR) [7] are some of the most common genetic changes in GBM. The loss of heterozygosity on chromosome 10, namely at the 10q23 region containing the PTEN gene, is a characteristic genetic hallmark of GBM. The pathobiology of GBM is also significantly influenced by epigenetic changes; in particular, methylation of the O-methylguanine-DNA methyltransferase (MGMT) promoter has been found to be a predictive biomarker for response to alkylating drugs like TMZ [8]. GBM has been molecularly subclassified into four main subtypes based on extensive genomic and transcriptomic research, especially those carried out under The Cancer Genome Atlas (TCGA) effort. These subtypes are each distinguished by unique genetic and transcriptomic markers. Frequent EGFR amplification and a comparatively low frequency of TP53 mutations define the classical subtype. The mesenchymal subtype is characterized by increased expression of mesenchymal and inflammatory genes as well as deletion or mutation of neurofibromin 1 (NF1) [9]. Amplification of platelet-derived growth factor receptor alpha (PDGFRA) [10] and mutations in isocitrate dehydrogenase 1 (IDH1) are common in the proneural subtype, which is usually linked to younger patients and better prognoses. The expression of neuronal lineage markers identifies the neural subtype, which is less well defined but may be partially due to contamination by normal brain tissue. Every molecular pathway exhibits unique biological behavior, response to treatment, and clinical trajectory, highlighting the necessity of therapeutic approaches tailored to each subtype and expanding the application of precise oncology in the treatment of GBM [11][12].

1.1.3 Types of GBM

GBM can be classified based on both clinical origin and molecular gene expression profiles. These classifications have important implications for prognosis, therapeutic response, and personalized treatment strategies. This aggressive brain tumor is further divided into primary and secondary GBM by their origin. Specifically, based on gene expression, GBM is classified in four categories such as classical, mesenchymal, proneural and neural. **Figure 2** shows the types of GBM.

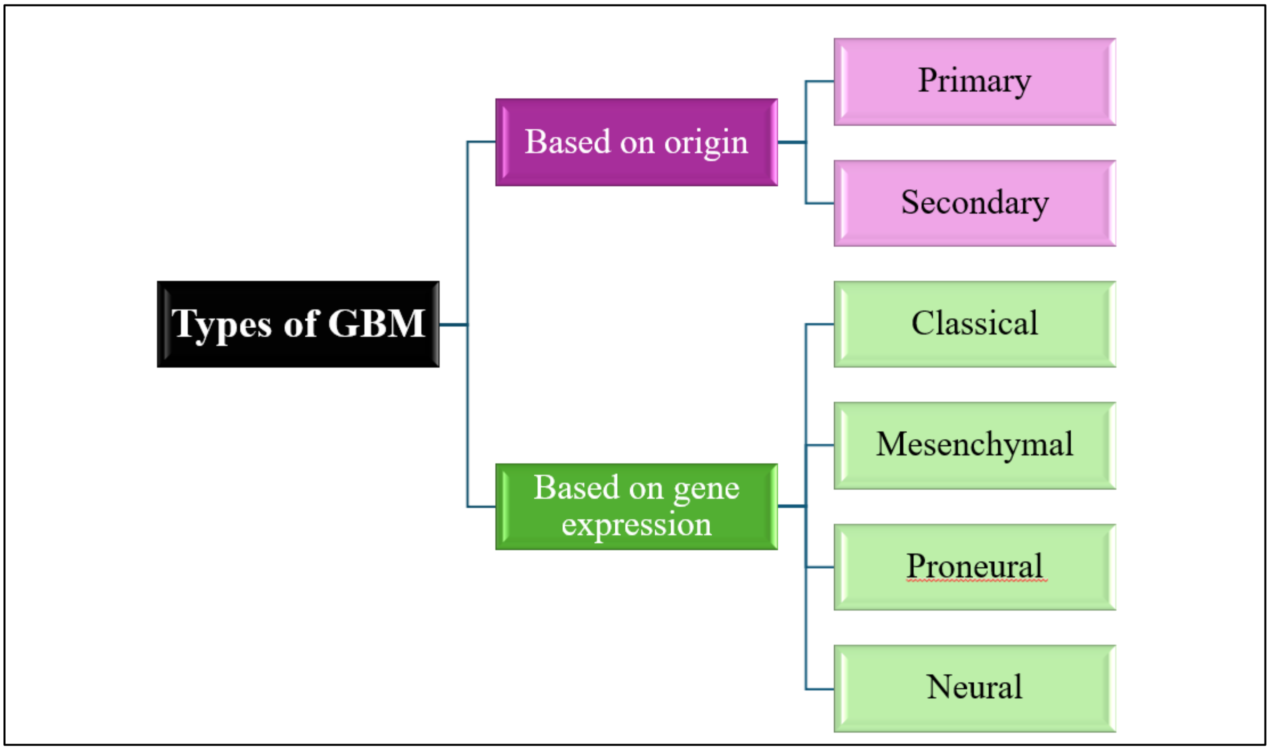


Figure 2 Classification of GBM

This figure illustrates the classification of GBM based on clinical origin (primary vs. secondary) and molecular subtypes (classical, mesenchymal, proneural, and neural), highlighting their distinct genetic features and clinical relevance.

1.1.3.1 Classification based on origin

Primary (de novo) and secondary GBM are the two main types of GBM that can be distinguished by their clinical and pathological development. Variations in tumor genesis, patient demographics, molecular changes, and disease progression are all reflected in this classification. Both types develop through separate biological processes and have different prognostic implications, even though they are histologically identical at diagnosis.

i. **Primary GBM:** About 90% of cases are primary GBM, which develops quickly and shows no histological or clinical signs of a previous lower-grade glioma. It is usually identified by an IDH-wildtype status and primarily affects older persons [13]. IDH-wildtype status, or the absence of mutations in the isocitrate dehydrogenase (IDH1 or IDH2) genes, is one of the most unique genetic characteristics of primary GBM. Chromosome 10q deletions, TERT promoter mutations, PTEN loss, and EGFR amplification are among the molecular characteristics commonly seen in primary GBM [14]. This subtype is the most prevalent in clinical practice, characterized by aggressive behavior, rapid progression, and poor prognosis. Here, primary GBM presents with a rapid onset of neurological symptoms such as seizures, focal deficits, or cognitive changes. Primary GBM has been the target of most studies in the current literature due to its high incidence and clinical urgency [15]. This has led to the development of biomarkers, molecular classifications, and therapeutic methods that predominantly reflect the biology of this subtype.

ii. **Secondary GBM:** Secondary GBM is more frequently observed in younger people and develops gradually from lower grade World Health Organisation (WHO) grade II or III) IDH-mutant diffuse astrocytoma. IDH mutations, most frequently IDH1 R132H, are the defining molecular characteristic of secondary GBM and are seen in more than 80–90% of secondary GBM patients [16]. D-2-hydroxyglutarate (D-2HG), an oncometabolite produced by IDH mutations, interferes with DNA repair, epigenetic control, and cellular differentiation, all of which promote carcinogenesis. However, IDH mutations are also linked to improved prognosis, slower tumor development, and increased reactivity to some treatments, including as radiation and alkylating medication. In contrast to primary GBM, secondary GBM frequently has TP53 mutations, ATRX deletion, and IDH1 or IDH2 mutations. Despite being histologically identical to main GBM at diagnosis, secondary GBMs typically have a delayed clinical course and a better prognosis [11]. The updated WHO classification of gliomas depends heavily on the molecular differences between primary and secondary GBM, which have significant diagnostic and prognostic implications.

1.1.3.2 Classification based on gene expression

The Cancer Genome Atlas (TCGA) and other large-scale transcripts profiling tools have made it possible to molecularly subclassify GBM into several gene expression subtypes. The four categories like classical, mesenchymal, proneural, and neural, reflect biological variability and are linked to variations in cellular origin, molecular changes, and clinical results. It is crucial to understand these subtypes to create individualized and focused approaches to therapy.

i. **Classical subtype:** The Classical subtype is genomically defined by amplification of chromosome 7, deletion of chromosome 10, and striking overexpression and mutation of EGFR, with EGFRVIII mutations found in over half of the tumors. A deletion of exons 2–7 results in EGFRvIII, a shorter mutant form of EGFR that lacks a part of the extracellular ligand-binding domain. Increased invasion, proliferation, and resistance to targeted treatments are all impacted by constitutive, ligand-independent receptor activation. It is considered as a characteristic change in the classical subtype of GBM. The absence of TP53 mutations and a high prevalence of EGFR amplification and chromosome 10 deletion characterize the classical subtype. It shows increased expression of genes related to proliferation and cell cycle regulation. Another hallmark is the homozygous deletion of CDKN2A, which disrupts the RB regulatory pathway often co-occurring with EGFR alterations in up to 94% of samples. This subtype also shows elevated activity in neural precursor pathways such as Notch and Sonic Hedgehog, supporting a stem-like cellular origin. Clinically, this form of tumor has a generally bad prognosis and is frequently resistant to conventional treatments [17] [18].

ii. **Mesenchymal Subtype:** The NF1 gene is frequently mutated or lost in this subtype, and mesenchymal and inflammatory markers including MET and CHI3L1 are highly expressed. These mutations often co-occur with PTEN loss, affecting the PI3K-AKT pathway. The transcriptomic profile is rich in mesenchymal and astrocytic markers such as CHI3L1 (YKL40), MET, CD44, and MERTK, indicating a resemblance to an epithelial-to-mesenchymal transition. Gene expression shows activation of inflammatory pathways particularly TNF, NF-κB, and related factors mirroring the necrosis and immune infiltration seen histologically. It is frequently linked to more aggressive tumor behavior and greater immunological infiltration. Because of the inflammatory environment, patients with mesenchymal GBM may react differentially to immunotherapeutic approaches [17] [18].

iii. **Proneural Subtype:** This subtype harbors frequent alterations in PDGFRA, including amplifications and high expression levels some with Ig-domain point mutations that potentially disrupt ligand interaction. Proneural GBMs are enriched for mutations in IDH1 and amplification of PDGFRA. This subtype is typically found in younger patients and exhibits a gene expression profile resembling that of oligodendrocyte progenitor cells. TP53 mutations and loss of heterozygosity are prevalent, reinforcing a distinct tumorigenic pathway. Unlike other subtypes, chromosome 7 gain and chromosome 10 loss are less frequent here. Despite its association with better prognosis in some contexts, proneural GBMs are paradoxically less responsive to aggressive therapy and may exhibit resistance to conventional treatments [17] [18].

iv. **Neural subtype:** Neural GBMs exhibit expression profiles that strongly resemble normal brain tissue, with elevated levels of neuronal markers. The expression of neuronal migration markers such NEFL, GABRA1, and SYT1 characterizes the neural subtype. Its classification is still debatable, though, as some research indicates that the expression patterns could not represent a specific tumor subtype but rather contamination with healthy brain tissue. Although less is known about its therapeutic responsiveness, the subtype shows modest benefit from aggressive treatment. It may represent a GBM that arises from more differentiated neural cell types. However, this category emphasizes the complex nature of GBM transcriptomics and the necessity of additional molecular classification improvement [17] [18].

1.2 GBM: Pathophysiology and Challenges

1.2.1 Epidemiology and Prevalence

GBM, responsible for more than half of all gliomas and 15% of all intracranial tumors, is the most common and deadly primary malignant brain tumor in adults [1]. As this number varies by region and ethnic group, the highest rates have been recorded in North America and Europe [13]. The estimated global incidence is approximately 3 to 4 cases per 100,000 people [19]. Most situations occur during the fifth and seventh decades of life, according to epidemiological data, and a slight male predominance has been continuously noted. The tumor is extremely unusual in children, but because of its aggressive clinical behavior and high recurrence rates, it causes a serious health risk to adults [20]. With median survival rates below two years and just a slight improvement in long-term survival over the previous 20 years, the general prognosis for GBM is still poor despite technical breakthroughs in diagnostic neuroimaging and histological classification. The statistics show that GBM is still deadly and emphasize the critical need for better molecular knowledge and more potent treatment approaches [21] [1].

1.2.2 Current therapeutic approaches and their limitations

The multimodal approach known as the Stupp protocol, which consists of maximally safe surgical resection, radiation, and associated chemotherapy with TMZ, defines the therapeutic landscape for GBM. Even while this treatment plan is still the primary strategy for managing GBM, it only provides temporary control over tumor growth, and most patients experience local recurrence a few months after therapy [22]. A failure to completely remove GBM without impairing neurological function is due to its extensive infiltration of closest brain tissue, which presents considerable surgical obstacles. Furthermore, a strong barrier that is frequently caused by epigenetic and molecular mechanisms like overexpression of MGMT (O6-methylguanine-DNA methyltransferase), activation of the DNA damage response, and the presence of glioma stem-like cells that aid in tumor repopulation is intrinsic and acquired resistance to radiation and TMZ. The bioavailability of many chemotherapeutic drugs is further limited by the blood–brain barrier's (BBB) impermeability, and the tumor microenvironment's immunosuppressive properties present further obstacles to the effectiveness of immunotherapeutic interventions. Furthermore, due to its molecular complexity and lack of consistent, druggable mutations, GBM has demonstrated little efficacy with targeted treatments and checkpoint inhibitors, despite its success in other cancers. All these drawbacks highlight the drawbacks of traditional methods and the necessity of investigating different therapy approaches [23].

1.2.3 Need for novel molecular targets, including lncRNAs

There is an increasing demand for new molecular targets that can address the heterogeneity and invasive nature of GBM due to its complicated resistance mechanisms and treatment ineffective.

lncRNAs, a family of RNA transcripts which have more than 200 nucleotides, have been shown to play important roles in the regulation of gene expression networks involved in tumor progression by recent developments in transcriptomics and epigenetics [24]. lncRNAs can act as tumor suppressors or oncogenes and have context and tissue specific expression patterns. They can affect a variety of cellular functions, such as chromatin remodeling, transcriptional activation or repression, post-transcriptional regulation, and signaling cascade modulation. Dysregulated lncRNAs in GBM have been linked to glioma stemness maintenance, invasion and angiogenesis promotion, and TMZ and radiation resistance [25]. They can regulate the activity of vital pathways including PI3K/AKT, Wnt/β-catenin, and p53, which are frequently changed in glioma genesis, through their capacity to interact with DNA, RNA, and proteins. Furthermore, lncRNAs are interesting candidates for use as predictive and diagnostic biomarkers as well as possible targets for RNA-based therapies due to their specific expression profiles and stability in body fluids. Thus, addressing lncRNA-mediated regulatory networks presents a novel and potentially revolutionary approach to the hunt for GBM treatments that are precisely targeted [26].

1.3 Long non-coding RNAs: Structure and Function

1.3.1 Definition and classification of lncRNAs

A broad class of RNA molecules longer than 200 nucleotides that do not encode proteins and do not have a functional open reading frame are known as long non-coding RNAs, or lncRNAs. Although RNA polymerase II generates lncRNAs similarly to mRNAs and they are frequently polyadenylated, lncRNAs show far more structural variety and spatiotemporal specificity in expression. lncRNAs are conventionally divided into various kinds according to their chromosomal location in relation to protein-coding genes. This classification is illustrated in **Figure 3**.

i. **Intergenic lncRNAs (lincRNAs):** These can be found in the genomic intervals between genes that code for proteins. They are independently transcribed and frequently control distant or nearby genes in either cis or trans. HOTAIR and linc-PINT are two examples [27].

ii. **Intronic lncRNAs:** Without overlapping with exons, these come only from the intronic sections of genes that code for proteins. They might function independently or control the host gene [27].

iii. **Sense lncRNAs:** An adjacent protein-coding gene may partially or fully overlap with these, which are transcribed from the same strand. They might affect the overlapped gene's splicing or transcription [27].

iv. **Antisense lncRNAs:** They are transcribed from the opposite strand of a coding gene and frequently use chromatin modification, transcriptional interference, or RNA-RNA interactions to control the expression of their sense counterpart. BDNF-AS, which inhibits BDNF expression, is a prominent example [27].

v. **Bidirectional lncRNAs:** These are transcribed in the opposite direction to a nearby coding gene, usually within 1 kb of its promoter. Such transcripts may share regulatory elements and participate in reciprocal regulation [27].

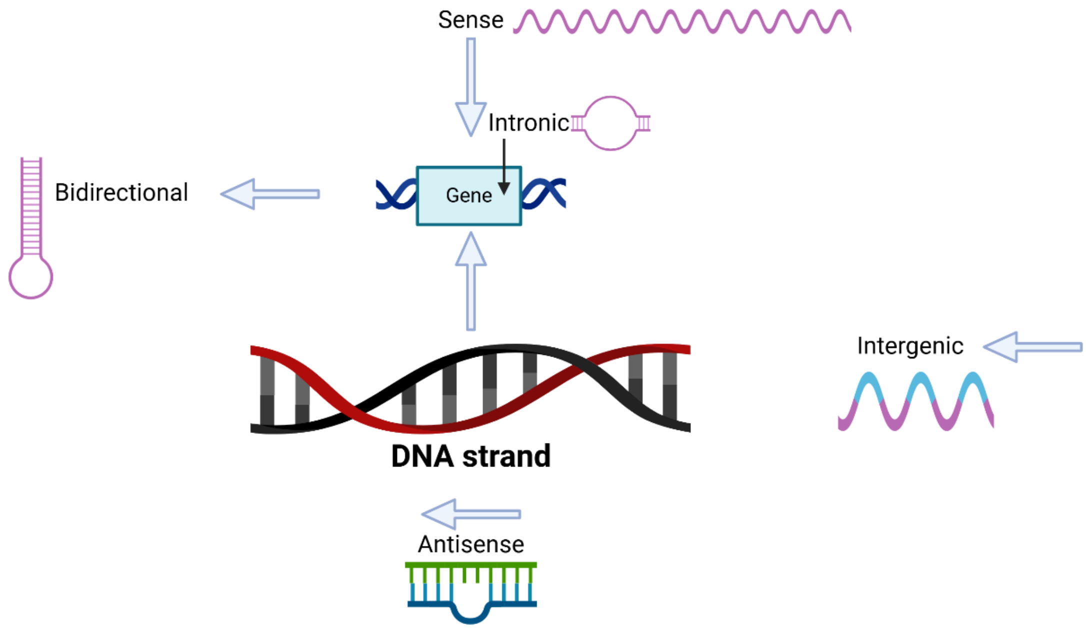


Figure 3 Classification of lncRNAs

This figure categorizes lncRNAs based on their genomic location (intergenic, intronic, sense, antisense, etc.) and their functional roles (cis/trans acting, nuclear/cytoplasmic localization, etc.), showing their diverse mechanisms in gene regulation.

In addition to this genome-based classification, functional and subcellular localization-based classifications have become increasingly important.

i. **Cis acting vs. Trans-acting lncRNAs:** Cis-acting lncRNAs regulate genes on the same chromosome, often near their site of transcription, while trans-acting lncRNAs can affect distant genes located on different chromosomes. A trans-acting lncRNA known HOTAIR epigenetically silences genes on many chromosomes, while XIST is a traditional cis-acting lncRNA that is implicated in X-chromosome inactivation [28] [29].

ii. **Nuclear vs. Cytoplasmic lncRNAs:** Nucleus-based lncRNAs are commonly implicated in transcriptional control, epigenetic regulation, and chromatin remodeling. Cytoplasmic lncRNAs, on the other hand, play a larger role in post-transcriptional regulation, which includes microRNA sponging, translation, and mRNA stability. TUG1, which operates in both compartments, and NEAT1 (nuclear paraspeckle assembly) are two examples [29].

iii. **Enhancer lncRNAs (eRNAs):** These are transcribed from active enhancer regions and frequently control the expression of genes by recruiting transcriptional coactivators or altering enhancer-promoter looping. Although being non-polyadenylated and typically unstable, eRNAs are essential for dynamic gene regulation in both disease and development [30].

iv. **Circular lncRNAs (circRNAs):** CircRNAs are non-linear RNAs created via back-splicing, however they are not necessarily regarded as classical lncRNAs. Many come from non-coding areas and can act as decoys for RNA-binding proteins or as microRNA sponges. Certain circRNAs are unique to the brain and are linked to the pathophysiology of gliomas and neural development [31].

v. **Pseudogene-derived lncRNAs:** Non-functional copies of coding genes called pseudogenes are the source of some lncRNA transcription. These lncRNAs function as ceRNAs (competing endogenous RNAs) and can control the parental gene or other genes. As an example, consider PTENP1, a pseudogene lncRNA that sequesters select microRNAs to control PTEN levels [32].

vi. **Small peptide-encoding lncRNAs (SEPs):** Recent research indicates that just a few percent of lncRNAs may encode micropeptides through small open reading frames (sORFs), even though they are characterized by their inability to code for proteins. The strict distinction between coding and non-coding is called into question by the discovery of these micro peptides, which can exhibit biological activity [33].

This broad and dynamic classification underlines the multifunctional and context-dependent characteristics of lncRNAs, which make them important regulators in both physiological and pathological circumstances, such as the progression of GBM and neural growth.

1.3.2 Mechanisms of lncRNA action (e.g., chromatin remodeling, transcriptional regulation, post-transcriptional control)

lncRNAs regulate gene expression through a variety of frequently overlapping methods, impacting both distant (trans-acting) and close (cis acting) genes. At the epigenetic level, nuclear lncRNAs can attract chromatin-modifying enzymes to genomic loci, such as DNA methyltransferases, histone acetyltransferases, or Polycomb Repressive Complex 2 (PRC2). This results in changes to histone marks or DNA methylation patterns that affect transcriptional activity. A well-known example is XIST, which attracts repressive chromatin remodelers and spreads throughout the X chromosome to mediate X-chromosome inactivation. By directly interacting with transcription factors, RNA polymerase II, or transcriptional co-regulators, lncRNAs can function as co-activators or repressors at the transcriptional level, dynamically modifying gene expression in response to cellular factors [28]. Cytoplasmic lncRNAs control mRNA shifts, splicing, translation efficiency, and localization in the post-transcriptional realm. As ceRNAs, a sizable portion of lncRNAs behave as microRNA sponges, modifying microRNA availability and thus regulating target mRNA translation. Furthermore, lncRNAs could attach to RNA-binding proteins (RBPs) to create ribonucleoprotein complexes that affect the stability or degradation of mRNA. An additional layer of functional complexity is added by the fact that structural motifs within lncRNAs, rather than their primary sequence, frequently drive their interactions [29]. Furthermore, recent research has expanded the functional landscape of lncRNAs by highlighting them as scaffolding that organize nuclear bodies.

lncRNAs contribute to several levels of cellular regulation by controlling gene expression via cytoplasmic and nuclear processes. lncRNAs participate in transcriptional repression and chromatin remodeling in the nucleus, frequently via complexes like the Polycomb Repressive Complex 2 (PRC2). Histone methylation and transcriptional silence of target genes can result from these lncRNAs' ability to attract PRC2 to genomic locations. Additionally, by preventing transcription factors from accessing DNA, they may interact with transcription factors and repress transcription. Although these nuclear functions are crucial for preserving cell identity, carcinogenesis, particularly GBM, has been linked to their dysregulation.

Error! Reference source not found.lncRNAs interact with messenger Ribonucleic Acid (mRNAs) a nd micro–Ribonucleic Acid (miRNAs) in the cytoplasm to affect post-transcriptional regulation. As "miRNA sponges," lncRNAs trap miRNAs and stop them from breaking down their target mRNAs, so indirectly facilitating translation. This is a frequent process. As an alternative, lncRNAs can attach directly to mRNAs and either target them for degradation or stabilize them to improve protein synthesis. lncRNAs can adjust protein synthesis in response to cellular inputs due to these cytoplasmic activities. An outline of these dual functions is given in **Figure 4**, which highlights how lncRNAs, depending on their subcellular location, mediate both transcriptional and post-transcriptional gene regulation.

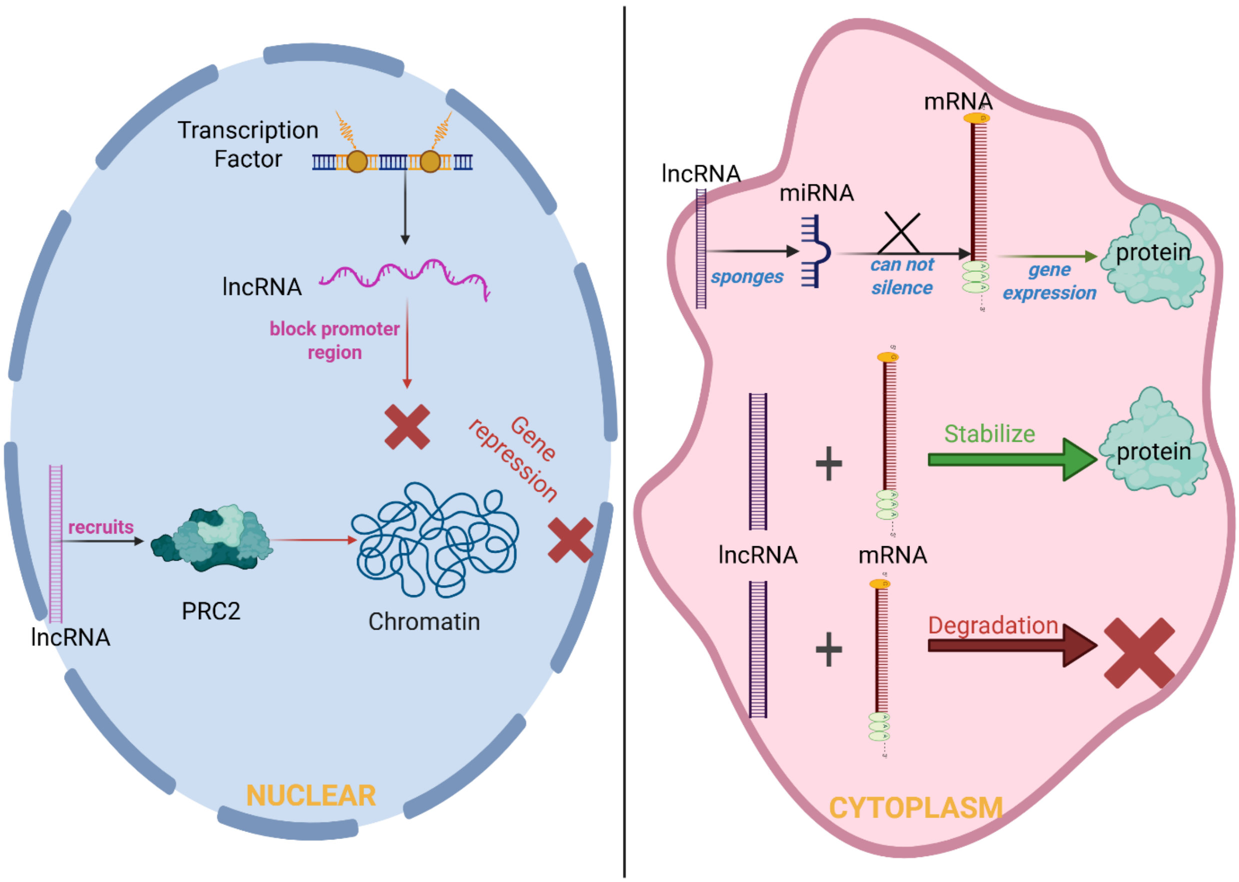


Figure 4 Mechanism of lncRNA action

This figure summarizes the nuclear and cytoplasmic mechanisms of lncRNAs. It shows how lncRNAs regulate chromatin structure, transcription, and post-transcriptional processes, impacting tumor growth and therapy resistance in GBM.

1.3.3 Role in normal brain function vs. pathological conditions

Compared to other organs, the central nervous system expresses a disproportionately large number of lncRNAs, highlighting their significance in brain development and function. Through the regulation of lineage-specific transcription factors and epigenetic landscapes, lncRNAs play crucial roles during neurogenesis, regulating the shift from neural stem cells to adult neurons and glial cells. For example, lncRNAs PANDA and MALAT1 control cell cycle exit and synaptogenesis, while RMST promotes neuronal development by interacting with the transcription factor SOX2. By altering neurotransmitter signaling pathways and activity-dependent gene expression, lncRNAs in postnatal brain tissue support synaptic plasticity, learning, memory formation, and circadian rhythm modulation. Functional compartmentalization and precise neuronal connections are supported by the temporal and spatial specificity of lncRNA expression. This tightly regulated lncRNA network becomes dysregulated in pathogenic situations, especially brain tumors and neurodegenerative disorders. For instance, certain lncRNAs are silenced in GBM, leading to the loss of tumor suppressor capabilities, while others are overexpressed and contribute to pro-oncogenic signaling. In contrast, lncRNAs like BACE1-AS and 17A have been linked to amyloid processing, neuroinflammation, and mitochondrial dysfunction in neurodegenerative illnesses including Alzheimer's, Parkinson's, or Huntington's disease. Because lncRNAs are both crucial regulators of neural physiology and possible causes of neuropathology, their dual nature shows their importance as mechanistic contributors, diagnostic biomarkers, and therapeutic targets in illnesses relating to the brain [5] [25].

1.4 Hypothesis and objective of the review

1.4.1 Hypothesis

Dysregulation of LncRNAs contributes to GBM pathogenesis by modulating transcriptional, post-transcriptional, and epigenetic processes, thereby influencing key hallmarks such as proliferation, invasion, stemness, angiogenesis, and treatment resistance. Elucidating the functional roles of lncRNAs in GBM may reveal novel therapeutic targets and prognostic biomarkers to overcome current treatment limitations.

1.4.2 Objective

The primary objective of this study is to conduct a systematic literature review, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, to comprehensively evaluate current research on the molecular and functional roles of lncRNAs in GBM. The review specifically aims to:

- **i.** Classify lncRNAs according to their subcellular location, molecular function, and genetic origin.
- **ii.** Describe how PI3K/AKT, p53, Wnt/β-catenin, NF-κB, and other important signaling pathways involved in the progression of GBM are regulated by oncogenic and tumor suppressive lncRNAs.
- **iii.** Examine how lncRNAs contribute to the mechanisms of therapeutic resistance, such as radio resistance and chemoresistance to TMZ.
- **iv.** Highlight recent developments and translational prospects for RNA-based therapies and describe the therapeutic and diagnostic potential of lncRNAs in GBM.

Chapter 2: Methodology

A comprehensive systematic literature search was conducted using PubMed, ScienceDirect, and Google Scholar in accordance with the PRISMA guidelines [34]. The initial search used the keywords "Glioblastoma" and "long non-coding RNA", resulting a total of 679 articles, including original research papers, review articles, clinical trials, meta-analyses, and book chapters. Then, an advanced search was performed on PubMed using the Boolean query: ((Glioblastoma[Title/Abstract]) AND (((long non-coding RNA*[Title/Abstract])) OR (lncRNA*[Title/Abstract]))) NOT (Review[Publication Type]), which retrieved 558 non-review articles. After removing 14 duplicate records, 544 unique studies remained. Titles and abstracts were screened to assess the relevance of each article to the role of lncRNAs in GBM. During this step, 129 articles were excluded due to insufficient information on the systematic roles of lncRNAs in GBM. The remaining 415 full-text articles were assessed for eligibility. Among these, 26 articles were excluded because they focused only on lncRNA biology without discussing downstream pathways or their functional relevance to GBM pathogenesis was unclear. Therefore, 389 articles were included based on their detailed descriptions of how lncRNA affect the regulation of GBM related pathways, including apoptosis, DNA damage response, cell survival, invasion, angiogenesis, therapy resistance, epigenetic regulation, and ceRNA networks. This review primarily focuses on the molecular and therapeutic implications of these pathways and underscores the potential of specific lncRNAs as biomarkers or therapeutic targets in GBM. The study selection process is summarized in **Figure 5** followed by PRISMA guidelines.

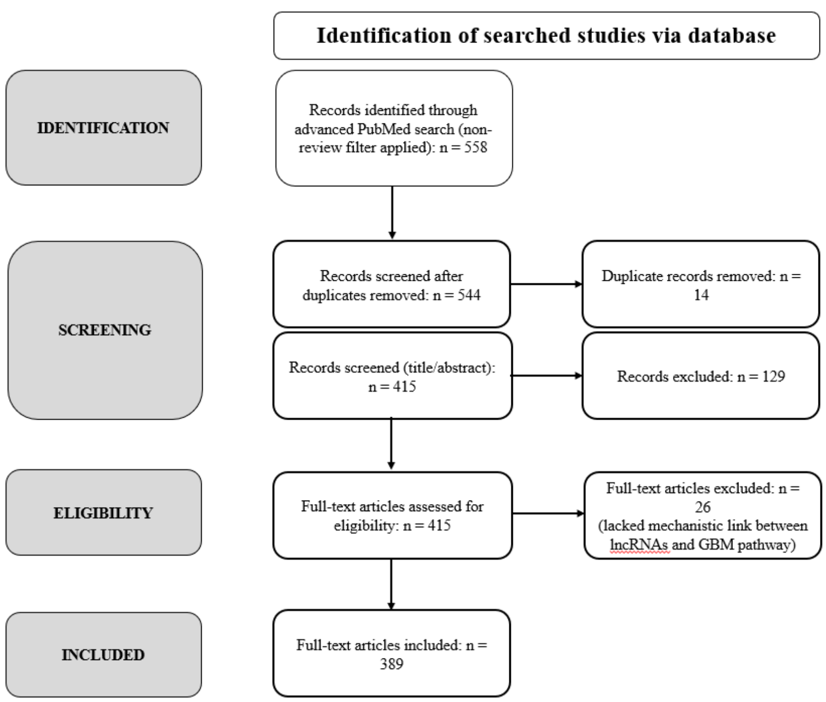


Figure 5 PRISMA diagram.

This figure depicts the article selection process for this review. Out of 679 initial articles, 389 were included based on strict inclusion criteria focused on lncRNAs and their role in GBM pathogenesis and treatment.

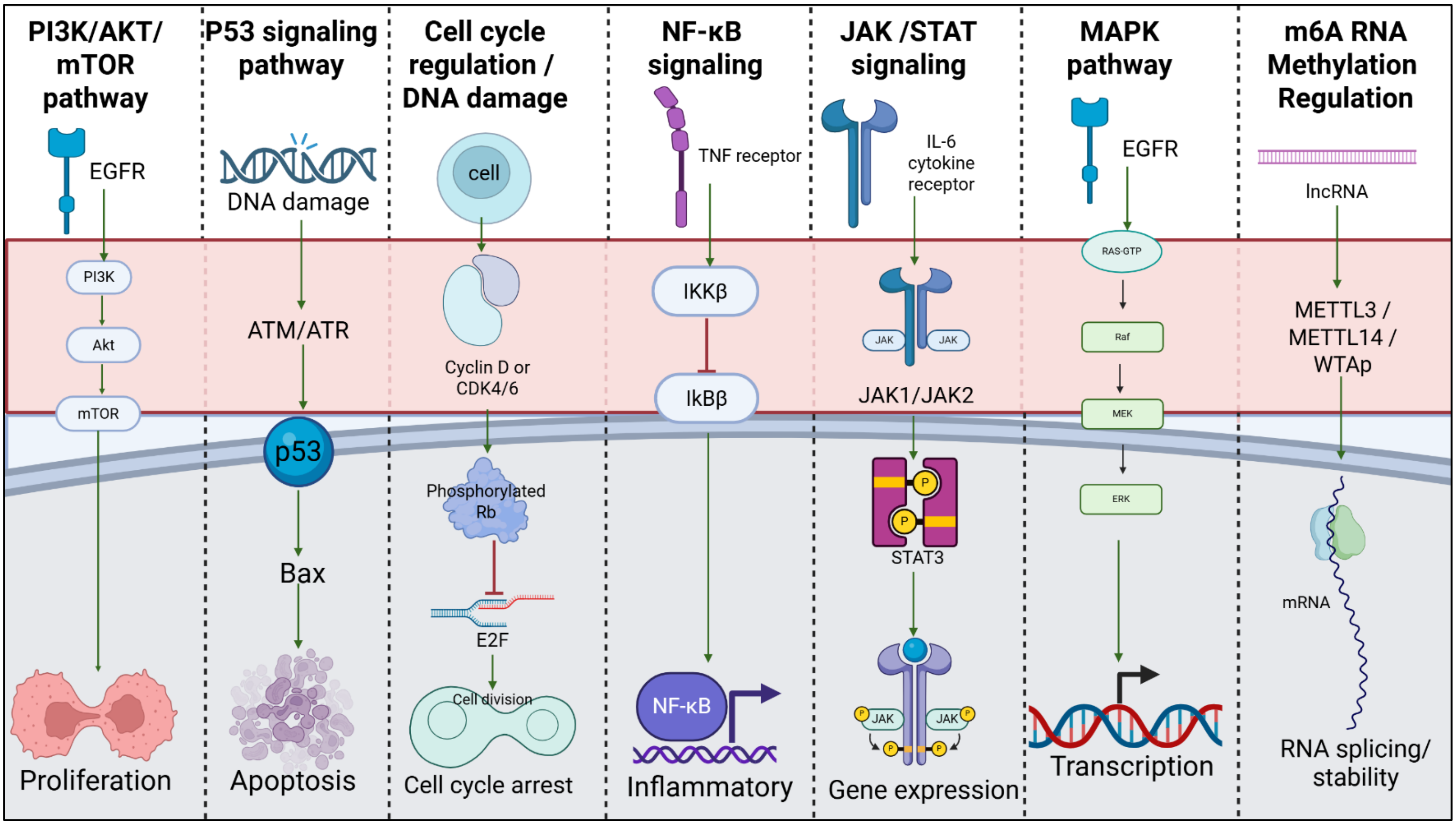
Chapter 3: Results

3.1 Interaction between lncRNAs and key molecular pathways in GBM

In GBM, combination of miRNAs and lncRNAs have been shown in all characteristics of tumor malignancy, containing resistance to apoptosis, cell proliferation, angiogenesis and drug resistance [35]. The aim of lncRNAs and their key mechanisms are varied. For an example, many of lncRNAs either promote or suppress glioma progression [36]. By considering those pathways like PI3K/AKT/mTOR, Notch, p53, NF-κB, Wnt/β-catenin are observed often and contribute to the malignant phenotype of GBM cells. Many articles are witness that lncRNAs are the key challenging regulators of these pathways which can activate by various mechanisms such as miRNA sponging, transcriptional regulation, and epigenetic modification. To explore novel therapeutic targets and biomarkers in GBM, the study of correlation between lncRNAs and these signaling pathways is important. This section illustrates numerous pathways along with functional gene targets. The pathways are categorized by their role in biological processes, for an instance, some pathways are directly related to apoptosis / DNA damage / cell survival and some other are indirectly affects them.

3.1.1 Directly related to apoptosis / DNA damage / cell survival.

GBM can evade cell death and repair DNA damage efficiently that can lead to increase unchecked tumor growth and resistance to any standard therapy which is the major undeniable fact about GBM [37] [38]. lncRNAs promote the activity or expression of key regulators like p53, PI3K/AKT, ATM/ATR, and caspases. Moreover, they have been gradually recognized as important modulator of these networks. This section depicts lncRNAs that can directly participate in DNA repair mechanisms, regulation of apoptosis and mentioning their major role to promote tumor progression or resistance in GBM. Some studies show that lncRNA influences GBM via multiple pathways and each pathway has their own significance which describes below in Error! Reference source not found..



This figure illustrates seven core oncogenic signaling pathways in GBM that are directly modulated by lncRNAs. These include PI3K/AKT/mTOR, p53 signaling, cell cycle regulation/DNA damage response, NF-κB signaling, JAK/STAT, MAPK, and m6A RNA methylation regulation. lncRNAs influence these cascades through transcriptional, post-transcriptional, and epigenetic mechanisms, impacting GBM proliferation, apoptosis, inflammation, gene expression, and RNA stability.

3.1.1.1 PI3K/AKT/mTOR pathway

This pathway stands for Phosphoinositide 3-Kinase (PI3K), Protein Kinase B (PKB), and Mechanistic Target of Rapamycin (mTOR). The PI3K/AKT/mTOR pathways have a vital role in evolution, expansion and therapy resistance of GBM. This pathway gets activated in multiple steps which are highlighted in **Figure 6.** Initially, growth factors like epidermal growth factor (EGF) and platelet derived growth (PDGF) are detected by proteins on the cell surface. EGFR is frequently amplified or mutated in GBM that can active it even in the absence of signals. After the activation of receptor tyrosine kinases (RTKs), the attraction towards PI3K occur. PI3K known as lipid kinase enzyme and its coverts PIP2 into PIP3. Then, AKT attaches itself to PIP3 and is phosphorylated (activated) by PDK1 and other kinases. AKT promotes cell survival, metabolism and cell growth, once its activated and it can activate mTOR directly or indirectly. Eventually, tumor suppressor gene PTEN lock this pathway by removing PIP3. PTEN is frequently lost or altered in GBM, which results in uncontrolled PI3K/AKT/mTOR activation.

GBM is influenced by lncRNAs through DDR, apoptosis, and modulation of oncogenic signaling pathway that can mainly focus on drug resistance in addition PI3K/AKT is the essential pathway observed frequently in GBM. For an example, by sponging miR-190a-3p, LINC00657 functions as a tumor suppressor, preventing GBM cell motility and invasion by upregulating PTEN, suppressing PI3K/AKT signaling, and enhancing apoptosis through active caspase-3 [6]. Similarly, Oncogenic lncRNAs LINC01198 and SAMMSON contribute to tumor growth and chemoresistance by activating PI3K/AKT signaling via improving DNA repair processes and sponging miR-129-5p to raise PIK3CA, respectively [39] [40]. In contrast, by inhibiting AKT, CASC2 suppresses the same pathway, eventually promotes apoptosis and minimise proliferation whereas maintains glioma stem cell (GSC) identity and facilitates resistance under hypoxia [37]. PITPNA-AS1 also binds with miR-223-3p and by sponging with it, upregulates EGFR, leading to the activation of PI3K/AKT signaling pathway. This activation prevents apoptosis, by increasing BCL2 levels, reducing Bax/caspase 3 expression, and influencing DDR [7].

Many lncRNAs control EGFR related oncogenic axes. By binding miR-373, HOXA-AS2 increases EGFR signaling, enhancing the production of VE cadherin and MMP-2/-9, and boosting apoptosis resistance and vasculogenic mimicry (VM). Similarly, INHEG supports GSC persistence and resistance to therapy by promoting the expression of EGFR, IGF1R, CDK6, and PDGFRB through increased RNA 2'-O-methylation mediated by TAF15/NOP58 [41]. Notably, LINC02283 collaborated with PDGFRA, increasing downstream AKT and ERK signaling. It refers tumorigenic potential, resistance to apoptosis, particularly in PDGFRA mutated gliomas [10]. lncRNAs are also regulate DDR and modulation of apoptosis, specifically towards to chemotherapeutic resistance. Upregulation of cisplatin, AC023115.3 acts as a ceRNA for mi-26a, permitting GSK3β to degrade anti apoptotic Mc11, therefore, promoting apoptosis and minimising chemoresistance [42].

While its reduction improves treatment sensitivity, Linc-RoR, which is highly active during the G2/M phase, enhances GBM stemness, proliferation, and resilience to DNA damage [43]. On the other hand, NONHSAT159592.1 suppresses invasion and proliferation by inhibiting ITGA3/FAK/PI3K/AKT axis [44], and GBM progresses because LINC00470 promotes AKT activation, inhibits autophagy, and increases glycolysis [45].

The major hallmark of GBM therapy is TMZ resistance which influence by lncRNAs. Lnc-TALC increases c-Met via sponging miR-20b-3p, which in turn triggers the Stat3/p300 complex to increase MGMT, improving DNA repair and decreasing apoptosis. The AKT/FOXO3 axis supports this and increases the expression of lnc-TALC [46]. Likewise, during TMZ therapy, PSMG3-AS1 maintains c-Myc in the nucleus, facilitating apoptosis avoidance and survival. GBM cells are sensitized to TMZ by knockdown, indicating its potential significance in recurrence. Furthermore, JPX stabilizes PDK1 mRNA through its association with the m6A demethylase FTO, promoting aerobic glycolysis and TMZ resistance. This represents a targetable axis (JPX/FTO/PDK1) in drug-refractory GBM [47].

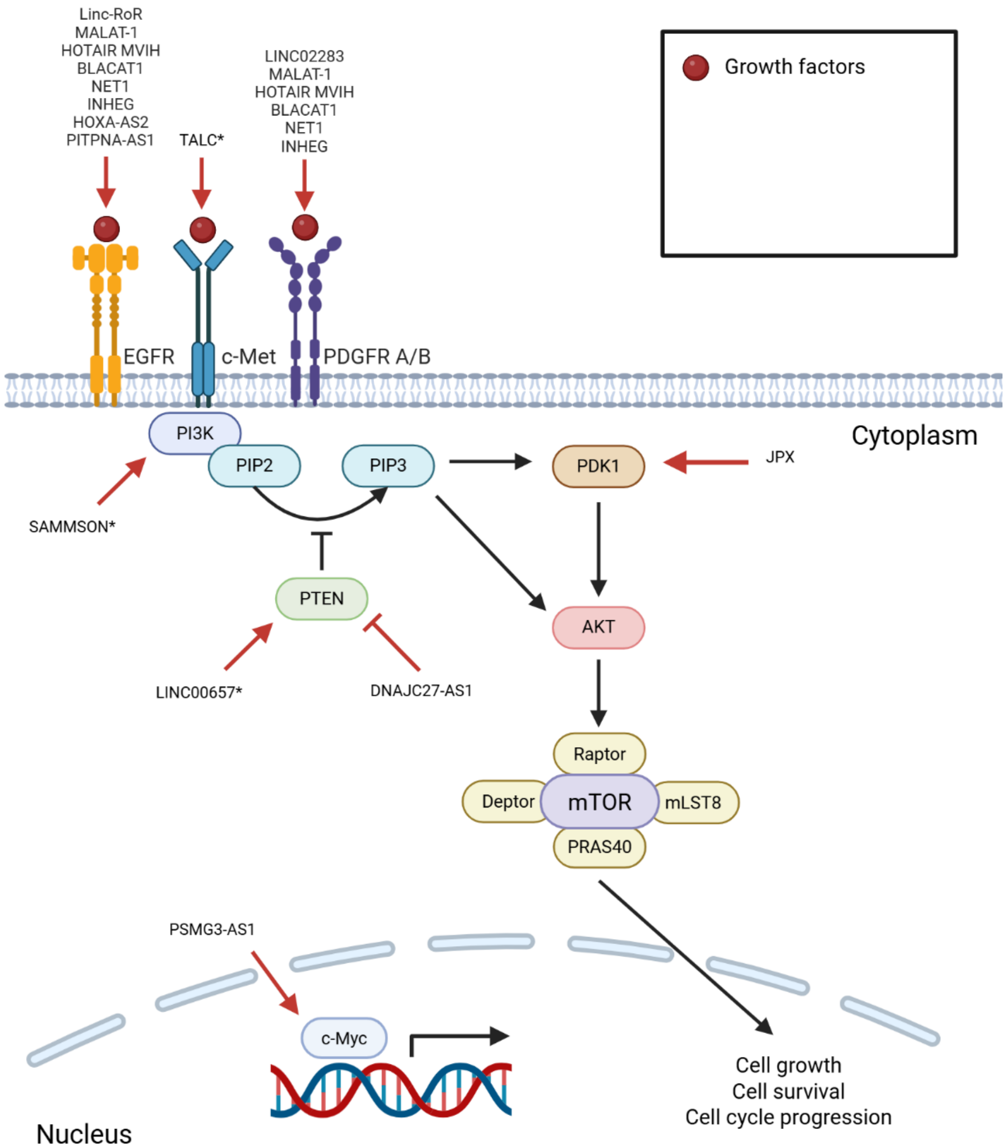


Figure 6 Mechanism of PI3K/AKT/mTOR pathway

Beyond drug interaction, other lncRNAs act as prognostic biomarker. For an instance, CRNDE influences TMZ resistance through ABCG2 and autophagy regulation [48], while HOTAIR and MALAT-1 associated with regulation of DNA repair, poor survival, metastasis and apoptotic pathway [49]. ENSG00000261924.1 and P2RX5-TAX1BP3 impact the mTOR component RPTOR and proteasome function respectively, affecting repair responses and tumor growth [50]. Moreover, the relevance of a four-lncRNA pseudo uridine related signature (DNAJC27-AS1, GDNF-AS1, ZBTB20-AS4, DNMBP-AS1) in GBM prognosis and immunotherapy design is highlighted by the way it affects immune infiltration, tumor purity, IDH1, EGFR, and PTEN alterations, as well as treatment sensitivity [51]. In addition to, a five-lncRNA signature (LNC01545, WDR11-AS1, NDUFA6-DT, FRY-AS1, TBX5-AS1) stratifies patient outcomes, along with TBX5-AS1 associating with poor prognosis [52].

In conclusion, these mentioned disclose that lncRNAs orchestrate multiple layers of GBM biology from metabolism and signal transduction to treatment resistance and stemness, frequently through miRNA sponging, protein stabilization and epigenetic modulation. They are highly valuable targets for precision therapeutics and personalized medicine in GBM because of their strong interaction with important pathways like PI3K/AKT, EGFR, c-Met, PDGFRA, and mTOR, as well as their impact on the efficacy of drugs like TMZ and cisplatin. More detailed information of articles mentioned in the **Appendix**

Table 1.

3.1.1.2 p53 signaling pathway

This cellular signaling pathway centered around p53, a tumor suppressor protein, also known as the “guardian of genome”. The dysregulation of p53 pathway is observed often, and this refers to its malignancy.

Figure 7 depicts mutations in the TP53 gene, which codes for the p53 protein, have been identified in about 30–35% of GBM patients. Gain of function mutations cause p53 to lose its tumor-suppressive capabilities and may develop carcinogenic characteristics. Even when TP53 is not altered, the pathway is functionally suppressed in many GBM cases. This enables GBM cells to continue growing despite genetic defects and avoid programmed cell death. Chemotherapy and radiation therapy damage DNA. Generally, an undamaged p53 pathway would detect this damage and initiate apoptosis. Therapy resistance results from GBM cells surviving treatment when p53 is not functioning properly. The p53 pathway is modulated by numerous lncRNAs, including LINC-ROR, TP73-AS1, and lncH19. Certain lncRNAs increase tumor survival by inhibiting p53 activation whereas others increase apoptosis by stabilizing or activating p53.

In GBM, TP73-AS1 is significantly overexpressed, especially in glioma CSC, and is related to a poor prognosis as well as chemoresistance to the common chemotherapy medication TMZ. Mechanistically, TP73-AS1 prevents glioma CSCs from undergoing TMZ induced apoptosis by regulating the expression of genes linked to metabolism and ALDH1A1. Its significance in TMZ resistance and the therapeutic potential of targeting TP73-AS1 are highlighted by the fact that its loss downregulates ALDH1A1, improving sensitivity to TMZ and inducing apoptosis [53]. Similarly, through its interaction with the p53 pathway, LINC-ROR enhances cell survival and suppresses apoptosis, thus promoting GBM development. Because p53 also transcriptionally activates LINC-ROR, LINC-ROR suppresses p53 translation by binding to hnRNP I, creating a feedback loop. Because of this modulation, LINC-ROR is another important modulator of p53-mediated apoptosis in GBM, contributing to decreased caspase 3 activity and poor survival outcomes [54].

In another p53-related pathway, lncH19 enhances apoptosis triggered by the histone deacetylase inhibitor (HDACi) ITF2357 by stabilizing TP53. This HDACi significantly causes apoptosis in GBM cells by upregulating annexin-V, splitting caspase 3, and encouraging PARP-1 degradation. The interaction between HDAC inhibition and lncH19 indicates a combined approach for reducing chemoresistance, even if ITF2357 also influences autophagy independently of lncH19 [55].

In GBM, radiotherapy also alters lncRNA expression and activity; TP53TG1 is one important lncRNA linked to radiosensitivity. The p53 pathway drives transcriptional reactions involving lncRNA gene combinations during radiation exposure, indicating their potential as biomarkers and therapeutic targets to increase radiosensitivity and better outcomes for patients [56]. PTCSC3 has shown a tumor-suppressive effect in GBM by suppressing the Wnt/β-catenin signaling pathway, which reduces tumor growth and invasion, despite being mostly researched in oral cancer. Although PTCSC3's direct links to p53 or DNA damage in GBM are still unclear, the fact that it causes autophagy and apoptosis in other malignancies suggests that it may also have a functional significance in GBM [57].

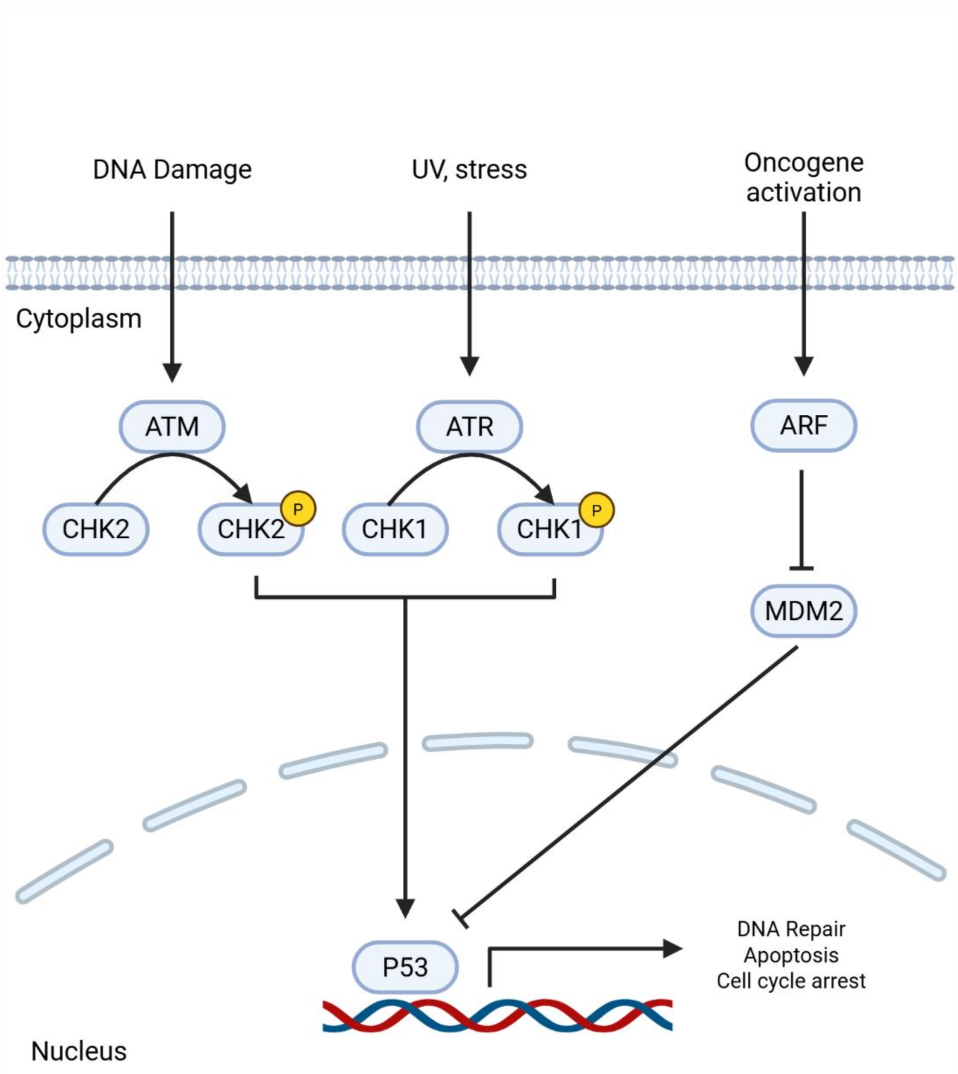


Figure 7 Mechanism of p53 pathway

Together, these results demonstrate the complexity of lncRNA-mediated control in GBM, especially through the p53 signaling pathway, and show how treatments such as TMZ and ITF2357 may affect or be impacted by lncRNA expression and activity. In addition to offering new ways to make tumors more sensitive to chemotherapeutic and radiotherapeutic treatments, addressing certain lncRNAs such as TP73-AS1, LINC-ROR, lncH19, and TP53TG1 may help overcome resistance to existing treatments. Additional specific details on the articles included in **Table 2**.

3.1.1.3 Cell Cycle Regulation / DNA Damage

By recognizing and correcting DNA damage and controlling cell cycle progression, the cell cycle regulation/DNA damage response (DDR) pathway plays a crucial role in maintaining genomic integrity. This pathway is usually disturbed in GBM, leading to tumor aggressiveness, uncontrolled proliferation, and resistance to treatment. Essential regulators include p53, which controls repair, arrest, or apoptosis; ATM/ATR, which detects DNA breaks; and CHK1/CHK2, which blocks the cycle for repair. Unchecked cell cycle entrance is made possible by CDK dysregulation or the loss of tumor suppressors. Mutations in DDR genes (such as ATM, BRCA1/2, and TP53) are frequently found in GBM, resulting in genomic instability. Surprisingly, a lack of DDR can make a person more vulnerable to substances that damage DNA, such as TMZ. However, by mending damage caused by therapy, insufficient DDR activity can result in chemoresistance. Combination of radiotherapy or TMZ and DDR inhibitors may sensitize GBM cells by DNA repair prevention.

The resistance of GBM to the prevalent chemotherapeutic drug TMZ is influenced by several types of lncRNAs. lncRNAs like AC093278.2, LINC01116, and AC017104.1 regulate TMZ resistance in the DNA damage response pathway by controlling the DNA repair enzyme MGMT. They are also responsive to interferon-β (IFN-β), which can restore TMZ sensitivity by causing apoptosis and decreasing MGMT expression [58]. With lncRNAs like CRNDE and XIST (upregulated) and MIR7-3HG and MIR124-2HG (downregulated) influencing tumor suppressor genes like TP53, CDK1, and CCNB1 which are essential for cell cycle regulation and DNA repair, the ceRNA network also plays a major role [59].

Numerous lncRNAs either directly or through miRNA intermediates alter the apoptotic mechanism. For example, FAS-AS1 is downregulated in GBM, indicating its tumor-suppressive role, whereas LINC01605 stimulates proliferation by preventing apoptosis. MiR-17-5p and miR-

20-5p regulate Caspase-3, a crucial apoptosis effector, which links the lncRNA–miRNA–mRNA axes to GBM resistance [60]. CREB-activated LINC00473 increases MGMT expression via the CEBPα pathway, promoting TMZ resistance. It can also be carried by exosomes, indicating intercellular drug resistance propagation. To re-sensitize GBM cells to TMZ, it is suggested to break the CREB/LINC00473/CEBPα/MGMT loop [61]. Similarly, UCA1 raises γ-H2AX and ATM activation, which enhances DNA damage and TMZ efficacy, while its silencing or overexpression of miR-182-5p stabilizes MGMT and encourages survival [8]. Another carcinogenic lncRNA, HOTAIR, promotes DNA repair and cell cycle progression by repressing miR-214-3p and activating the β-catenin/MGMT axis. Methotrexate (MTX) increases sensitivity to TMZ and decreases HOTAIR [62].

Another factor that leads to resistance is structural modification of lncRNAs. When CHK1 is activated by TMZ, LINC01956 takes on a conformation that makes MGMT mRNA export easier. By breaking this structure function interaction, suppressing CHK1 with SRA737 restores TMZ sensitivity [63]. With predictive significance based on integrated miRNA-lncRNA-mRNA profiles, MCM3AP-AS and MIR17HG regulate apoptosis related genes such as MATR3 and XPO1 in a larger network context [64]. Resistance is further increased by epigenetic silencing mechanisms, as AGAP2-AS1 promotes survival by suppressing TFPI2 through EZH2 and LSD1 recruitment. TFPI2 is reactivated by inhibition of these enzymes or knockdown of AGAP2-AS1, which triggers apoptosis [65]. On the other hand, the tumor suppressor AC003092.1 increases the activity of TMZ by sponging miR-195, upregulating TFPI2, and reducing drug efflux through P-glycoprotein. By influencing PD-L1 and TIM-3, it also modifies immunology responses, correlating lncRNA activity to immune evasion and prognosis [66,67].

Regarding the regulation of the cell cycle, lncRNAs like FOXD2-AS1 and FOXD3-AS1 stimulate the G2/M transition by sponging miRNAs like miR-31 and miR-128-3p, which raise CDK1 and WEE1, respectively two important regulators of DNA repair and mitotic entry. GBM is re-sensitized to TMZ when these lncRNAs or WEE1 are targeted [68,69]. Similarly, VIM-AS1 suppresses miR-105-5p to upregulate WEE1, and its knockdown encourages apoptosis. Adavosertib (AZD-1775), a WEE1 inhibitor, is effective in stopping the growth of GBM [70]. Palbociclib, a CDK6 inhibitor, decreases both SNHG15 and CDK6 expression, restoring chemosensitivity, whereas SNHG15 raises CDK6 levels via blocking miR-627-5p, causing TMZ resistance [71]. Similarly, UCA1 influences the PI3K/AKT, MAPK, and Notch pathways to promote cell cycle progression and survival via the miR-193a/CDK6 axis [68].

Further integrating lncRNA roles in microenvironmental modification, other lncRNAs such as HOXA-AS3 and H19 affect tumor growth and angiogenesis, the latter through miR-29a/VEGFA [72]. By suppressing PDCD4 and raising CDK4/CCND1 levels via EZH2 and LSD1, HOTAIR also promotes proliferation. By upregulating P21 and PUMA through histone modification that induces apoptosis, nanoparticle-based downregulation or combination therapy with AQB and GSK-LSD1 alters this epigenetic axis [73,74]. Additionally, TOP2A and BCL2 expression are modulated by LINC00461, which is stabilized by HDAC6. MPT0B291 inhibits HDAC6 by downregulating LINC00461, which results in tumor regression and cell cycle arrest [75].

In general, lncRNAs impact p53, ATM, CDC25C, E2F1, CDKN1A, and telomere repair pathways, confirming their function in TMZ resistance and highlighting their potential as a treatment for GBM [76]. **Table 3** has more detailed information about all articles.

3.1.1.4 NF-κB Signaling

One important mechanism that controls inflammation, immunological response, cell survival, and proliferation is the NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) signaling pathway. Hyperactivation of NF-κB is frequently seen in GBM and plays a role in angiogenesis, invasion, tumor growth, and treatment resistance. It encourages the production of genes that improve DNA repair, maintain tumor cell survival under stress, and inhibit apoptosis (cell death). Additionally, NF-κB contributes to the development of an inflammatory tumor microenvironment, which helps GBM evade immune detection. To affect tumor behavior, it interacts with lncRNAs, which can either promote or suppress this pathway. The mechanism part of this pathway highlighted in **Figure 8**.

Oncogenic lncRNAs like LINC00470 and LINC01057 play a major role in NF-κB activation. By interacting with IKKα, enabling its nuclear translocation, and inducing chromatin accessibility at NF-κB-responsive promoters, LINC01057 promotes mesenchymal transition and increases GBM invasiveness and radio resistance. LINC01057 is an acceptable therapeutic target because its knockdown decreases DNA repair efficiency and downregulates NF-κB target genes such as CCL2, CXCL2, CXCL8, and ICAM1 [9]. Despite being primarily investigated in hepatocellular carcinoma, LINC00470 has also been shown to accelerate the growth of GBM by increasing AKT activity, blocking HK1 ubiquitination, and reducing autophagy. Although its relationship to NF-κB in GBM is less obvious, it indirectly influences autophagic pathways via controlling ELFN2 expression by targeting miR-101 [77].

On the other hand, by activating AMPK, tumor-suppressive lncRNAs like DRAIC block the NF-κB pathway, which results in mTOR suppression, reduced protein translation, and increased autophagy. DRAIC decreases glucose absorption and carcinogenic potential by downregulating

NF-κB targets such as GLUT1. In this regard, pharmacological NF-κB suppression with Bay11-7082 and AMPK activation with AICAR or metformin show great therapeutic promise [78]. By blocking RELA through the E2F6 connection, MATN1-AS1 also suppresses tumors by downregulating ERK1/2, Bcl-2, surviving, and MMP-9 and encouraging the production of pro-apoptotic Bax. This axis reveals MATN1-AS1 as a potential therapeutic intervention through its interaction with NF-κB and MAPK signaling [79].

By downregulating IκBα through NDH2-mediated recruitment and enhanced H3K27me3 methylation, lncRNA XTP6 leads to NF-κB hyperactivation in GBM, creating a feedback loop with c-myc. Tumor growth is efficiently suppressed by using tiny molecules to inhibit NF-κB in cells that express XTP6 [80]. TNF alpha/NF-κB signaling and immunological responses are linked to NEAT1, which is broadly expressed in tumor and immune cells. It influences immunotherapy responses by promoting TNF alpha production and M1 macrophage polarization. NEAT1 is a biomarker and a modulator of treatment success due to its silencing interferes with these immune processes [81].

It is expected that additional lncRNAs, including LINC01366 and LINC01433, which have been identified in GBM, would control RELA through ceRNA networks. RELA is still essential for GBM cell survival and angiogenesis even though a direct relationship has not been verified. This pathway may be used by anti-angiogenic medications such as bevacizumab, sunitinib, and imatinib to indirectly influence lncRNA expression and tumor behavior [82]. By reducing RELB and boosting proneural behaviors while suppressing mesenchymal indicators, LOXL1-AS1 promotes the growth of GBM. It is a poor prognostic predictor because its suppression decreases cell proliferation and may change NF-κB-mediated tumor aggressiveness [83]

FAM66C affects TNF-α signaling, angiogenesis, and EMT by modifying transcription factors such SMAD3, RELA, and STAT3 in the presence of hypoxia. ADAMTS9-AS2, LINC00968, and LUCAT1 are examples of hypoxia-related lncRNAs that have been found to be prognostic biomarkers that are associated with immune infiltration and progression of GBM. NF-κB activity and hypoxia-driven tumor evolution may be impacted by medications that target these axes [84].

Necroptosis related lncRNAs, including RP11-131L12.4, have been studied and found to decrease necroptosis while strengthening migration, proliferation, and resistance to treatment. These lncRNAs influence drug resistance and NF-κB-driven immune escape, which supports their targeting in tailored treatment [85]. Similarly, lncRNAs linked to PYCARD are linked to tumor growth and chemotherapy resistance. Immune cell infiltration is correlated with PYCARD expression, and malignancy is accelerated by its overexpression in TMZ resistant GBM cells. In some situations, NF-κB pathway targeting may improve therapeutic outcomes [4].

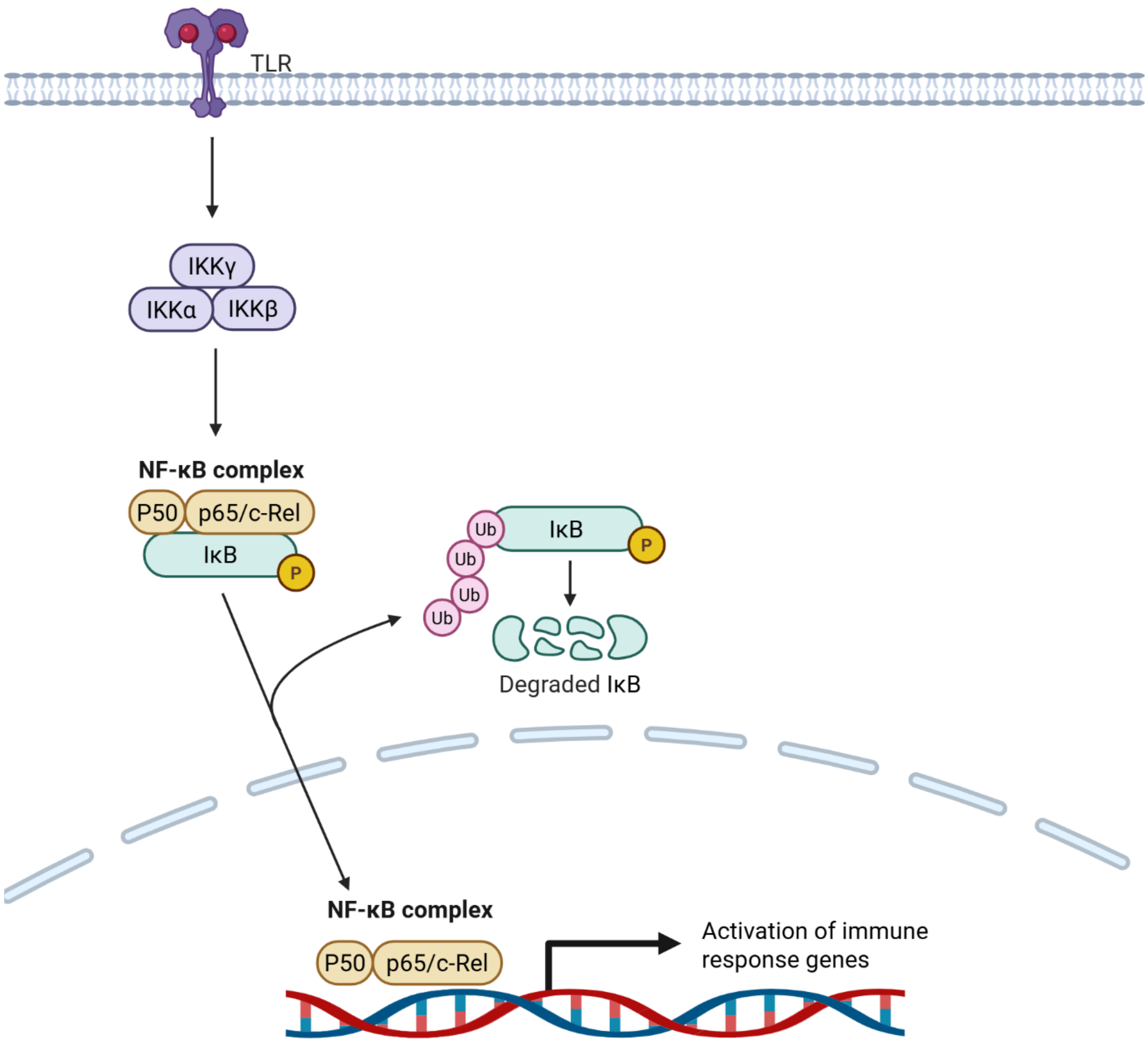


Figure 8 Mechanism of NF-κB Signaling pathway

Lastly, epigenetically regulated lncRNAs such as CD109-AS1 and LINC02447 are identified as immune-evasive markers in GBM by genome-wide analysis. These lncRNAs affect tumor immunity and survival with interacting with DNA methylation patterns and NF-κB signaling. This axis is also associated with HOTAIR, a recognized NF-κB activator that promotes phosphorylation and nuclear translocation of NF-κB components [86]. **Table 4** provides detailed information about each article.

3.1.1.5 JAK / STAT signaling

A crucial intracellular cycle, the JAK/STAT (Janus kinase / Signal Transducer and Activator of Transcription) signaling pathway transfers signals from growth factors and cytokines at the cell surface to the nucleus, where they alter gene expression. The in-detail part of this pathway is mentioned in **Figure 9**. Growth factors like EGF and cytokines like IL-6 frequently activate STAT3, a major oncogenic driver in GBM. In GBM, lncRNAs can change the behavior of the tumor by either increasing or decreasing the activity of the JAK/STAT pathway. GBM cells proliferate, go through, and evade the immune system with the support of the JAK/STAT pathway. It is a crucial target for GBM treatments as it contributes significantly to the tumor's increased aggressiveness and resistance to therapy.

The malignancy of GBM is mainly affected by the JAK/STAT signaling pathway, with many lncRNAs affecting tumor growth, immunological evasion, and treatment resistance. In GSCs, MIR222HG promotes the proneural to-mesenchymal transition, increasing radio resistance while establishing an immunosuppressive tumor environment. It promotes mesenchymal transition by inducing H4 deacetylation through its interaction with the YWHAE/HDAC5 complex.

Furthermore, transcribed miR221 and miR222 are carried to macrophages in exosomes, where they decrease the expression of SOCS3 and indirectly activate the JAK/STAT pathway, both of their roles in suppressive polarization and tumor growth. The study's RAF inhibitor, PLX-4720, increases radiosensitivity in mesenchymal GSCs by inhibiting SPI1-mediated transcription of MIR222HG, pointing to a potential treatment approach for resistant GBM subtypes [87].

Similarly, via interacting with DHX9 and enriching the promoter regions of STAT1 and CX3CL1, PVT1, which is overexpressed in GBM because of copy number amplification, regulates immune response and tumor growth. PVT1 activity is further linked to JAK/STAT-mediated immune suppression and poor prognosis because of decreased expression of interferon-stimulated genes (ISGs) and increased macrophage infiltration [88]. Through the TLR9/NEAT1/STAT3 axis, NEAT1 is another lncRNA that contributes to the aggressiveness of GBM. Through STAT3 activation, which enhances GSC self-renewal and stemness and increases cell survival and resilience to apoptosis and DNA damage, NEAT1 expression rises in response to adenoviral stimulation. These actions are significantly hindered by STATTIC's suppression of STAT3, demonstrating the significance of STAT3 in GSC survival [89].

In GBM, LINC00152 behaves differently according on the subtype. Although it is known to be an oncogene in several malignancies, it suppresses tumor growth in A172 GBM cells. While LINC00152 knockdown has little effect on cell survival, it does promote invasion and migration. By binding to its pre-mRNA, it increases the expression of STAT3, showing a regulatory feedback loop; however, in GBM, unlike in other malignancies, STAT3 does not regulate LINC00152, proving tumor heterogeneity and cell-specific processes [90].

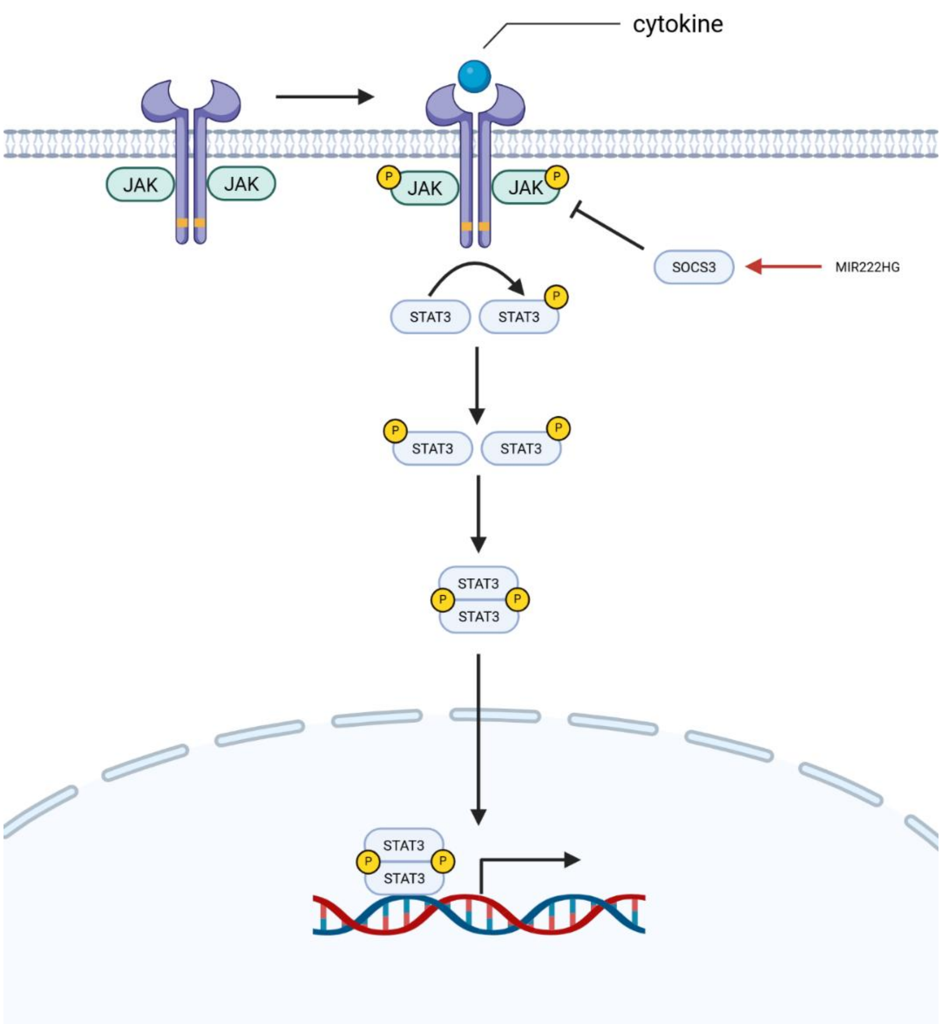


Figure 9 Mechanism of JAK/STAT signaling pathway

Additionally, TMZ resistant GBM cells have increased LINC00520, which helps them evade apoptosis and tolerate DNA damage. While LINC00520 stabilizes LIN28B to prevent autophagy and maintain DNA repair, hence contributing to TMZ tolerance, STAT3 binds to the LINC00520 promoter, increasing its expression. Cells become more sensitive to TMZ when LINC00520 is silenced because it increases apoptosis and causes G1/S phase arrest. To reverse chemoresistance in GBM, this STAT3/LINC00520/LIN28B regulatory axis offers a prospective target [91]. More detailed information of articles mentioned in the **Table 5**.

3.1.1.6 MAPK pathway

One important intracellular interaction pathway that delivers information from the cell surface to the nucleus and controls a variety of cellular functions, including as migration, apoptosis, differentiation, proliferation, and survival, is the MAPK (Mitogen-Activated Protein Kinase) signaling pathway. The ERK1/2 pathway is most frequently implicated in GBM. It promotes angiogenesis, invasion, and tumor growth by regulating transcription factors such as Elk-1, c-Fos, and c-Myc. Additionally, resistance to treatments like radiation and TMZ is a result of dysregulated MAPK signaling. Matrix metalloproteinases, or MMPs, are expressed more when MAPK is activated, which facilitates GBM cell invasion and migration. Additionally, MAPK amplifies oncogenic signals by interacting with other pathways, such as PI3K/AKT.

By influencing important cellular functions like proliferation, apoptosis, migration, and DNA damage response, the MAPK signaling pathway contributes significantly to the development and resistance to treatment of GBM. It has been demonstrated that a few lncRNAs control this pathway, impacting the malignancy of GBM and the results of treatment **Figure 10**. For instance, lncRNA NEAT1 is increased in GBM and suppresses let-7g-5p, a microRNA that targets MAP3K1, a component of the MAPK pathway, to improve GSC survival and TMZ resistance. While NEAT1 knockdown raises TMZ sensitivity and decreases tumor cell viability, migration, and invasion, the NEAT1/let-7g-5p/MAP3K1 axis contributes to increased tumor aggressiveness [92]. Like this, abnormal lncRNA DNA methylation in GBM modifies MAPK related gene expression, hence boosting carcinogenic processes through epigenetic regulation. The activation of MAPK signaling and the upregulation of hypomethylated lncRNAs signal possible therapeutic targets and small molecule therapies that can reverse these epigenetic modifications [93]. Through their control of DNA damage repair pathways, lncRNAs also affect radiation resistance in GBM. This process involves MAP2K6, a part of MAPK signaling, and the pathway is further modulated by radiation induced alterations in kinase activity. By modifying MAPK signaling and lncRNA expression patterns, clinically relevant small medicines like Sitravatinib and Brigatinib have demonstrated effectiveness in treating radiation resistant GBM [94].

Further research supports the oncogenic function of SNHG5, which is transcriptionally activated by YY1 and stimulates the p38/MAPK axis to enhance the growth of GBM cells. The therapeutic importance of targeting this signaling cascade is demonstrated by the fact that inhibition by SB203580 reduces proliferation, whereas activation of this pathway by TNF-α reverses the inhibitory effects of SNHG5 knockdown [95]. Through upregulating MAP4K4 and recruiting POLR2A to the MAP4K4 promoter, LINC01127, which is controlled by histone acetylation through the Warburg effect, promotes GBM cell survival and self-renewal. By inhibiting this axis with SP600125, tumor growth is suppressed, suggesting a possible treatment strategy for GBM [96]. Another study found that lncRNAs such HOTAIRM1 and LOXL1-AS1 function as competing endogenous RNAs, affecting gene expression linked to the MAPK pathway and accelerating the development of GBM. Drugs such as GSK2256098, a focal adhesion kinase inhibitor, have shown promise in blocking MAPK-driven cancer by targeting these lncRNAs [97].

Moreover, by promoting apoptosis and preventing the epithelial–mesenchymal transition (EMT), TCONS00020456 inhibits the growth of tumors. Through interactions with Smad2 and PKCα, its downregulation promotes ERK and JNK signaling, indicating that this lncRNA can be modulated to influence tumor aggressiveness and MAPK pathway activation. According to Chuanxi Tang et al. (2019) [98], it also interacts with hsa-miR-1279, providing another layer of post-transcriptional regulation significant to GBM therapy. Finally, via controlling RRAS and increasing MAPK14 activity, which affects cell invasion, proliferation, and survival, HULC overexpression in GBM encourages oncogenesis. Another promising approach for therapeutic intervention in GBM is to target HULC-RRAS-MAPK signaling [92]. **Table 6** provides more articles related this pathway.

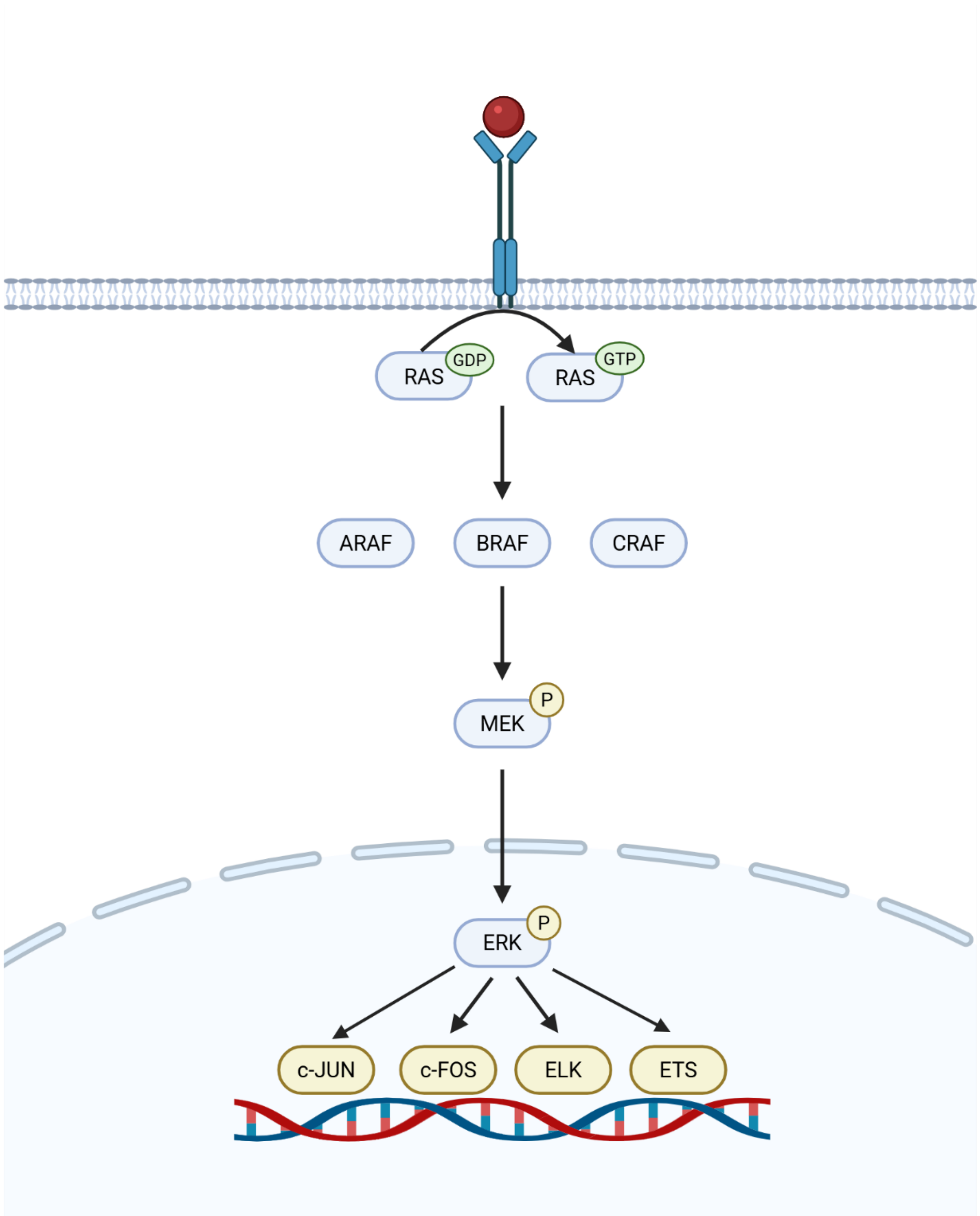


Figure 10 Mechanism of MAPK pathway

3.1.1.7 m6A RNA Methylation Regulation

The N6-methyladenosine (m6A) modification on RNA, the most common internal modification in eukaryotic messenger RNA (mRNA), is referred to as m6A RNA methylation regulation. It has an impact on mRNA stability, splicing, export, translation, and destruction, and it is essential for post-transcriptional gene control. A chemical alteration on RNA called m6A RNA methylation regulates the expression of genes during transcription. This pathway enhances the stability and translation of RNAs linked to malignancy in GBM, which in turn promotes tumor growth. It helps the tumor grow and withstand treatment by supporting GSCs. It promotes resistance to treatment, particularly to TMZ, by improving cell survival and DNA repair. increases PD-L1 expression, for instance, assisting in immune evasion. As a potential therapy for GBM, targeting m6A regulators (such as suppressing METTL3 or ALKBH5) is being investigated.

Methyltransferases ("writers"), demethylases ("erasers"), and binding proteins ("readers") interact dynamically to control m6A methylation, which impacts RNA stability, splicing, and gene expression. m6A-modified lncRNAs have been found in numerous investigations to be important modulators in GBM. For instance, 24 m6A-modified lncRNAs, such as MALAT1, NEAT1, and NORAD, were found in U87-MG cells. These lncRNAs exhibited high modification frequencies and were linked to tumor progression and cell survival, indicating that they may be used as therapeutic targets or biomarkers in the treatment of GBM [99]. Another study found that the prognosis of patients was highly associated with four lncRNAs such as AC005229.3, SOX21-AS1, AL133523.1, and AC004847.1. In high-risk patients, these m6A-related lncRNAs were associated with immunosuppressive characteristics like T-cell checkpoint dysregulation and APC co-inhibition. Furthermore, the therapeutic importance of m6A-lncRNA interactions was highlighted by the changed efficacy of targeted medications like AZD8055 and Vorinostat, as well as chemotherapeutic treatments like Doxorubicin and Methotrexate [100].

Additional research shows that via influencing important regulators, lncRNAs can indirectly modify m6A methylation. A micro peptide called AF127577.4-ORF, which is encoded by the lncRNA AF127577.4, inhibits the growth of GBM cells by destabilizing METTL3 and interfering with the ERK2/METTL3 connection. Inhibiting METTL3 decreases oncogenic m6A signaling and slows tumor growth because it increases m6A methylation and promotes tumorigenic processes, such as resistance to apoptosis and DNA damage repair. In addition to reducing METTL3 expression, ERK inhibition enhances the effects of the micro peptide [101]. Similarly, FGD5-AS1 was found to enhance tumor growth by upregulating HNRNPK, activating the Wnt/β-catenin pathway, and functioning as a molecular sponge for miR-129-5p, even though it was not clearly related to m6A in the study that was published. As m6A alterations are known to control gene expression and RNA stability, this pathway may interact indirectly with m6A dynamics in GBM [102].

Furthermore, it has been demonstrated that m6A methylation influences the regulation of alternative splicing and chromatin remodeling in GBM by lncRNAs such MALAT1, TUG1, and CRNDE. The epigenetic complexity of GBM is further reinforced by m6A marks, which alter the expression and splicing of tumor-related RNAs. To modify lncRNA activity and get past treatment resistance in GBM, researchers are investigating pharmacological approaches that target m6A regulators, such as methyltransferase and demethylase inhibitors [103]. Together, these results demonstrate the critical function of m6A-modified lncRNAs in controlling the course of GBM and emphasize their potential as therapeutic targets and prognostic markers across a variety of molecular axes. Additional specific details on the articles included in **Table 7**.

3.1.2 Indirectly related to apoptosis / survival / resistance

In GBM, lncRNAs affect transcription factors, regulatory molecules, or signaling pathways which can lead to indirect role in apoptosis, cell survival, and resistance to therapy. These indirect effects are often equally important as direct gene targeting, as they influence the tumor environment and cellular reactions to stress, treatment, and DNA damage. While certain lncRNAs, like LINC00461, support oncogenic pathways like MYC to promote proliferation, others improve tumor cell movement and survival through activation of the TGF-β pathway. LncRNAs control metabolic reorganization and autophagy in response to cellular stress [104]. For example, H19 supports glucose metabolism to maintain energy production and survival, while FOXD2-AS1 encourages autophagy and TMZ resistance [105]. Furthermore, lncRNAs promote glioma stemness and radiation resistance by activating the Wnt/β-catenin signaling pathway. Through the coordinated activation of TGF-β, Wnt, and Notch pathways, they also contribute to the EMT, a process associated with invasion and resistance, in which lncRNAs such as HOTAIRM1 and MIR222HG play important roles [106,107]. lncRNAs like TUG1 assist the maintenance of glioma stem-like cells and further resistance to TMZ by enhancing notch signaling itself. lncRNAs such as HIF1A-AS2 are increased in hypoxic environments, stabilizing the hypoxia-inducible factor HIF-1α which promotes angiogenesis and tumor cell survival [108–110]. These lncRNAs work together to coordinate a network of indirect molecular connections that inhibit apoptosis and improve the resistance of GBM to treatment. **Figure 11** indicates the list of pathways are indirectly involve in apoptosis and resistance.

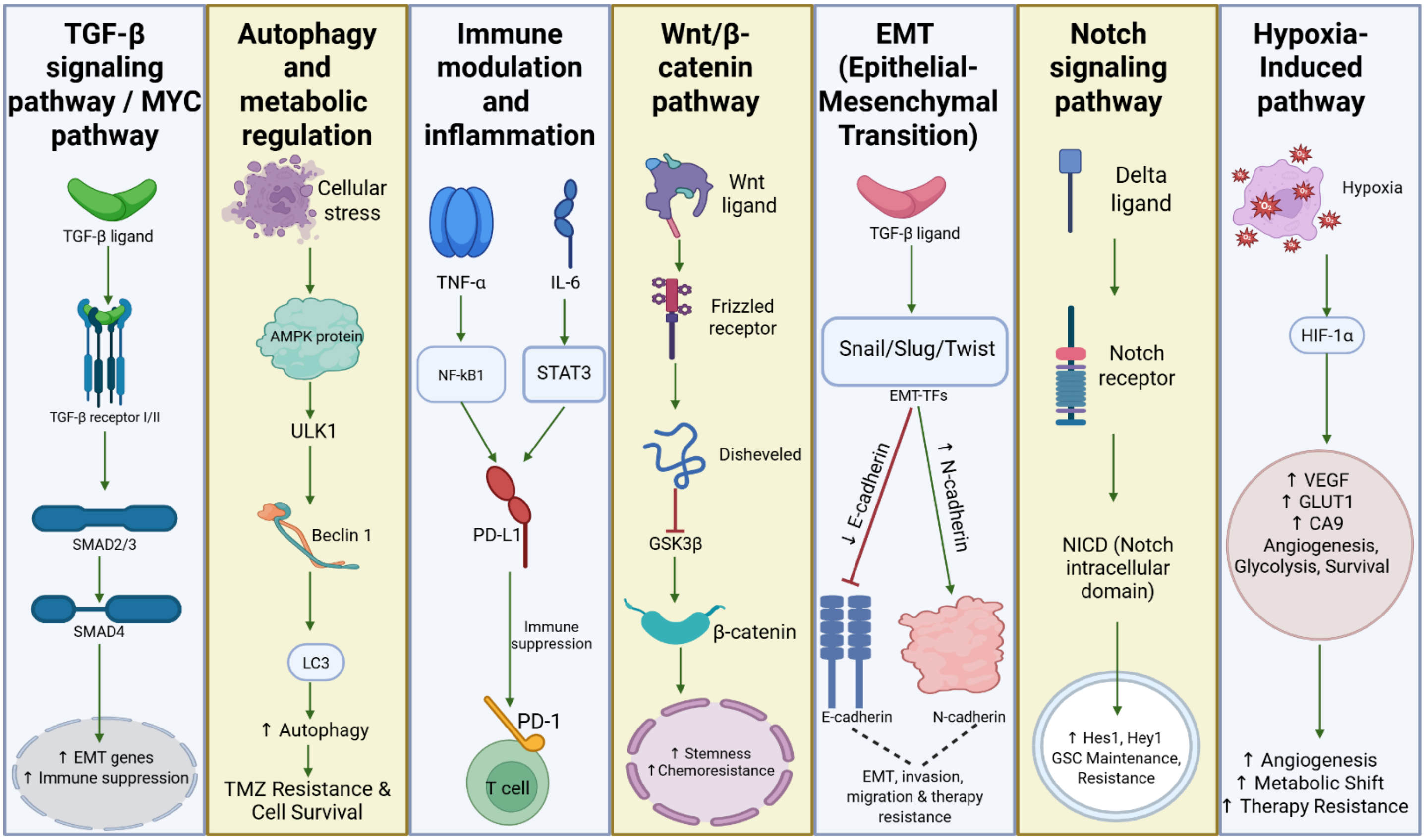


Figure 11 Additional lncRNA-regulated pathways involved in therapy resistance, stemness, and immune modulation in GBM

This figure highlights additional pathways affected by lncRNAs in GBM that contribute to tumor aggressiveness and treatment resistance. These include the TGF-β/MYC pathway, autophagy and metabolic regulation, immune evasion (PD-1/PD-L1 axis), Wnt/β-catenin, EMT, Notch, and hypoxia-induced signaling. lncRNAs modulate these networks to enhance immune suppression, stemness, invasion, metabolic adaptation, and resistance to therapy.

3.1.2.1 TGF-β Signaling Pathway / MYC Pathway

TGF-β signaling is linked to cell survival, apoptosis, and DNA damage response, and RPSAP52, which is significantly increased in GBM, stimulates TGF-β1 production, increasing CD133+ stem-like cell populations and tumor stemness [111]. The TGF-β and MYC pathways, that drive EMT, immune evasion, and carcinogenic transcriptional processes, are impacted by the ceRNA networks that regulate gene expression through six lncRNAs such as AC021739.2, AL031722.1, AL354740.1, FGD5-AS1, LINC00844, and NEAT1. Potential treatments that target these pathways include irinotecan, camptothecin, mitoxantrone, azacitidine, mestranol, and enilconazole [112].

By suppressing its negative regulators (Axin2, ICAT, and GSK3B) and promoting proliferation and invasion, NEAT1 also improves WNT/β-catenin signaling via EZH2-mediated H3K27 trimethylation [113]. High-grade gliomas overexpress ANCR, which suppresses apoptosis and cell cycle arrest, interacts with EZH2, and links to the TGF-β and MYC pathways to promote tumor maintenance [114]. Through PRC2/EZH2-mediated suppression of DNA damage repair genes, HOTAIR accelerates the progression of GBM, is associated with a poor prognosis, and is targeted by DZNep to stop tumor growth [106]. Additionally, HOTAIR controls MGMT expression, which contributes to TMZ resistance. By inhibiting MGMT expression by EPIC-0628, cells become resistant by upregulating CDKN1A and decreasing DNA repair (ATF3-p38-E2F1) [115].

Likewise, among these, lncRNA Smyca promotes chemoresistance and proliferation by increasing the transcriptional activity of MYC and TGF-β. According to Yilei Xiao et al. (2020) [105], H19, which is extensively expressed in GBM, is associated with a poor prognosis, controls immune infiltration, and promotes radiation resistance and TGF-β-driven EMT. Although there is no evidence of a direct connection between TRG-AS1 and MYC or TGF-β, SUZ12's epigenetic role raises the possibility of an indirect effect [116]. TRG-AS1 acts as a ceRNA for SUZ12 via miR-877-5p, promoting proliferation and survival. Tumor suppressor motility, invasion, and repression are facilitated through different oncogenic lncRNAs, including HOTAIR, HOTTIP, and ANRIL [117]. Through methods that go beyond traditional routes, such as protein scaffolding, immunological regulation, metabolic adaption, ceRNA activity, and epigenetic remodeling, these lncRNAs influence oncogenesis. By upregulating IGF1 and sponging miR-302a-3p, for example, HOXA-AS2 promotes TMZ resistance. It also promotes GSC self-renewal by transcriptionally regulating E2F1, STAT1, and ATF3 [118,119]. MIR210HG improves invasion, stemness, and chemoresistance in hypoxic environments by interacting with OCT1 to activate IGFBP2 and FGFR1 [120].

Collectively, these studies highlight the ways in which lncRNAs control GBM pathophysiology via the TGF-β and MYC pathways, chromatin modifiers like EZH2 and SUZ12, and mediators of the cell cycle and DNA repair like MGMT and CDKN1A, identifying important targets for treatment [107]. More detailed information of articles mentioned in the **Table 8**.

3.1.2.2 Autophagy and metabolic regulation

Numerous studies have demonstrated the critical roles that lncRNAs have in GBM malignancy by influencing metabolic reprogramming and autophagy. Through the CXCL14/UCA1/miR-182/PFKFB2 axis, UCA1 promotes glycolysis and invasion. CXCL14, which is produced from stromal cells, upregulates UCA1 and inhibits miR-182, which causes GBM cells to express higher PFKFB2 and become metabolically activated [121]. By maintaining HK2 mRNA through association with the m6A reader IGF2BP2, CASC9 further improves aerobic glycolysis and tumor aggressiveness, establishing the CASC9/IGF2BP2/HK2 axis as a metabolic driver [122].

By interacting with significant protein-coding genes and participating in metabolic and autophagy-related pathways, especially when exposed to TMZ chemoradiation, other prognostic lncRNAs including LINC00618, LINC02015, AC068888.1, CERNA1, and CTD-2140B24.6 modulate GBM survival and therapy response [104]. Transcriptionally controlled by NFE2L2, LINC00978 offers a therapeutic window for metabolic targeting and increases glucose metabolism and autophagy via AKR1B1, sensitizing GBM cells to 2-deoxyglucose [123]. On the other hand, through non-metabolic but glycolysis-related pathways, ARST suppresses tumors by interfering with ALDOA-actin connections, changing cytoskeletal integrity, and reducing aggressiveness [124].

By altering mitochondrial respiration and copper-induced cell death, cuproptosis-related lncRNAs also contribute to the pathophysiology of GBM; for example, lncRNA ZFAS1 promotes the growth of gliomas by invasion and proliferation [125]. By suppressing PPARα through the EZH2-H3K27me3 complex, HOTAIR promotes the growth of GBM; si-HOTAIR and fenofibrate therapy together have optimistic therapeutic outcomes [126]. Parallel to this, GLIDR indirectly influences autophagy and metabolic signaling, sponging miR-342-5p and upregulating PPARGC1A to contribute to chemoresistance [127]. Through chromatin remodeling and resistance mechanisms including autophagy and metabolism, aberrant splicing mediated by lncRNAs like MALAT1, CRNDE, and MEG3 further drives GBM [103]. Stabilized by m6A alteration, LINREP improves PTBP1 activity and encourages RTN4 alternative splicing, which affects metabolic and cytoskeletal remodeling [128]. Through its links to the AMPK/mTOR and PI3K/AKT pathways, which are essential for metabolic regulation and treatment resistance, FGD5-AS1 enhances the aggressiveness of GBM via the miR-129-5p/HNRNPK/Wnt/β-catenin axis[102]. By maintaining FUS and blocking its degradation via MDM2, ADAMTS9-AS2 promotes TMZ tolerance, highlighting the importance of autophagy and metabolic pathways in drug response [129]. Additionally, ZFAS1 returns in research associated to cuproptosis because of its activity in metabolism and Notch signaling, further combining autophagy and lncRNA function [125].

As a GBM-associated regulator, pan-cancer risk lncRNA SNHG1 affects chromatin dynamics and interacts with PI3K/AKT and AMPK/mTOR signaling, which is compatible with other metabolic and autophagy-related pathways [130]. Lastly, IDH1-AS1 links with larger networks of metabolic control and autophagic balance in GBM cells by promoting apoptosis and cell cycle arrest while increasing IDH1 enzymatic activity[131]. While examined as a whole, these studies highlight the complex function of lncRNAs in the pathophysiology of GBM and present encouraging opportunities for therapeutic intervention through the alterations of metabolic and autophagy pathways. More detailed information of articles mentioned in the **Table 9**.

3.1.2.3 Immune modulation and inflammation

In GBM, lncRNAs have become important modulators of inflammatory signaling and immune regulation, impacting tumor development, immune escape, and responsiveness to treatment. Zhao-Mu Zeng et al. (2023) [132] used whole-transcriptome sequencing and ceRNA structure design to identify variation in lncRNAs and their interactions with miRNAs and mRNAs, especially major regulatory nodes hsa-miR-296-5p and hsa-miR-874-5p. These work together in pathways including calcium signaling and neuroactive ligand-receptor interactions, which are essential for controlling immune responses and reshaping the tumor microenvironment. Yongsheng Li et al. (2016) [133] also showed that immune-related gene expression, such as CD58 and NCAM1, is influenced by lncRNA-TF-gene triplets, including HOTAIR interacting with transcription factors MXI1 and ATF5, both of which are linked to the prognosis of GBM. Furthermore, lncRNAs like MALAT1 influence P53 signaling, an essential pathway linked to inflammation, via regulating E2F1, which in turn controls the cell cycle and apoptotic responses.

According to Xiaolong Zhu et al. (2020) [134], lncRNAs RP11-547C13.1, RP11-268F1.3, and RP11-90M5.4 are miRNA sponges in ceRNA networks that impact immune-related pathways such as Ras signaling and T cell receptor. Immune-modulatory mRNAs such as C1S and HSD3B7 are also highlighted in the study as prognostic markers. The primary chemotherapeutic medication used to treat GBM, TMZ, changes the expression of lncRNA and is implicated in immune-mediated tumor cell death and DNA damage. In GBM, Kai Yu et al. (2021) [135] observed 2,577 lncRNAs that were differently expressed, emphasizing the MIR155HG/miR-129-5p/C1S axis. C1S knockdown decreased invasion and proliferation, indicating a role in inflammatory and immunological pathways. Victor Enciso-Mora et al. (2013) [136] additionally emphasized the importance of the rs55705857 SNP in the lncRNA CCDC26, which affects glioma risk through changes in immune cell activation, leukocyte function, apoptosis, and inflammation, all of which are especially important in the transformation and progression of low-grade gliomas.

Xiaoping Xu et al. (2021) [137] studied the immune-regulatory role of MEG3 and found that glioma downregulation is associated with a poor prognosis. MEG3 expression showed a negative correlation with dendritic cells and a positive correlation with CD8+ T cells, suggesting a role in immunological infiltration. Variations in its copy number affected patient survival as well as immunological activity. According to Wu Xu et al. (2019) [138], UBE2R2-AS1, which functions via the miR-877-3p/TLR4 axis, is significantly downregulated in GBM. Its overexpression highlighted its immune-modulatory function through the TLR4-mediated inflammatory pathway by promoting apoptosis, increasing caspase activity, decreasing BCL2 expression, and suppressing proliferation. According to Fan Hong et al. (2021) [139], IL10RB-AS1 is a survival-associated lncRNA that is connected to Toll-like receptor pathways and cytokine signaling. It is a promising biomarker and therapeutic target as it affects immune response, tumor growth, and drug resistance through the IL10RB-AS1/hsa-miR-26a-5p/GBP1 and IL10RB-AS1/hsa-miR-93-5p/DPYD networks. ANRIL and RP11-571M6.8 were identified by Yong Zhang et al. (2019) [140] as immunosuppressive lncRNAs in GBM. ANRIL, that regulates miR-375 and miR-637 and is frequently deleted in GBM, is linked to immunological checkpoints such as CTLA-4, PD-1, and PD-L1. It was discovered that RP11-571M6.8 affects regulatory T cell (Treg) markers such IL2RA and FCGR2B, which helps to decrease the immune system. The study by Kaikai Yi et al. (2022)

[141] concentrated on NEAT1, which is stabilized by PTRF/Cavin-1 and results in PD-L1 overexpression and NF-κB activation, two important processes in immune evasion. Additionally, NEAT1 inhibits UBXN1, which improves NF-κB signaling and makes T-cell suppression even easier. Anti-tumor immunity in GBM may be restored by focusing on this PTRF-NEAT1-PD-L1 axis.

According to Wanghao Chen et al. (2020) [142], HOXA-AS3 acts as a sponge for miR-455-5p, upregulating USP3 and promoting GBM cell proliferation, migration, and EMT. This pathway involves USP3-associated oncogenic signals to increase immune evasion and decrease apoptosis. According to FAN HONG et al. (2023) [143], miR-6072 is competitively bound by UBDP1, a pseudogene-derived lncRNA, which inhibits UBD. With implications for inflammatory and DNA repair processes, UBD improves tumor cell motility, survival, and immune evasion. Lastly, the immunosuppressive function of MIR222HG, which is transcriptionally controlled by SPI1 and stimulates proneural-to-mesenchymal transition and radio resistance in GSCs, was highlighted in the study of Yang Fan et al. (2023) [87]. Additionally, MIR222HG promotes the downregulation of SOCS3 and the induction of immunosuppressive polarization by facilitating the exosome delivery of miR-221 and miR-222 to macrophages. One potential therapy that is effective against this process is PLX-4720, which makes mesenchymal GBM cells more sensitive to radiation.

Together, these investigations clarify the various and intricate ways that lncRNAs influence the immune environment and inflammatory signaling in GBM, exposing several pathways by which they regulate cytokine signaling, immune checkpoint activation, and immune infiltration. Regarding the complex interactions among lncRNA-mediated transcriptional and post-transcriptional control, tumor immune microenvironment modification, and treatment response, lncRNAs have been identified as both therapeutic targets and biomarkers in GBM. More detailed information of articles mentioned in the **Table 10**.

3.1.2.4 Wnt/β-catenin pathway

The progression of GBM is significantly influenced by the Wnt/β-catenin signaling pathway, which modifies cellular functions such as stemness, apoptosis resistance, survival, proliferation, and response to therapy. Many lncRNAs, or long noncoding RNAs, have been found to be important regulators of this system. In the research they did of 301 EMT-related lncRNAs in GBM, XinJie Yang et al. (2021) [144] focused on SOX2OT because of its capacity to stimulate Wnt/β-catenin signaling and upregulate SOX2, which in turn promotes resistance to TMZ. According to Hanshuo Zhu et al. (2021) [126], LINC-PINT is a tumor-suppressive lncRNA that suppresses the expression of β-catenin, CD44, and C-Jun and blocks Wnt/β-catenin activity. Its effects are reversible by LiCl-induced pathway activation, confirming its upstream regulatory role. Oncogenic Wnt signaling and resistance to apoptosis are indirectly promoted by lncEPAT, an EGFR-induced lncRNA that suppresses USP16-mediated histone H2A deubiquitinating [145]. After TMZ treatment, NEAT1 is increased via the HMGB1/TLR2 axis, activating Wnt/β-catenin signaling to improve glioma stemness and chemoresistance [146]. Similarly, it has been found by Mingzhi Han et al. (2019) [147] that MIR22HG promotes tumor growth by sponging miR-22-3p and miR-22-5p, inhibiting Wnt inhibitors SFRP2 and PCDH15, and thereby increasing pathway activation. The carcinogenic role of H19, which recruits EZH2 to silence NKD1, a negative regulator of Wnt/β-catenin is highlighted [148]. This promotes tumor growth and invasiveness.

Furthermore, it was demonstrated that LINC01503 and CRNDE increased CD44/OLIG2 regulation and proneural-to-mesenchymal transition (PMT) through Wnt/β-catenin signaling, indicating a pathway-dependent immunosuppressive shift in GBM [149]. Through immune suppression and subtype regulation, the SNHG family, particularly SNHG18 was associated with GBM stemness and poor prognosis, tumors with high SNHG results responded to inhibitors of the EGFR-ERK pathway, suggesting upstream control over Wnt-related networks [150]. PXN-AS1 epigenetically suppresses DKK1, an antagonist of the Wnt pathway, via recruiting EZH2, which increases β-catenin activity and stimulates proliferation [151]. LiCl tests that restored inhibition of DKK action provided more evidence for this, underlining the importance of Wnt signaling. Weiguo Li et al. (2016) [152] and Jiang et al. (2016) [153] further implicated the Wnt/β-catenin axis in GBM malignancy by demonstrating the oncogenic role of H19 and its relationship with cancer stemness, angiogenesis, and apoptosis inhibition.

Wnt signaling was not specifically linked in some investigations, but their results on CD44, FANCD2, and ICAM-1 demonstrate downstream interaction with this pathway [154,155]. All together, these studies highlight the key function of Wnt/β-catenin signaling in the pathophysiology of GBM, which is mainly driven by dysregulated lncRNAs that either promote or reduce oncogenic outcomes. With the possibility for combinatorial therapies incorporating lncRNA regulation and Wnt/β-catenin inhibitors like PORCN inhibitors, mDKN-01, and AC1L6JTK, this pathway represents a promising therapeutic target. More detailed information of articles mentioned in the **Table 11**.

3.1.2.5 EMT (Epithelial-Mesenchymal Transition)

lncRNAs are essential upstream regulators of the EMT signaling system, which is involved in the progression, invasion, resistance to therapy, and stemness of GBM. To enable increased migration, invasion, and treatment evasion, EMT is typified by the loss of epithelial characteristics (such as E-cadherin and ZO-1) and the acquisition of mesenchymal markers (such as N-cadherin, vimentin, fibronectin, and α-SMA). Through the upregulation of mesenchymal markers and the suppression of E-cadherin, LncRNA ASB16-AS1 has been demonstrated to activate EMT signaling, promoting GBM cell growth, migration, and invasion, its silencing inhibits the proliferation of glioma stem-like cells, indicating potential therapeutic significance [156]. Through its regulation of MDR-associated proteins (MDR1, MRP5, LRP1) and important EMT transcription factors like ZEB1, Snail, and SLUG, MALAT1, which is overexpressed in TMZ resistant GBM cells, promotes to EMT and multidrug resistance (MDR). EMT is decreased, epithelial markers are restored, and cells become re-sensitive to TMZ when MALAT1 is suppressed [146,157]. By acting as a ceRNA for miR-34a, LINC01711 promotes EMT and survival through the TGF-β signaling pathway, resulting in increased invasion, TMZ tolerance, and ZEB1 overexpression [158]. On the other hand, DGCR5 is an EMT suppressor that promotes cell cycle arrest and inhibits tumor development and invasion by improve E-cadherin and decreasing N-cadherin expression [159]. By regulating targets including ZEB1, PTEN, and AKT and promoting intercellular transmission of EMT-related phenotypes, exosome lncRNAs such SBF2-AS1 and MALAT1 increase cell survival and apoptosis resistance [160].

The complexity of this regulatory axis is further highlighted by additional EMT-promoting lncRNAs. By interacting with WASF3 to rearrange the cytoskeleton, LINC03045 promotes invasion and connects EMT to TMZ resistance [161]. MMP7, a metalloproteinase essential to EMT and GBM invasiveness, is upregulated because of BCAR4's ceRNA-sponging action on miR-2276 [162]. Through the miR-185-5p/ANXA2/STAT3 axis, miR155HG controls EMT; its EMT-enhancing actions reduce when STAT3 is inhibited by SH-4-54 [163]. By stabilizing HMMR mRNA and enhancing the formation of homologous repair proteins (ATM, RAD51, and BMI1), HMMR-AS1 facilitates EMT and radio resistance [164]. Through the sponging of miR-137 and miR-520f-3p, respectively, HOTAIRM1 and WEE2-AS1 both influence EMT via SP1, a transcription factor that drives mesenchymal gene expression, and are associated with a poor prognosis [165,166]. Additionally, MIR155HG increases TMZ resistance via PTBP1 and links EMT to immune evasion and DNA repair through supporting EMT and immunological regulation through the miR-155/PCDHs/β-catenin axis [167]. LOC541471 promotes GBM migration and invasiveness by activating EMT via PLEK2 and extracellular matrix components (COL1A1, FN1, MMP9, ITGA5) [168]. By upregulating ZEB1 and ALDH1A1 under TMZ-induced stress via YY1 promoter activation, TP73-AS1 promotes EMT and chemoresistance, resulting in in stemness and treatment evasion [169]. By modifying MDR1, MRP5, PTEN, and ZEB1, other lncRNAs such CASC2, H19, TUSC7, and XIST control EMT and impact autophagy, DNA repair, and chemoresistance [170]. Through the miR-3681-5p/MALT1/NF-κB axis, HOXD-AS2 promotes EMT and invasion, whereas its knockdown inhibits tumor growth and increases apoptosis [171]. Lastly, through SNAI2 and TGM2, HOTAIRM1 regulates EMT and mitochondrial dynamics, supporting radiation resistance, mitochondrial function, and the regulation of reactive oxygen species (ROS) [172].

These results together demonstrate a strong and associated EMT regulation network in GBM, which is controlled by lncRNAs interacting with transcription factors, miRNAs, DNA damage response pathways, cytoskeletal regulators, and extracellular matrix components. Since these lncRNAs promote intercellular communication, resistance propagation, cellular invasion, and plasticity, EMT is a crucial axis for therapeutic targeting in GBM. More detailed information of articles mentioned in the **Table 12**.

3.1.2.6 Notch signaling pathway

GBM pathogenesis is significantly influenced by the Notch signaling pathway, which also affects tumor growth, apoptosis resistance, cancer stem cell maintenance, and treatment failure. Through transcriptional and post-transcriptional mechanisms, lncRNAs play a crucial role in regulating this pathway. RAMP2-AS1 regulates tumor growth by downregulating NOTCH3 and its downstream effector HES1 through interaction with DHC10, it is significantly downregulated in GBM and inversely correlates with prognosis. This tumor suppressive impact can be prevented by co-expression of NOTCH3, indicating that RAMP2-AS1 is a modulator of Notch signaling and a possible target for therapy [173]. Similarly, via sponging miR-642a-5p, MAFG-AS1 increases radio resistance in GBM by upregulating Notch1 and activating its downstream targets, such as Hes1. GBM cells become more sensitive to radiation when MAFG-AS1 is silenced or miR-642a-5p is restored, highlighting this axis as a potential target for radio sensitization methods [174]. Another carcinogenic long noncoding RNA, FEZF1-AS1, promotes cell invasion, migration, and proliferation by sponging the tumor suppressor miR-34a, which derepresses Notch1. Its functional role in the progression of GBM and its potential as a therapeutic target in conjunction with Notch1 are supported by the correlation of high FEZF1-AS1 levels with a poor prognosis [175]. Furthermore, by controlling MAML2, a co-activator in the Notch transcriptional complex, LINC01152 promotes GBM growth and prevents apoptosis. LINC01152 upregulates MAML2 via sponging miR-466 and recruiting SRSF1, which then interacts with NICD and RBPJ to activate Notch target genes, such as p21 and HES1.

Surprisingly LINC01152 expression is further amplified by Notch signaling feedback, producing a self-reinforcing oncogenic loop [176]. Moreover, GBM treatment resistance is a result of lncRNA dysregulation in the Notch pathway. The complex role of Notch signaling in chemoresistance is shown by the fact that EFEMP1 has been linked to improving TMZ resistance through Notch activation[177]. Together, these results point to a complex regulatory network in which lncRNAs control Notch signaling at several levels, including through interacting co-factors (like MAML2), downstream transcription factors (like HES1, p21), and ligand/receptor expression (like NOTCH1/3). There is great potential for overcoming drug resistance and improving GBM treatment results by targeting this lncRNA-Notch axis with strategies like γ-secretase inhibitors or lncRNA-targeted therapies. More detailed information of articles mentioned in the **Table 13**.

3.1.2.7 Hypoxia-Induced pathway

By promoting the continuing existence of GSCs, resistance to apoptosis, increased glycolysis, and resistance to therapy, hypoxia-induced signaling is essential to the progress of GBM. Multiple lncRNAs strongly regulate the stability and activity of the transcription factor hypoxia-inducible factor-1α (HIF-1α), which is crucial to this pathway. Significantly elevated in GBM tissues and cell lines, PCED1B-AS1 promotes the Warburg effect, increases cell survival, and speeds up tumor growth by binding to the 5′-UTR of the HIF-1α protein and improving its translation. PCED1B-AS1-mediated carcinogenic effects are reduced by HIF-1α knockdown, indicating a direct reliance [178]. By establishing a transcriptional complex with HIF-1α and its co-activator CBP, LUCAT1 also plays a role in tumor growth and is significantly expressed in hypoxic regions of GBM. HIF-1α signaling is amplified, GSC self-renewal is improved, and metabolic tolerance to low oxygen levels is encouraged by this positive feedback loop [109,179]. Depletion of LUCAT1 breaks this loop, decreases glucose absorption and lactate generation, enhances apoptosis, and prevents tumor growth in xenograft models. GBM aggression under hypoxia is also modulated by other lncRNAs, including uc003tnq.3. uc003tnq.3, one of six dysregulated lncRNAs, interacts with RNA-binding proteins (RBPs) and microRNAs, including TIA1, SRSF3, A1CF, and FUS, to form a lncRNA–miRNA–mRNA axis that regulates HIF-1α signaling indirectly. Its functional role in hypoxia-mediated tumor growth is further supported by the fact that its knockdown decreases GBM proliferation, migration, and invasion [180].

Although they were first investigated in non-small cell lung cancer, XIST and HIF1A-AS1 have also been linked to GBM. While HIF1A-AS1 is activated during hypoxia and interacts with apoptotic proteins to increase GBM cell survival, XIST is highly expressed in GBM and its silencing inhibits tumor growth [181]. Through the long-term stability of FOXM1, the lncRNA HULC contributes to the hypoxic response in GBM by activating AGR2 and, in turn, HIF-1α expression. This FOXM1/AGR2/HIF-1α axis links hypoxia to increased stemness and tumorigenicity by promoting glycolysis and GSC maintenance. Glycolytic flux and GBM viability are decreased when this axis is targeted, for instance, by the GLUT1 inhibitor WZB117 [182]. Additionally, NEAT1, an exosome lncRNA, is increased in GBM after chemotherapy and radiation damage to DNA. It creates an immune-evasive, hypoxia-adapted tumor microenvironment by promoting immunosuppressive macrophage M2 polarization through STAT3 activation and miR-125a suppression [183]. This hypoxia-linked exosome signaling also promotes GSC resistance and survival. The complex network of hypoxia-induced lncRNAs that regulate HIF-1α-dependent transcription, metabolic reprogramming, GSC maintenance, and immunological evasion in GBM is highlighted by these findings taken together. A possible therapeutic approach to address the aggressive and treatment-resistant characteristics of GBM is to target key components of the lncRNA-HIF-1α regulatory axis. More detailed information of articles mentioned in the **Table 14**.

3.1.3 Other

In GBM, lncRNAs influence many different types of regulatory networks in addition to the typical signaling pathways, which contribute to a variety of biological outcomes. To modify pathway gene expression in tumor growth and resistance, lncRNAs control or activate transcription factors (e.g., SOX2, HIF-1α, and STAT3). LncRNAs frequently regulate epigenetic regulators, like EZH2 and

DNMTs, to change chromatin states and inhibit tumor suppressor genes. An additional layer of post-transcriptional regulation influencing death or cell proliferation is expressed by non-coding RNA networks, such as ceRNA interactions with miRNAs or circRNAs. Additionally, lncRNAs affect translational efficiency, mRNA stability, and RNA binding proteins, which indirectly controls protein synthesis that is essential for tumor proliferation.

3.1.3.1 Transcription factors

lncRNAs in GBM intricately regulate transcription factor (TF) signaling pathways, which are essential for tumor growth, immune evasion, cellular plasticity, and resistance to treatment. Through a variety of methods, such as direct interactions, epigenetic modification, miRNA sponging, and transcriptional feedback loops, lncRNAs affect TF dynamics. For example, SOX2-OT increases the aggressiveness of GBM by suppressing tumor-suppressive miRNAs (miR-122-3p and miR-194-5p), which in turn causes TFs like FOXO1, FOXA1, and SOX3 to be upregulated. Additionally, it activates the JAK/STAT and Wnt5a/β-catenin signaling pathways, which contributes to stemness and TMZ resistance [133,184,185]. Similarly, MIAT suppresses apoptosis and modulates pluripotency TFs (Oct4, Sox2, Nanog) by controlling the Nanog/Sox2/let-7a-5p/miR-29b-3p axis, which improves stem-like characteristics [186]. TF–epigenetic crosstalk is highlighted by HOTAIR, which is activated by HOXA9, epigenetically silences tumor suppressors via PRC2 (EZH2), and is affected by DNA demethylation [187]. By sequestering epigenetic repressors (G9a, EZH2, DnmTs) and maintaining HOXA9 expression by enhancer-like looping, HOTAIRM1 promotes invasion, TMZ resistance, and HOXA1–3 expression [188–190]. At the same time, HOXD10 and related lncRNA networks control immunological signaling and cytokine interaction, with changed protein–RNA correlations in GBM tissues [191], whereas HOXB13-driven HOXC-AS3 overexpression promotes invasion and proliferation [192].

Additionally, REST induced transcriptional repression suppresses HAR1A, which when reactivated triggers apoptosis via the TP53 and MAPK pathways as well as CNS TFs like SYN1, linking REST to resistance to therapy [193]. Other lncRNAs stabilize TFs to provide chemoresistance: DANCR, stabilized by IGF2BP2, represses FOXO1 and its downstream target PID1 via ubiquitination, contributing to etoposide resistance [194]; PDIA3P1, upregulated by p38α-MAPK under TMZ, stabilizes C/EBPβ to promote proneural-to-mesenchymal transition (PMT), which is reversed by neflamapimod [195]. CeRNA interactions additionally regulate TF activity: RNCR3 targets miR-185-5p to upregulate KLF16 and cause apoptosis [196]; HOXA-AS2 sponges miR-885-5p to upregulate RBBP4, a chromatin-associated TF effector [197]; and CHRM3-AS2 sponges miR-370-5p, derepress oncogenic TF KLF4 [198]. While TP73-AS1 modifies RFX1 expression through ceRNA activity, TRPM7-induced HOTAIR further activates TF FOSL1 by suppressing miR-301a-3p [199–201]. According to Yang Ji et al. (2020) [202], MCM3AP-AS1 is known to control TFs SIX1 and ZBTB20 by miRNA sponging, which impacts the PI3K/AKT and ERK1/2 pathways via downstream targets like AGGF1 and KLF5.

LncRNAs are also involved in the TF pathways for the immune system and the stress response. C1RL-AS1, LINC00968, and MIR155HG modulate immune escape and apoptotic regulation by activating NF-κB signaling [203]. LncRNAs such as H19, LEF1-AS1, MALAT1, and NEAT1 change the expression of TF-driven genes associated with angiogenesis and stemness during hypoxic stress and oncolytic virotherapy (HSV-G47Δ) [204]. TMZ resistance is promoted by LINC00021, which is increased by E2F1 and recruits EZH2 to mute p21 and stimulate Notch signaling [205]. Chromatin remodeling and angiogenesis are linked by the lncRNA MANTIS, which is controlled by JARID1B and interacts with BRG1 to regulate TFs like SOX18 and SMAD6 [206]. Through ceRNA networks, differential lncRNA expression also regulates HMG-box TFs, particularly SOX6, which affects immunological infiltration and medication resistance [207]. While PR-lncRNAs function as tumor suppressors by downregulating SOX1/2/9, and TF knockdown alters glioma stem-like traits[208], H19 and its derivative miR-675-5p support CSC-TFs (SOX2, Nestin, Musashi-1) and downstream ERK1/2 and JNK signaling, enhancing invasion [209]. This network complexity is further supported by transcriptome-wide investigations. In U87 cells, knockdown of different lncRNAs modifies DNA repair and ribosome growth via influencing splicing through RBPs and TFs [210]. According to genome-wide profiling, TMZ resistant cells have abnormalities in DNA repair, ECM interaction, and MMR/NER pathways involving TFs like SOX2, as well as hundreds of dysregulated lncRNAs controlling TFs like PAK1 through PI3K/Akt and p53 signaling[211,212]. Lastly, SLC7A11 is elevated and ferroptosis resistance is promoted using DLEU1's participation in a CAF-driven axis involving HSF1–ZFP36–ATF3[213]. Additionally, MIR4435-2HG promotes TF KLF6 via miR-513a-5p sponging, which has significance for cross-cancer TF regulation, despite being examined in renal cancer [214,215]. The clinical significance of TF lncRNA interaction in chromatin architecture and drug response is highlighted by the observation that lncRNA-mediated TF regulation is resilient across experimental conditions such as MGMT promoter methylation status and HOXA locus silencing [216]. The detailed list of mention papers is in **Table 15**.

3.1.3.2 Epigenetic regulators

GBM progression and treatment resistance are significantly influenced by epigenetic control, with lncRNAs acting as important modulators of DNA methylation, histone modification, and chromatin dynamics. As a ceRNA in this situation, HAS2-AS1 inhibits miR-137's ability to downregulate LSD1, a histone demethylase involved in transcriptional reprogramming. This new epigenetic vulnerability in GBM is identified by the fact that the HAS2-AS1/miR-137/LSD1 axis promotes GBM proliferation both in vitro and in vivo, and that its disruption reduces tumor growth and increases survival [217]. On the other hand, the tumor suppressive lncRNA LINC00998 stabilizes CBX3, a Chromebox protein that increases H3K9 trimethylation at the c-Met promoter, therefore epigenetically suppressing the c-Met/Akt/mTOR pathway. The Akt inhibitor MK2206 mimics the effects of suppressing this oncogenic signaling cascade, which results in decreased tumor development and cell proliferation, indicating therapeutic synergy. This regulatory axis is further refined by the significant negative regulation of LINC00998 by miR-34c-5p [218]. Similarly, NEAT1 uses an epigenetic ceRNA pathway to increase TMZ resistance and GBM progression. NEAT1 stops the downregulation of GJA1 (Connexin 43), a gene linked to gap junction integrity and chemoresistance, by sponging miR-454-3p. While its knockdown restores miRNA function and makes cells less resistant to apoptosis, elevated NEAT1 expression in recurrent GBM is associated with a poor prognosis and decreased TMZ efficacy [219].

OBI1-AS1, which is expressed less in GBM than in low-grade glioma (LGG), demonstrates another layer of epigenetic regulation. Its overexpression is related with altered topologically associated domains (TADs), and it is epigenetically regulated through CTCF-mediated chromatin border architecture and IDH1 mutation-dependent DNA methylation. According to these results, OBI1-AS1 may decrease tumors by maintaining chromatin integrity in signaling pathways arising from astrocytes[220]. As a ceRNA that sequesters miR-19a-5p, AC016405.3 supports this tumor-suppressive paradigm by restoring the production of TET2, a DNA demethylation enzyme with recognized involvement in epigenetic remodeling. In GBM, downregulating AC016405.3 and TET2 increases tumor aggressiveness, but restoring this axis prevents metastasis and proliferation, indicating that it may be used therapeutically to epigenetically remodel GBM cells [221]. Certain lncRNAs affect the formation of GBM by multifunctional or highly context-specific processes that do not just map onto regular molecular pathways. For instance, LINC00174 has been linked to epigenetic chromatin interactions that promote glioma migration and proliferation, although it has no clear connection to classical signaling cascades like as p53 or PI3K/AKT. Like this, ZEB1-AS1 is known to increase the aggressiveness and stemness of gliomas, but its varied mechanistic roles in various studies make it difficult to categorize it into a single signaling pathway. All this research indicates chromatin remodeling factors and lncRNA-miRNA-protein axes as potential targets for upcoming therapeutic treatments, revealing a dynamic and intricate lncRNA-centered epigenetic network that controls GBM etiology and response to treatment. **Table 16** indicates the details of all articles.

3.1.3.3 non-coding RNAs

By activating within ceRNA networks that control the availability of miRNA and downstream oncogenic signaling, lncRNAs play a crucial role in the pathophysiology of GBM. To derepress oncogenic targets associated in invasion, proliferation, apoptosis evasion, and therapy resistance, these lncRNAs essentially act as molecular sponges, sequestering tumor-suppressive miRNAs. For instance, LINC00599 reduces EMT via the miR-185-5p/KLF16 axis [222], while tumor suppressive lncRNAs like CASC2 prevent proliferation and EMT by sponging miR-18a and regaining tumor inhibitory gene expression [223]. On the other hand, LINC00606 increases PI3K/AKT signaling by sponging miR-486-3p, derepressing TCF12, and interacting with ATP11B [224], while oncogenic lncRNAs such as FLVCR1-AS1 promote invasion by suppressing miR-30b-3p, which results in increased MMP-2/MMP-9 expression [225]. Several lncRNAs affect key pathways such as SNHG7 uses the miR-5095/CTNNB1 axis to activate Wnt/β-catenin signaling [226]; SEMA3B-AS1 causes cell cycle arrest by regulating miR-195 and cyclin D1 [174]; and TALNEC2, which is upregulated by E2F1, downregulates miR-124 and miR-137 while promoting miR-21/miR-191, which promotes mesenchymal transition, proliferation, and radio resistance [227]. Numerous types of lncRNAs control therapeutic resistance and stemness. For example, NEAT1 increases NRAS and SOX2 expression by sequestering miR-132 and let-7e, which contributes to TMZ resistance, and XIST increases GSC self-renewal by sponging miR-152, which enhances KLF4 expression [228].

Similarly, HOTAIRM1 drives EMT by creating a feedback loop with miR-153-5p/SNAI2 [229]. HOTAIR also modulates vascularization, glycolysis, and TMZ resistance through a variety of miRNA interactions, such as those with miR-526b-3p/EVA1, miR-125/HK2, and miR-519a-3p/RRM1 [223,230,231]. Other lncRNAs mediate therapy resistance by targeting miRNA processing or DNA repair: TGF-β1/Smad-induced H19 and HOXD-AS2 disrupt the miR-198/MGMT axis through KSRP inhibition [232], MAFG-AS1 inhibits miR-34a processing through DICER/Drosha inhibition [233], and ZEB1-induced SBF2-AS1 secreted via exosomes suppresses miR-151a-3p/XRCC4 [174]. Other ceRNA networks that activate PI3K/AKT signaling are EGFR-AS1/miR-133b/RACK1 [234], TTN-AS1/miR-320b/PKP2, and LINC01410/miR-370-3p/PTEN [235,236].

LINC00680/miR-568/AKT3–mTOR–EIF4EBP1, NCK1-AS1, and PSMB8-AS1/miR-22-3p/DDIT4 pathways all are involved in resistance [92,95,237]. Axes like LINC00645/miR-205-3p/ZEB1 and LINC00525/miR-338-3p control EMT regulation, whereas GAPLINC promotes EMT by sequestration of miR-331-3p [238]. The H19/miR-326/PKM2 axis promotes glycolysis and tumor growth [239], while SNHG9 regulates glycolysis via the miR-199a-5p/Wnt2 pathway [223]. LncRNAs also control metabolic rewiring. Immunosuppressive microenvironments are promoted by immune modulation involving PCED1B-AS1/miR-433-3p/MS4A6A and AL161785.1/miR-139-5p/MS4A6A [240]. While SATB2-AS1 inactivates miR-671-5p, restoring pro-apoptotic CDR1 and VSNL1 [241], tumor suppressive lncRNAs like MEG3 and UNC5B-AS1 block EMT and proliferation via the miR-6088/SMARCB1 and miR-24-3p/MAPK axes, respectively [242]. These complex interactions between lncRNA, miRNA, and mRNA converge on important signaling pathways, such as PI3K/AKT, Wnt/β-catenin, MAPK, EMT, mTOR, EGFR, and JAK/STAT, which together control the growth of GBM, stemness, immune evasion, and resistance to treatment. These ceRNA pathways' potential as RNA based therapeutic targets and diagnostic indicators for GBM is highlighted by the mechanistic insights about them. More information about articles is mentioned in **Table 17**.

3.1.3.4 RNA Binding / Translation / Post-transcriptional Regulation

Recent data emphasize how important lncRNAs are in regulating translation, RNA binding proteins, and post-transcriptional regulatory systems that influence the pathophysiology of GBM. According to Esparza-Garrido et al. (2018) [243], lncRNAs, such as linc-RoR, are elevated in pediatric GBM and affect the expression of PHLDA1 and ELAV1, two important regulators of cell survival and stress response. Additionally, these lncRNAs interact with circular RNAs and miR-101-1-3p, which influences targets including CDK6 and VEGFA and suggests that they are involved in the PI3K-Akt and MAPK signaling pathways. Similarly, copy number variations (CNVs) cause ceRNA network dysregulation, as demonstrated by Xu et al. (2019) [244], where lncRNAs such as ELAVL2 and MARCH9 change post-transcriptional regulation by competitively binding miRNAs shared with mRNAs such as STMN1, MTMR1, and CECR2 genes implicated in tumor proliferation and cell cycle progression. Drug resistance and a poor prognosis have been linked with CNV deletions in CDKN2A/B and MTAP, which interrupt the p53 and TGF-β pathways.

Further research identifies lncRNAs as central ceRNA regulators, for an instance, FOXD1-AS1 supports glioma cell survival by sequestering miR-339/342, which increases translation of eIF5A, an essential translation factor involved in oncogenesis; LINC01446 enhances tumor growth through the LINC01446/miR-489-3p/TPT1 axis; and HAS2-AS1 promotes GBM progression by sponging miR-608, thereby upregulating PRPS1, a gene involved in purine biosynthesis and cell proliferation [245–247]. By either directly controlling translation mechanism or indirectly affecting mRNA stability and expression through miRNA sponging, these results highlight a convergent mechanism in which lncRNAs function as post-transcriptional modulators. The involvement of targets like CDK6, eIF5A, and TPT1 indicates potential for combining lncRNA targeted approaches with current therapies like CDK4/6 inhibitors or TMZ, particularly for GBMs with defined CNV or ceRNA imbalances, even though no drugs were directly tested in these studies. More detail of used papers is articulated in **Table 18**.

3.1.3.5 Neurotrophic / Growth Factors

lncRNAs play a major role in the dysregulation of neurotrophic and growth factor signaling in GBM, which affects tumor progression, resistance to therapy, and microenvironmental remodeling. By downregulating BDNF, a crucial neurotrophic factor, the tumor suppressive lncRNA BDNF-AS, which is increased by the anesthetic propofol, prevents GSC proliferation, self-renewal, and mesenchymal growth. GSCs become more sensitive to TMZ and radiation when propofol increases BDNF-AS delivery through extracellular vesicles (EVs). Conversely, BDNF-AS silencing reverses these effects, underscoring its essential role in inhibiting neurotrophic signaling between GSCs and microglia [248]. Similarly, by controlling EGFR and PDGFR, two essential growth factor receptors in GBM, MEG3, an epigenetically silenced lncRNA in GSCs, acts as a tumor suppressor. Cell invasion and proliferation are decreased when it is replaced with valproic acid (VPA), suggesting that epigenetic treatments can reactivate lncRNAs to alter growth factor signaling [249]. By using miR-454-3p sponging to upregulate Connexin 43 (Cx43/GJA1), the lncRNA NEAT1 aids in chemoresistance. This establishes the NEAT1/miR-454-3p/Cx43 axis as a critical regulator of growth factor-linked apoptotic resistance by enhancing TMZ-induced apoptosis and promoting mitochondrial survival signaling and drug efflux [219]. Furthermore, RP11-838N2.4 (LINC01198) restores EphA8 expression and apoptosis by indirectly regulating neurotrophic signaling through miR-10a sponging.

Growth factor suppression and increased TMZ sensitivity are linked by this dual mechanism, which also involves TGF-β pathway repression[250]. Another example is the m6A-regulated lncRNA RP11-552D4.1 (LINC01736), which is linked to immunosuppressive tumor environments and neuronal proliferation through MAP2 and β-tubulin. Its involvement with neurogenesis-related tumor dynamics and therapeutic response is suggested by the fact that high expression enhances proliferation and resistance to PARP inhibitors [12]. A transcriptome studies found HOXB-AS3, LINC00311, and other lncRNAs linked to poor prognosis and growth factor intersecting pathways like calcium signaling and Wnt in GBM, even though they were not directly mapped to typical neurotrophic pathways. In an eight-mRNA prognostic model, genes such as ASIC5 and CLDN16 affect barrier function and ion homeostasis, which in consequence affect neurotrophic signaling networks [11]. **Table 19** has more data about this pathway.

3.1.3.6 Novel Uncharacterized lncRNAs

Although most of lncRNAs in GBM are classified based on how they interact with identified oncogenic signaling pathways, other lncRNAs in GBM do not have a unique biological relationship with any signaling axis. These uncharacterized lncRNAs are still important, but their roles are either uniquely underexplored or represent novel mechanisms of action independent of established signaling frameworks.

In addition, certain lncRNAs exhibit non-recognised molecular activity, such as affecting RNA editing, telomere maintenance, or nucleolar dynamics, without directly activating or repressing pathways, or have been identified clinical subgroups (e.g., pediatric GBM or IDH mutant gliomas). Taken together, these uncharacterized lncRNAs highlights the need for more studies to examine the unique, non-classical roles of lncRNAs in GBM history, therapeutic resistance, and clinical outcomes. This is in keeping with the evolving characteristics of GBM molecular research. All the articles with no clear pathway are include in **Table 20**.

3.2 Role of lncRNAs in GBM

We identified total 378 studies in which 165 articles mentioned oncogenic lncRNAs, 93 discussed tumors suppressive lncRNAs, 14 studies focused on therapy resistance, and 99 papers were related to tumor growth. Approximately 26 studies could not be clearly classified into these categories. **Figure 12** summarizes the classification of all reviewed studies according to the functional role of lncRNAs in GBM. The discussion below explores how these lncRNAs contribute to GBM pathogenesis through distinct mechanisms.

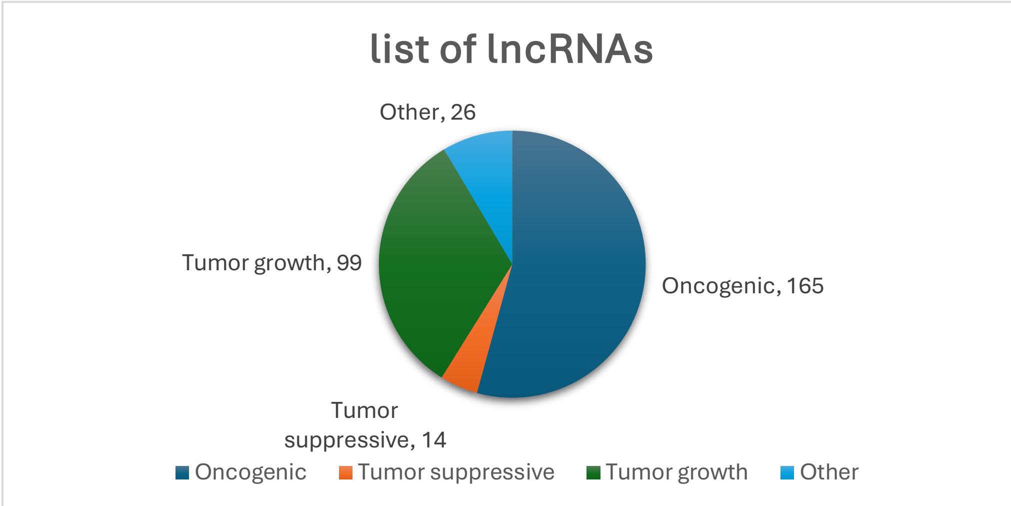


Figure 12 Classification of lncRNAs based on their role in GBM

This figure classifies lncRNAs into oncogenic, tumor-suppressive, therapy resistance-associated, and tumor growth-related groups, illustrating their diverse functions and regulatory targets in GBM.

3.2.1 Oncogenic lncRNAs (upregulated in GBM)

Oncogenic lncRNAs are key regulators in GBM, significantly contributing to tumor progression through their diverse molecular functions. While some lncRNAs act as proto-oncogenes under normal physiological conditions, their aberrant expression, mutation, or epigenetic dysregulation in GBM transforms them into potent oncogenes. These lncRNAs promote uncontrolled cell division, survival, invasion, angiogenesis, stemness, and resistance to therapy, making them crucial components in the GBM tumorigenic network. In GBM, oncogenic lncRNAs exert their functions through several mechanisms. Many acts as ceRNAs that sponge tumor suppressive microRNAs, thereby releasing oncogenic mRNA targets from suppression. Others function as epigenetic regulators by recruiting histone modifiers such as EZH2 or LSD1 to silence tumor suppressor genes. In addition, some lncRNAs serve as scaffolds or stabilizers of transcription factors and mRNA transcripts, enhancing the translation or stability of oncogenic proteins. These lncRNAs integrate into and modulate major oncogenic pathways such as PI3K/AKT/mTOR, Wnt/β-catenin, MAPK, STAT3, and p53 signaling cascades.

For example, several lncRNAs promote GBM proliferation and survival via the PI3K/AKT/mTOR pathway. We observed 23 papers which focus on that pathway. LINC01198 [39] and SAMMSON [40] activate this pathway, while NONHSAT159592.1 enhances glioma cell motility through the ITGA3/FAK/PI3K/AKT axis [44]. LINC00470 contributes to tumor growth by activating AKT signaling and inhibiting autophagy [45]. CRNDE, a frequently upregulated lncRNA in GBM, activates both PI3K/AKT and Wnt/β-catenin pathways and plays a central role in metabolic reprogramming and glioma stemness [251].

The Wnt/β-catenin pathway, a major driver of EMT and tumor aggressiveness is activated by lncRNAs such as H19, which sponges miR-675 and facilitates invasion, proliferation, and stemness [244]. Similarly, LINC00689 targets the MAPK pathway to enhance glioma aggressiveness, and MIR155HG promotes c-Myc expression via the miR-185-5p axis, supporting cell proliferation [174]. PVT1 is another well-characterized oncogenic lncRNA that stabilizes c-Myc mRNA, driving glioma growth [252].

Oncogenic lncRNAs also modulate tumor suppressive pathways, particularly those involving the p53 axis. TUG1 sponges miR-145, disrupting the MDM2/p53 feedback loop and reducing apoptosis, ultimately enhancing glioma progression [245]. FOXD2-AS1 promotes cell cycle progression by recruiting EZH2 to repress CDKN1B [53]. Under hypoxic conditions, MIR210HG enhances HIF-1α stability, facilitating tumor adaptation to low oxygen environments [253].

Furthermore, several oncogenic lncRNAs enhance glioma stemness and therapy resistance. LINC01426 and LINC00511 activate STAT3 and Notch signaling, which are essential for maintaining stem-like properties in glioma cells [97,253]. TP73-AS1 is associated with chemoresistance through the miR-142/MGMT axis, affecting DNA repair and TMZ response [254]. AC092718.4 regulates both JAK/STAT and NF-κB pathways in a hypoxia-dependent manner, promoting tumor survival under stress [198], while LINC01711 enhances angiogenesis via VEGFA mRNA splicing.

Several additional lncRNAs demonstrate ceRNA activity by sequestering specific microRNAs. These include OIP5-AS1 (miR-129-5p/E2F1 axis), HOTTIP (miR-101/ZEB1), LINC00152 (miR-16/IGF1R), NEAT1 (miR-107/CDK14), and HOTAIRM1 (miR-129-5p/STAT3), each regulating critical pathways linked to proliferation, migration, and immune evasion [174,185,233,255,256]. Other oncogenic lncRNAs include ZFAS1 (MAPK/ERK signaling) [9], CASC19 (EMT via Snail/Slug) [257], SOX2-OT (stemness), and MALAT1 (AKT/mTOR and autophagy regulation)[258].

In mesenchymal subtypes of GBM, LINC00665 plays a key role in regulating EMT [87]. Similarly, MIR22HG, ZEB1-AS1, ZNF667-AS1, and MYLK-AS1 promote glioma genesis via transcriptional and post-transcriptional modifications including methylation and histone remodeling. Several SNHG family lncRNAs (SNHG20, SNHG7, SNHG12) activate both PI3K/AKT and Wnt signaling pathways, indicating pathway crosstalk. Additionally, lncRNAs such as KTN1-AS1 promote EMT and cell proliferation through the miR-505-3p/ZNF367 axis [259], and Linc-RoR maintains glioma stemness by sponging miR-145 to preserve SOX2 expression[37] [198].

In conclusion, oncogenic lncRNAs regulate nearly all malignant traits of GBM from unchecked proliferation to chemoresistance by modulating major signaling cascades and interacting with miRNAs, transcription factors, and chromatin modifiers. Their cell and cancer specific expression, combined with diverse mechanisms of action, highlights their potential as both diagnostic biomarkers and therapeutic targets. Targeting these lncRNAs could offer innovative treatment strategies for overcoming resistance and halting GBM progression.

3.2.2 Tumor-Suppressive lncRNAs (Downregulated in GBM)

In GBM, tumor-suppressive lncRNAs are often downregulated. These lncRNAs play an important role in inhibiting the progression of tumors by promoting apoptosis, stopping proliferation, controlling cell cycle checkpoints, and increasing sensitivity to radiation and chemotherapy. Through a multitude of molecular processes, including as transcriptional regulation, chromatin modifier recruitment, miRNA sponging, and modification of important tumor-suppressive signaling pathways, these lncRNAs carry out their suppressive functions. By sponging miR-181a and altering the STAT3 axis, CASC2 has been shown to improve TMZ sensitivity while reducing glioma cell proliferation, hence reversing drug resistance and increasing apoptotic signaling [37,200]. Similarly, the miR-106a-5p/PTEN/AKT axis is how LINC00657 (also called NORAD), a lncRNA that is frequently downregulated in gliomas, suppresses tumors.

By the restoration of PTEN expression through miR-106a-5p sponging, PI3K/AKT signaling is suppressed, tumor cell survival is decreased, and chemosensitivity is improved [116]. As a ceRNA for miR-10a, the p53-induced lncRNA TUSC7 prevents invasion, migration, and the EMT in GBM cells. MEG3 is another accurate tumor suppressor lncRNA that increases p53-mediated transcriptional activity to induce apoptosis. Because promoter hypermethylation frequently silences MEG3 in GBM, its reactivation highlights its therapeutic potential by activating caspase and causing cell death [260].

TP53TG1, a p53-target gene that regulates the cell cycle and reduces proliferation [56], and TPTEP1, which inhibits glioma growth via the miR-148a-3p/HIPK1 axis [252], are other tumor-suppressive lncRNAs with several methods. Glioma stemness is negatively regulated by DNAJC27-AS1, which is involved in RNA pseudouridylation and may be a factor in stem cell fatigue[51]. HNF1A-AS1 also reduces glioma stemness by blocking the Wnt/β-catenin signaling pathway [255]. According to Sun et al. (2020) [235], GAS5, a well-established lncRNA, sponges miR-222 to activate caspase-dependent cell death and upregulate pro-apoptotic factors like BCL2. Remarkably, ZFAS1 exhibits tumor-suppressive action in gliomas via inhibiting Notch1 signaling, despite being carcinogenic in other cancer. Similarly, AC099850.3, DLEU1, and LINC01088 repress glycolysis and GSC traits by targeting the mTOR pathway [257].

lncRNAs that are epigenetically controlled also aid in the inhibition of tumors. PANDAR interacts with the transcription factor NF-YA to promote apoptosis brought on by DNA damage [261]. While C2dat1 prevents hypoxia-induced survival by suppressing NF-κB activity[262], KCNQ1OT1 decreases EMT and invasiveness by downregulating β-catenin signaling [263]. Other suppressive lncRNAs, such as PTENP1 and NCRNA00085, are linked to genomic stability and immunological modulation. For example, NBAT1 uses EZH2 regulation to epigenetically repress oncogenic targets, hence preventing tumor development and migration [95]. Additional lncRNAs that influence important tumor-suppressive pathways like p53, PI3K, and TGF-β signaling have been found using multi-omics research. These include AC011472.4, RP11-334E6.12, FER1L4, MIAT, and FENDRR [198,264].

Additionally, immune regulation and tumor microenvironment adaptation are controlled by several tumor-suppressive lncRNAs. SLC26A4-AS1, for example, improves antigen presentation and upregulates MHC-I molecules, which may improve immunological recognition [247].

lncRNAs that control metabolic adaptability and cellular stress responses, including ADAMTS9-AS2 and LINC01271, limit glioma plasticity in hypoxic or nutrient-deficient environments. Other lncRNAs, such as LINC00998, ZBTB20-AS1, NCK1-AS1, RHPN1-AS1, and AC007728.1, upregulate tumor-suppressive genes including PDCD4 and SOX11 and use miRNA sponging (e.g., miR-21, miR-155) to suppress glioma cell movement and invasion or cause cell cycle arrest.

Together, these tumor-suppressive lncRNAs provide a rich and diverse class of regulators that work to keep glioma cells in a homeostatic state. In GBM, treatment resistance, aggressive phenotypes, and poor patient outcomes are all closely linked to their downregulation. Significantly, several of these lncRNAs particularly those that are p53-regulated, participate in the PI3K/AKT/mTOR and Notch pathways, or influence the immune system have potential as therapeutic targets and prognostic indicators, opening new treatment options for GBM personalized medicine.

3.2.3 lncRNAs involved in therapy resistance

Chemoresistance and radio resistance are two major categories of therapy resistance in GBM, each of which reflects the tumor's capacity to overcome specific therapeutic approaches. The term "chemoresistance" describes the decreased sensitivity or total resistance of GBM cells to chemotherapeutic drugs, particularly TMZ, the common chemotherapy medication used to treat GBM. The upregulation of the DNA repair enzyme O6-methylguanine-DNA methyltransferase (MGMT), which mitigates the cytotoxic effects of TMZ-induced DNA alkylation, is one of several intrinsic and acquired processes that contribute to TMZ resistance. Additionally, resistance is promoted by the enrichment of glioma stem-like cells (GSCs) with intrinsic drug-resistant traits, enhanced autophagic activity, evasion of apoptosis, and activation of pro-survival signaling pathways such PI3K/AKT. Notably, lncRNAs such as MALAT1, NEAT1, and TP73-AS1 have been implicated in chemoresistance by modulating these pathways [204].

On the other hand, radiation resistance refers to capacity of GBM cells to tolerate and rebound back from ionizing radiation, which is frequently used after surgery to remove any remaining tumor cells. While radiation-induced double-strand breaks are the main cause of tumor cell death, GBM cells frequently exhibit increased DNA damage repair pathways that allow them to survive radiation. Furthermore, the suppression of reactive oxygen species (ROS), avoidance of radiation-induced apoptosis, and the initiation of signaling pathways linked to stemness all contribute to resistance. Several lncRNAs have been shown to modulate these responses [265].

One of the primary challenges to treating GBM is therapy resistance, which can result in a high recurrence rate and a limited patient life. Even with the standard of care, which includes TMZ chemotherapy and radiotherapy after maximal surgical resection, GBM almost always returns, frequently with a more aggressive and drug-resistant characteristics. According to recent research, lncRNAs regulate a few molecular processes, such as DNA damage repair, autophagy, apoptosis, GSC maintenance, and epigenetic modification, and they are essential in mediating resistance to therapy.

HOTAIR is one of the most extensively researched lncRNAs linked to treatment resistance, and it plays a role in both TMZ and radiation resistance. HOTAIR increases the survival of glioma cells by activating the Wnt/β-catenin signaling pathway and epigenetically silencing tumor suppressor genes through interaction with EZH2, a part of the PRC2 complex. To methylate histones and inhibit transcription, it enlists the help of EZH2 and LSD1, which are parts of the polycomb repressive complex. Increased TMZ resistance is linked to HOTAIR-mediated PTEN suppression in GBM [259].

By triggering the PI3K/AKT pathway and preventing apoptosis, MALAT1 has also been demonstrated to increase TMZ tolerance and improve cell survival and autophagy in the context of chemotherapeutic stress. In TMZ-resistant GBM cells, MALAT1 is overexpressed. It does this by sponging miR-203 and activating the PI3K/AKT signaling pathway, which supports autophagy and cell survival. Glioma cells become more susceptible to TMZ-induced cytotoxicity when MALAT1 is suppressed [194].

By modifying the DNA repair machinery and inducing autophagy through the miR-107/ATG14 axis, NEAT1, another important lncRNA, modulates resistance and enhances cell survival in response to TMZ therapy. By promoting DNA damage repair, NEAT1 increases radio resistance in gliomas. It controls the formation of paraspeckles, nuclear substructures linked to stress responses and makes it easier for DNA repair proteins to be transported to damage sites[266].

GSCs are naturally more resistant to traditional therapies because of their stemness, which is maintained by TUG1, another lncRNA linked to therapy resistance. It functions through the miR-145/SOX2 signaling axis, and in resistant GBM models, it has been demonstrated that blocking it restores TMZ sensitivity. GAS5 and CASC2, on the other hand, are lncRNAs that inhibit tumors and have been linked to higher chemosensitivity. GAS5 stimulates apoptosis via the mTOR signaling pathway, whereas CASC2 decreases the AKT pathway by reducing miR-181a. Both are often downregulated in GBM tissues that are resistant to treatment. Additionally, through sponging tumor-suppressive microRNAs like miR-124, TP73-AS1 has been shown to increase glioma cell survival and proliferation while also promoting TMZ resistance[267].

All these results demonstrate a network of oncogenic and tumor-suppressive lncRNAs that significantly influence GBM treatment resistance. Most of these lncRNAs function mechanistically via modifying ceRNA activity, epigenetic alteration, and apoptotic or autophagy pathways. A promising treatment approach is to target these resistance-associated lncRNAs. Experimental research has demonstrated potential in overcoming resistance and resensitizing GBM cells to TMZ using lncRNA knockdown, siRNA-mediated silencing, or antisense oligonucleotides. Furthermore, resistance-associated lncRNAs' expression profiles could be used as prognostic biomarkers to customize treatment for GBM patients. To overcome therapeutic failure in GBM, it is necessary to comprehend the molecular interactions between lncRNAs and therapy resistance pathways. The involvement of these lncRNAs in therapy resistance underlines their importance as biomarkers for treatment response and potential targets for sensitizing GBM to existing therapies.

3.2.4 lncRNAs involved in tumor growth

Uncontrolled cellular proliferation, higher metabolic activity, and sustained tumor microenvironmental support are the main causes of tumor growth in GBM. These activities have been found to be critically regulated by lncRNAs, which through several molecular mechanisms contribute to the malignant growth of glioma cells. These consist of controlling the progression of the cell cycle, preventing apoptosis, altering oncogenic signaling pathways, and interacting with microRNAs that regulate genes linked to growth. Glioma cell proliferation and tumor mass expansion have been linked to a few lncRNAs, which are frequently associated with a poor prognosis and a high tumor grade [268].

CRNDE is one of the most widely studied growth-promoting lncRNAs in GBM. It is significantly increased in glioma tissues and cell lines. By altering the mTOR signaling pathway and sponging certain tumor-suppressive miRNAs, such as miR-136-5p and miR-384, CRNDE stimulates the growth of tumors by improving downstream targets like PI3K and STAT3. Another important lncRNA is PVT1, which stabilizes c-Myc, a master regulator of cell growth and metabolism, and speeds up the proliferation of glioma cells [41]. Furthermore, GBM growth is facilitated by LINC00152, sometimes referred to as CYTOR, which suppresses the expression of growth-inhibiting miRNAs including miR-103a-3p and activates the EGFR/PI3K/AKT pathway. In GBM tissues, elevated Ki-67 proliferation index and larger tumor sizes have been linked to high expression of LINC00152 [60].

Another lncRNA that has been demonstrated to promote the growth of gliomas is CCAT2, which affects the Wnt/β-catenin pathway, a crucial signaling axis in tumor development and cell proliferation. Similarly, by encouraging cell cycle progression and preventing p53-dependent growth arrest mechanisms, H19, an imprinted lncRNA that is expressed maternally, has been linked to the development of GBM tumors. It enhances tumor growth and migration through modifying the β-catenin/ZEB1 axis and sponging members of the miR-200 family [152].

Furthermore, by regulating EZH2, an epigenetic silencer, and controlling genes related to proliferation and brain development, TALNEC2, a tumor-associated lncRNA, has been shown to enhance GBM growth and stemness. Through ceRNA methods and modulation of pathways like AKT, TGF-β, and Notch signaling, it has been demonstrated that other lncRNAs, including LINC00467, SNHG1, and SOX2OT (SOX2 overlapping transcript), influence the growth of gliomas [185].

Overall, tumor growth-associated lncRNAs support the rapid development of GBM through many of frequently linked methods. Many of these lncRNAs work by interacting with chromatin-modifying complexes, controlling transcription factors, or sponging tumor-suppressive microRNAs. Their overexpression has a direct impact on tumor growth, glioma cell viability, and adverse clinical results. Growth-associated lncRNAs are interesting targets for anti-proliferative treatments and molecular diagnostics in GBM because of their functional significance and tumor-specific expression.

Chapter 4: Discussion

4.1 Summary of findings and key mechanisms

Research on GBM and lncRNA is a highly complex and diverse field of cancer biology. This intricacy results from the wide range of functions of lncRNAs as well as the extremely variable nature of GBM itself, both genetically and cellularly. Multiple sub clonal populations contribute to GBM tumors, and each has unique genetic changes, epigenetic markers, and therapeutic responses. Treatment is made more difficult by intratumorally variety, which also increases the risk of therapeutic resistance and early recurrence. However, lncRNAs can interact with DNA, RNA, and proteins in plenty of ways and display context-dependent, tissue-specific activities. In GBM, lncRNAs control cellular functions such invasion, angiogenesis, apoptosis, proliferation, and resistance to chemotherapy and radiation. They also function as tumor suppressors and oncogenic drivers.

It has been observed that lncRNAs regulate important signaling pathways such as PI3K/AKT/mTOR, p53, Wnt/β-catenin, Notch, and NF-κB directly, as well as through epigenetic remodeling, transcriptional regulation, and miRNA sponging. These pathways work together to create a complex regulatory network that allows tumor cells to resist common treatments, avoid immune surveillance, and adapt to environmental stress. This review examines how lncRNAs have been integrated into these essential signaling networks and how their dysregulation increases to the malignant characteristic of GBM by analyzing about 389 articles with peer review. It is essential to comprehend these complex molecular connections since they give new opportunities to find reliable biomarkers and create precision-targeted treatments for a condition that always causes enormous therapeutic challenges.

4.1.1 Dysregulated lncRNAs and their associated pathways in GBM

Identifying that which lncRNAs are frequently dysregulated in GBM and how they affect essential molecular pathways is a crucial first step towards the clinical translation of lncRNA-based treatments. Because of their frequent appearance in many independent searches, a few lncRNAs came out as having significant clinical value. Among the most researched oncogenic lncRNAs, HOTAIR (51 studies), MALAT1 (20), NEAT1 (13), H19 (22), CRNDE (10), and PVT1 (2) were frequently linked to activation of the PI3K/AKT/mTOR, NF-κB, Wnt/β-catenin, and STAT3 signaling pathways. It has been demonstrated repeatedly and again that these lncRNAs improve tumor recurrence, therapeutic resistance, and GBM cell survival. 51 studies found that HOTAIR is one of the most often identified oncogenic lncRNAs in GBM, stimulates PI3K/AKT and NF-κB pathway activation and EZH2-mediated chromatin remodeling, which advances tumor growth and resistance to TMZ [74,107]. MALAT1 has also been extensively researched, and it acts as a ceRNA for miR-199a and miR-101, activating mTOR and EMT-related signaling cascades to promote glioma cell invasion, proliferation, and stemness [171,269]. Another oncogenic lncRNA, PVT1, contributes to tumor aggressiveness and resistance to treatment by stabilizing MYC protein and influencing Wnt/β-catenin signaling [270]. Similarly, NEAT1 improves GSC maintenance and TMZ resistance through control of the Notch and STAT3 pathways [271], while CRNDE stimulates PI3K/AKT/mTOR signaling and is associated with metabolic reprogramming in glioma cells [38,251].

However, in GBM, a few lncRNAs function as tumor suppressors. Addressing tumor suppression, lncRNAs including MEG3 (14 studies), CASC2 (9), GAS5 (5) H19 (10), TP73-AS1 (6) and

LINC00461 (2) showed that they inhibited oncogenic pathways such PI3K/AKT, mTOR, and p53. They were also associated with improved patient outcomes and increased chemosensitivity. Additionally, some research has shown that downregulation of these lncRNAs is associated with more aggressive GBM characteristics and a worse prognosis. For example, MEG3 is known to inhibit the carcinogenic E3 ligase MDM2 and stimulate p53 signaling and its downregulation is associated with a poor prognosis [137]. GAS5 observed as reduce mTOR signaling and encourages apoptosis [272], whereas CASC2 inhibits the PI3K/AKT pathway and makes GBM cells more sensitive to TMZ [273]. TUSC7 recorded by 2 studies for sponging oncogenic miRNAs such as miR-10a and inhibits cell cycle progression. These lncRNAs not only represent critical nodes in glioma genic pathways but also serve as potential biomarkers or therapeutic targets [170,274]. GBM development and treatment resistance are significantly linked to the lncRNA H19. By sponging miR-675 and modifying Wnt/β-catenin signaling, it has been demonstrated to enhance invasion, cell proliferation, and the EMT. H19 is also linked to tumor aggressiveness and metabolic adaption since it is frequently increased in hypoxic environments and contributes to TMZ resistance through a variety of ceRNA interactions [152]. A family of tumor-causing lncRNAs, SNHG1 and SNHG12 (identify in 12 studies), are often overexpressed in GBM. By sequestering tumor-suppressive microRNAs like miR-140-5p, miR-194, and others, these lncRNAs function as ceRNAs, which in turn activates oncogenic pathways like Wnt/β-catenin, Notch, and PI3K/AKT. A poor prognosis and increased glioma cell migration and proliferation are associated with their overexpression [95]. By altering chromatin remodeling complexes and controlling genes related to cell cycle regulation, apoptosis inhibition, and treatment resistance, TP73-AS1 accelerates the growth of tumors. Additionally, it has been linked to the survival of GSCs, which promotes tumor recurrence and treatment failure [53,200]. LINC00461 is significantly downregulated in GBM tissues and cell lines. It functions as a sponge for oncogenic miR-216a, which normally inhibits tumor suppressor genes. By sponging miR-216a, LINC00461 restores the expression of PTEN, a critical tumor suppressor that negatively regulates the PI3K/AKT pathway [75].

Our review of more than 389 evaluated studies found that lncRNAs including HOTAIR, MALAT1, and NEAT1 were among the most often studied, highlighting their clinical significance.

4.2 Potential therapeutic targeting of lncRNAs in GBM

As lncRNAs play essential roles in controlling tumor development, invasion, apoptosis, and resistance mechanisms, they have become attractive therapeutic targets in GBM. Several therapeutic approaches, such as RNA-based treatments, gene-editing instruments, small molecule inhibitors, and modification of drug-lncRNA interactions, have been investigated to alter the activity of lncRNAs in GBM.

4.2.1 RNA-based therapies (siRNA, antisense oligonucleotides)

For the management of GBM, RNA-based therapies provide a promising method of modulating oncogenic or tumor-suppressive lncRNAs. Briefly, synthetic nucleic acids known as small interfering RNAs (siRNAs) and antisense oligonucleotides (ASOs) can silence target lncRNAs by RNA interference or RNase H-mediated degradation, respectively [199]. Glioma cell migration, proliferation, and chemoresistance have all been shown to be significantly decreased in preclinical GBM models when MALAT1, CRNDE, or NEAT1 are knocked down by siRNA. In a similar vein, ASOs that targeted HOTAIR or TP73-AS1 effectively increased apoptosis and restored sensitivity to TMZ [187]. Against lncRNAs with known sequences and structures, these compounds show outstanding specificity and are reasonably simple to synthesize. The weak permeability of the blood-brain barrier (BBB), sensitivity to nuclease degradation, and requirement for specialized delivery systems, however, continue to interfere with practical translation. Lipid nanoparticles, aptamers, and conjugated peptides are being investigated further to improve tumor selectivity and BBB crossing. However, these challenges, RNA-based methods provide a versatile and modular way to either restore tumor-suppressive lncRNAs or quiet carcinogenic ones in GBM [191].

4.2.2 CRISPR/Cas9-based editing of lncRNAs

The genome-editing approach CRISPR/Cas9 offers a novel platform for eliminating or permanently altering lncRNA loci in GBM cells. This method allows for either complete lncRNA gene deletion or epigenetic modification via CRISPR activation (CRISPRa) or interference (CRISPRi). Oncogenic lncRNAs including FOXD2-AS1 and PVT1 have been deleted in GBM studies using CRISPR-Cas9, which has improved chemosensitivity, decreased tumorigenic potential, and impaired stemness. CRISPRi techniques reduce the risk of genotoxicity by suppressing lncRNA transcription without causing DNA breaks. Additionally, CRISPRa-based lncRNA editing has been used to reactivate tumor-suppressor lncRNAs that have been silenced, such as MEG3, which increases apoptosis and inhibits the advancement of the cell cycle. However, transport limitations, off-target effects, and ethical concerns about germline editing limit the use of CRISPR in vivo. Notwithstanding these drawbacks, accuracy and flexibility of CRISPR system make them an effective tool for both functional validation of lncRNAs and, once delivery and safety issues are resolved, possible therapeutic therapy [161].

4.2.3 Small molecule inhibitors targeting lncRNA interactions

A new and undiscovered field of GBM treatment is represented by small molecule inhibitors that are intended to interfere with lncRNA's interactions with proteins or other RNAs. Numerous lncRNAs cause cancer by serving as scaffolds or guides for miRNAs, RNA-binding proteins (like HuR and IGF2BP2), or chromatin modifiers (like EZH2 and LSD1). For instance, PVT1 promotes chromatin remodeling and stabilizes MYC, whereas HOTAIR combines with EZH2 to cause gene silence by H3K27 trimethylation. Oncogenic signaling complexes or tumor suppressor genes may become unstable if these interactions are disrupted. It has been demonstrated that small compounds like AQB and BC11 hydrazone may interfere with RNA-protein interactions involving HOTAIR or MALAT1, which lowers the survival of glioma cells. The understanding of RNA primary structures is being enhanced by structural investigations employing NMR and cryo-EM, which is directing the logical development of small-molecule binders. However, because RNA structures are dynamic and variable and lack conserved binding sites, the discovery of RNA-specific medicines is still technically challenging. Nevertheless, these challenges, lncRNA interaction-targeting small molecule inhibitors present the possibility of extremely selective and reversible lncRNA activity control [275].

4.2.4 Drug-lncRNA interaction

By modifying the expression of resistance genes, adjusting signaling pathways, or controlling metabolic reprogramming in GBM, lncRNAs can have a direct impact on medication responsiveness. One excellent example is lnc-TALC, which increases the transcription of the MGMT promoter and, consequently, its ability to repair DNA by attracting STAT3 and p300 to it. This enables resistance to TMZ. The expression of drug-efflux transporters like ABCB1 has also been demonstrated to be enhanced by UCA1, which lowers the intracellular concentration of chemotherapeutic drugs. However, tumor-suppressive lncRNAs such as CASC2 enhance apoptosis by adversely regulating the PI3K/AKT pathway, which makes cells more sensitive to TMZ. The dual function of lncRNAs as resistance mediators and possible therapeutic adjuvants is highlighted by these drug-lncRNA interactions. By incorporating lncRNA profiling into personalized medicine techniques, it may be possible to predict resistance to traditional treatment or identify patients who will benefit from lncRNA-targeting medicines. Furthermore, lncRNA knockdown may improve therapy efficacy and postpone the emergence of resistance when combined with conventional chemotherapeutics [46].

4.3 lncRNAs as prognostic and diagnostic biomarkers

With major benefits for disease categorization, prognosis, and non-invasive diagnosis, lncRNAs have become important biomarkers in GBM. The clinical potential of lncRNAs is becoming more widely acknowledged because of their mechanistic involvement in carcinogenesis, relative stability in biofluids, and cancer-specific expression patterns. It has been demonstrated that a few lncRNAs correlate with significant clinical outcomes, including tumor grade, patient survival, recurrence risk, and resistance to treatment. For example, downregulation of tumor-suppressive lncRNAs like MEG3, CASC2, and GAS5 correlates with improved survival and increased therapy sensitivity, whereas high expression of oncogenic lncRNAs like HOTAIR, PVT1, and MALAT1 has been consistently linked to poor prognosis and resistance to TMZ. These findings highlight the predictive potential of lncRNAs and raise the possibility that they may be employed to categorize GBM patients into molecular subgroups with different clinical outcomes. Moreover, lncRNAs are being intensively investigated as diagnostic markers, particularly in the context of liquid biopsies, where their identification in circulating biofluids provides a dynamic and non-invasive means of evaluating the burden of disease and the effectiveness of treatment.

4.3.1 Clinical relevance and detection techniques (e.g., qRT-PCR, sequencing)

The capacity of lncRNAs to accurately reflect clinical outcomes and genetic tumor identification makes them clinically relevant biomarkers. Their abnormal expression in GBM, which is frequently distinct to a subtype or stage, makes them perfect candidates for tailored therapy. In predicting patient survival and response to treatment, lncRNA-based prognostic signatures have been shown in multiple studies to perform better than conventional markers like MGMT promoter methylation or IDH1 mutation [58]. The classification of GBM into prognostic subtypes has been proposed using multi-lncRNA expression panels, which combine data from lncRNAs such TUG1, LINC00665, and UCA1. More precision and strength are provided by these signatures than by single-gene markers.

Developments in detection technologies, which enable the sensitive and accurate quantification of lncRNAs from tumor tissue and biofluids, support the use of lncRNAs in therapeutic settings. The most used method is still quantitative real-time PCR (qRT-PCR) because of its excellent sensitivity, specificity, and suitability for clinical workflows. Although it requires more resources, RNA sequencing (RNA-seq) provides transcriptome-wide profiling, which makes it possible to identify new lncRNAs and precisely measure those that are already known [84]. Furthermore, droplet digital PCR has been used to detect circulating lncRNAs in plasma, serum, and cerebrospinal fluid (CSF) with extreme sensitivity, particularly when the lncRNAs are protected from degradation by exosomes or extracellular vesicles. These methods enable repeated sampling to study tumor dynamics, allowing for real-time evaluation of early recurrence, therapy response, and disease progression. Standardization of RNA extraction procedures, normalization techniques, and validation across sizable, heterogeneous patient populations are still necessary for clinical application, nevertheless. After these problems are resolved, lncRNAs may be used as reliability, less invasive biomarkers for GBM in diagnostic and prognostic pipelines.

4.4 Patient studies and clinical trial status of lncRNA-targeting therapies

Although preclinical GBM models have demonstrated promising outcomes with lncRNA-targeting techniques, clinical translation is still restricted, and there are presently no authorized lncRNA-specific medicines for the treatment of GBM. A rising number of patient-based studies, however, such as functional studies employing patient-derived material and retrospective cohort analyses, provides fundamental support for upcoming therapeutic applications.

Primary tumor cell cultures, organoids, and patient-derived xenograft (PDX) models have all proven crucial in confirming the functional roles of important lncRNAs and evaluating treatment approaches. For instance, in orthotopic xenograft models obtained from GBM patients, ASOs or siRNAs targeting NEAT1, CRNDE, or FOXD2-AS1 have shown considerable tumor growth suppression and restoration of TMZ sensitivity. The reversal of stem-like characteristics, induction of apoptosis, and decreased potential for self-renewal have all resulted from lncRNA knockdown in 3D GBM spheroids. Although these investigations are limited to experimental settings, they highlight the translational potential of lncRNA regulation [276,277]

There are currently no phase I or II clinical trials evaluating lncRNA-targeting therapies in GBM patients as of 2024. However, the safety and effectiveness of lncRNA-targeting ASOs, such as CCAT1-ASO and H19-DTA, are being assessed in several early-phase trials in various malignancies, such as liver, prostate, and breast cancer. Soon, glioma-specific trials are anticipated to be made possible by these investigations. Pilot studies utilizing circulating lncRNAs as non-invasive biomarkers for tumor identification and therapy monitoring are becoming more popular on the diagnostic front. Although they are not yet commonly used, some studies are investigating the use of lncRNA expression panels to classify glioma patients into risk groups or molecular subtypes.

The following are the main barriers for beginning clinical trials: (1) the challenge of delivering RNA-based agents across the blood-brain barrier; (2) the absence of approved intracranial delivery systems; (3) a lack of information regarding long-term safety and immunogenicity; and (4) the absence of regulatory guidelines for RNA therapeutics in CNS diseases. Therapeutic design is further complicated by the fact that many carcinogenic lncRNAs lack conserved sequences or defined functional domains. Collaborations between academic institutions, biotech organizations, and clinical trial networks will be essential to overcoming these obstacles. Determining the precise pharmacokinetic, pharmacodynamic, and toxicity profiles of potential lncRNA treatments in humans will also be essential to the clinical translation process.

4.5 Challenges in translating lncRNA-based therapies to the clinic

Clinical acceptance of lncRNA-targeted treatments for GBM has been limited by a few important issues, despite their enormous potential. First, lncRNAs frequently have cell-type-specific and context-specific activities, which means that the same lncRNA may behave differently according on the GBM subtype, signaling status, or cellular environment. Because of this diversity, it is challenging to generalize therapeutic procedures and requires precision targeting, which raises the expense and complexity of treatment.

Second, forecasting the functions of lncRNAs using animal systems is extremely difficult due to their poor sequence conservation across species. For lncRNAs without substitutes in mice or rats, this restricts the capacity to conduct preclinical safety and efficacy testing in vivo. As a result, many of the therapeutic effects shown in cell lines do not result in outcomes that are clinically meaningful.

Third, transporting RNA-based treatments across the blood-brain barrier is a recurring obstacle in brain tumor treatment. Large, negatively charged molecules that are difficult to enter the central nervous system are many siRNAs, ASOs, and CRISPR components. While exosome-mediated transport, viral vectors (like AAV), and nanoparticle design advancements provide some solutions, their immunogenic potential, off-target effects, and biodistribution are still issues. Although they have been investigated, intramural injection and convection-enhanced administration are invasive and not yet acceptable for general usage.

Fourth, there are safety risks from immune activation and off-target consequences. Even if these hazards are decreased by contemporary chemical modifications (such as 2′-O-methylation and phosphorothioate linkages), immunological detection by Toll-like receptors and unintentional gene regulation still arise. Long-term genomic instability, unwanted alterations, and double-strand breaks are still issues with CRISPR/Cas9-based methods.

Fifth, clinical acceptance is further delayed by regulatory obstacles. The FDA has no set standards for assessing the efficacy and safety of lncRNA-based treatments, particularly those that target non-coding areas. Furthermore, patient monitoring and trial inclusion criteria are made more difficult by the absence of standardized clinical-grade detection techniques for lncRNA biomarkers.

Collaboration between genetic biologists, doctors, delivery professionals, and regulatory experts will be necessary to overcome these complex challenges. Improving delivery methods, expanding lncRNA functional annotation, and assuring safety via thorough preclinical validation must be the main goals of future research. Instead of using a one-size-fits-all methodology, precision medicine is required due to the complex nature of lncRNA biology.

4.6 Future directions

Addressing the gap between molecular discovery and clinical application is crucial for the future of GBM lncRNA research. The thorough functional characterization of lncRNAs throughout the diverse environment of GBM is one of the most urgent needs. High-resolution mapping of lncRNA expression across various cell types, tumor areas, and microenvironmental niches can be accomplished by spatial transcriptomics and single-cell RNA sequencing (scRNA-seq). These technologies can reveal lncRNA-mediated cell-cell contact dynamics, spatiotemporal control, and context-specific activities.

Combining lncRNA expression with genomic, epigenomic, proteomic, and metabolomic profiles to create systems-level models of GBM biology is another crucial avenue for multi-omics data integration. This method can be used to anticipate synergistic interactions with current medications, find new therapeutic targets, and develop lncRNA-centered regulatory networks. High-throughput CRISPR screening can also be used in organoid models or GSCs to choose the most promising lncRNAs for treatment by carefully examining their functional relevance. The development of brain-specific delivery mechanisms for RNA-based medications is critically needed from a therapeutic perspective. BBB-permeable viral vectors, ligand-conjugated exosomes, and targeted nanoparticles are all fascinating platforms that are currently being studied. Another promising area of research is the development of RNA-based combination therapies, in which lncRNA inhibitors are given in conjunction with immunotherapy, radiotherapy, or chemotherapy. To improve the effectiveness of immunotherapy in GBM, lncRNAs that control immunological checkpoints, T cell infiltration, or antigen presentation may be addressed.

Developments in longitudinal patient cohort studies, which track lncRNA biomarkers in connection to treatment response, illness progression, and survival outcomes, are also necessary to enable clinical translation. Validating diagnostic and prognostic utility, improving patient selection standards, and creating biomarker-guided clinical trials will all depend on these kinds of investigations.

To sum up, future studies need to be multifaceted, mechanistic, and translational in nature, combining state-of-the-art technologies with reliable preclinical models and clinical collaborations. Only then may GBM be diagnosed and treated to the greatest extent possible using lncRNAs.

Chapter 5: Conclusion

This review includes results from 389 studies identified through a systematic PRISMA-based approach to thoroughly examine the diverse functions of lncRNAs in the molecular pathogenesis of GBM. The work illustrates how lncRNAs function as oncogenes or tumor suppressors in the progression of GBM based on their genomic origin, subcellular localization, and regulatory mechanisms through thorough categorization and mechanistic analysis. The findings show that lncRNAs are involved in important processes that affect angiogenesis, metabolic adaptability, apoptosis, DNA damage response, proliferation, and most importantly, resistance to TMZ and radiation therapy.

By activating PI3K/AKT, Wnt/β-catenin, and STAT3 signaling, oncogenic lncRNAs like CRNDE, HOTAIR, and LINC00470 promote glioma aggressiveness. They frequently do this by acting as chromatin remodelers or miRNA sponges. On the other hand, by stabilizing tumor suppressor pathways like p53 and PTEN, tumor-suppressive lncRNAs such as MEG3, TUSC7, and CASC2 improve apoptotic signaling and restore chemosensitivity. The conversation also emphasizes how lncRNAs control autophagy, DNA repair, and GSC maintenance to orchestrate therapeutic resistance. Notably, important connections with major oncogenic pathways, including p53, NF-κB, Notch, JAK/STAT, and PI3K/AKT/mTOR, indicate that lncRNAs function as both downstream effectors and upstream integrators within the complex GBM transcripts network.

Despite developments, delivery issues, off-target effects, and tumor heterogeneity continue to limit the translational applicability of lncRNA-based therapies. However, modern techniques like siRNA, antisense oligonucleotides, and CRISPR/Cas9-based editing present encouraging opportunities. Because of their high tissue selectivity and detectability in bodily fluids, many lncRNAs have great promise as biomarkers for diagnosis, prognosis, and treatment classification.

In conclusion, glioma biology and treatment resistance are significantly regulated by lncRNAs. To get over the current treatment obstacles, more research into lncRNA-targeting technologies, biomarker validation, and patient-specific expression profiles will be necessary. To fully realize the potential of lncRNAs in GBM therapy, future research should prioritize clinical translation, customized therapeutic design, and integration of multi-omics data.

References

1. Pinson, H.; Silversmit, G.; Vanhauwaert, D.; Vanschoenbeek, K.; Okito, J.-P.K.; De Vleeschouwer, S.; Boterberg, T.; De Gendt, C. Epidemiology and Survival of Adult-Type Diffuse Glioma in Belgium during the Molecular Era. *Neuro-Oncol.* **2024**, *26*, 191–202, doi:10.1093/neuonc/noad158.
2. Eraky, A.M.; Keles, A.; Goodman, S.L.; Baskaya, M.K. Serum Long Non-Coding RNAs as Potential Noninvasive Biomarkers for Glioblastoma Diagnosis, Prognosis, and Chemoresistance. *J. Integr. Neurosci.* **2022**, *21*, 111, doi:10.31083/j.jin2104111.
3. Xu, C.; Zhao, J.; Song, J.; Xiao, M.; Cui, X.; Xin, L.; Xu, J.; Zhang, Y.; Yi, K.; Hong, B.; et al. lncRNA PRADX Is a Mesenchymal Glioblastoma Biomarker for Cellular Metabolism Targeted Therapy. *Front. Oncol.* **2022**, *12*, 888922, doi:10.3389/fonc.2022.888922.
4. Liang, A.; Zhong, S.; Xi, B.; Zhou, C.; Jiang, X.; Zhu, R.; Yang, Y.; Zhong, L.; Wan, D. High Expression of PYCARD Is an Independent Predictor of Unfavorable Prognosis and Chemotherapy Resistance in Glioma. *Ann. Transl. Med.* **2021**, *9*, 986–986, doi:10.21037/atm-21-2346.
5. Subaiea, G.M.; Syed, R.U.; Afsar, S.; Alhaidan, T.M.S.; Alzammay, S.A.; Alrashidi, A.A.; Alrowaili, S.F.; Alshelaly, D.A.; Alenezi, A.M.S.R.A. Non-Coding RNAs (ncRNAs) and Multidrug Resistance in Glioblastoma: Therapeutic Challenges and Opportunities. *Pathol. - Res. Pract.* **2024**, *253*, 155022, doi:10.1016/j.prp.2023.155022.
6. Chu, L.; Yu, L.; Liu, J.; Song, S.; Yang, H.; Han, F.; Liu, F.; Hu, Y. Long Intergenic Non-Coding LINC00657 Regulates Tumorigenesis of Glioblastoma by Acting as a Molecular Sponge of miR-190a-3p. *Aging* **2019**, *11*, 1456–1470, doi:10.18632/aging.101845.
7. Geng, S.; Tu, S.; Fu, W.; Wang, J.; Bai, Z. LncRNA PITPNA-AS1 Stimulates Cell Proliferation and Suppresses Cell Apoptosis in Glioblastoma via Targeting miR-223-3p/EGFR Axis and Activating PI3K/AKT Signaling Pathway. *Cell Cycle* **2021**, *20*, 1988–1998, doi:10.1080/15384101.2021.1958503.
8. Cheng, M.; Wang, Q.; Chen, L.; Zhao, D.; Tang, J.; Xu, J.; He, Z. LncRNA UCA1/miR-182-5p/MGMT Axis Modulates Glioma Cell Sensitivity to Temozolomide through MGMT-Related DNA Damage Pathways. *Hum. Pathol.* **2022**, *123*, 59–73, doi:10.1016/j.humpath.2022.02.016.
9. Tang, G.; Luo, L.; Zhang, J.; Zhai, D.; Huang, D.; Yin, J.; Zhou, Q.; Zhang, Q.; Zheng, G. lncRNA LINC01057 Promotes Mesenchymal Differentiation by Activating NF-κB Signaling in Glioblastoma. *Cancer Lett.* **2021**, *498*, 152–164, doi:10.1016/j.canlet.2020.10.047.
10. Goenka, A.; Song, X.; Tiek, D.; Iglesia, R.P.; Lu, M.; Zeng, C.; Horbinski, C.; Zhang, W.; Hu, B.; Cheng, S.-Y. Oncogenic Long Noncoding RNA LINC02283 Enhances PDGF Receptor A-Mediated Signaling and Drives Glioblastoma Tumorigenesis. *Neuro-Oncol.* **2023**, *25*, 1592–1604, doi:10.1093/neuonc/noad065.
11. Gong, Z.; Hong, F.; Wang, H.; Zhang, X.; Chen, J. An Eight-mRNA Signature Outperforms the lncRNA-Based Signature in Predicting Prognosis of Patients with Glioblastoma. *BMC Med. Genet.* **2020**, *21*, 56, doi:10.1186/s12881-020-0992-7.
12. Zheng, P.; Zhang, X.; Ren, D.; Zhang, Y. RP11-552D4.1: A Novel M6a-Related LncRNA Associated with Immune Status in Glioblastoma. *Aging* **2022**, *14*, 7348–7363, doi:10.18632/aging.204177.
13. Thakkar, J.P.; Dolecek, T.A.; Horbinski, C.; Ostrom, Q.T.; Lightner, D.D.; Barnholtz-Sloan, J.S.; Villano, J.L. Epidemiologic and Molecular Prognostic Review of Glioblastoma. *Cancer Epidemiol. Biomarkers Prev.* **2014**, *23*, 1985–1996, doi:10.1158/1055-9965.EPI-14-0275.

14. Aldape, K.; Zadeh, G.; Mansouri, S.; Reifenberger, G.; Von Deimling, A. Glioblastoma: Pathology, Molecular Mechanisms and Markers. *Acta Neuropathol. (Berl.)* **2015**, *129*, 829–848, doi:10.1007/s00401-015-1432-1.
15. Amer, A.; Khose, S.; Alhasan, H.; Pokhylevych, H.; Fuller, G.; Chasen, N.; De Groot, J.; Johnson, J.M. Clinical and Survival Characteristics of Primary and Secondary Gliosarcoma Patients. *Clin. Neurol. Neurosurg.* **2022**, *214*, 107146, doi:10.1016/j.clineuro.2022.107146.
16. Hong, B.; Lalk, M.; Wiese, B.; Merten, R.; Heissler, H.E.; Raab, P.; Hartmann, C.; Krauss, J.K. Primary and Secondary Gliosarcoma: Differences in Treatment and Outcome. *Br. J. Neurosurg.* **2024**, *38*, 332–339, doi:10.1080/02688697.2021.1872773.
17. Verhaak, R.G.W.; Hoadley, K.A.; Purdom, E.; Wang, V.; Qi, Y.; Wilkerson, M.D.; Miller, C.R.; Ding, L.; Golub, T.; Mesirov, J.P.; et al. Integrated Genomic Analysis Identifies Clinically Relevant Subtypes of Glioblastoma Characterized by Abnormalities in PDGFRA, IDH1, EGFR, and NF1. *Cancer Cell* **2010**, *17*, 98–110, doi:10.1016/j.ccr.2009.12.020.
18. Wang, Q.; Hu, B.; Hu, X.; Kim, H.; Squatrito, M.; Scarpace, L.; deCarvalho, A.C.; Lyu, S.; Li, P.; Li, Y.; et al. Tumor Evolution of Glioma-Intrinsic Gene Expression Subtypes Associates with Immunological Changes in the Microenvironment. *Cancer Cell* **2017**, *32*, 42-56.e6, doi:10.1016/j.ccell.2017.06.003.
19. Tamimi, A.F.; Juweid, M. Epidemiology and Outcome of Glioblastoma. In *Glioblastoma*; De Vleeschouwer, S., Ed.; Codon Publications: Brisbane (AU), 2017 ISBN 978-0-9944381-2-6.
20. Capper, D.; Reifenberger, G.; French, P.J.; Schweizer, L.; Weller, M.; Touat, M.; Niclou, S.P.; Euskirchen, P.; Haberler, C.; Hegi, M.E.; et al. EANO Guideline on Rational Molecular Testing of Gliomas, Glioneuronal, and Neuronal Tumors in Adults for Targeted Therapy Selection. *Neuro-Oncol.* **2023**, *25*, 813–826, doi:10.1093/neuonc/noad008.
21. Fisher, J.P.; Adamson, D.C. Current FDA-Approved Therapies for High-Grade Malignant Gliomas. *Biomedicines* **2021**, *9*, 324, doi:10.3390/biomedicines9030324.
22. Roh, J.; Im, M.; Kang, J.; Youn, B.; Kim, W. Long Non-Coding RNA in Glioma: Novel Genetic Players in Temozolomide Resistance. *Anim. Cells Syst.* **2023**, *27*, 19–28, doi:10.1080/19768354.2023.2175497.
23. Cardon, T.; Fournier, I.; Salzet, M. Unveiling a Ghost Proteome in the Glioblastoma Non-Coding RNAs. *Front. Cell Dev. Biol.* **2021**, *9*, 703583, doi:10.3389/fcell.2021.703583.
24. Ghaemi, S.; Fekrirad, Z.; Zamani, N.; Rahmani, R.; Arefian, E. Non-Coding RNAs Enhance the Apoptosis Efficacy of Therapeutic Agents Used for the Treatment of Glioblastoma Multiform. *J. Drug Target.* **2022**, *30*, 589–602, doi:10.1080/1061186X.2022.2047191.
25. Mahinfar, P.; Baradaran, B.; Davoudian, S.; Vahidian, F.; Cho, W.C.-S.; Mansoori, B. Long Non-Coding RNAs in Multidrug Resistance of Glioblastoma. *Genes* **2021**, *12*, 455, doi:10.3390/genes12030455.
26. Yan, Y.; Xu, Z.; Li, Z.; Sun, L.; Gong, Z. An Insight into the Increasing Role of LncRNAs in the Pathogenesis of Gliomas. *Front. Mol. Neurosci.* **2017**, *10*, doi:10.3389/fnmol.2017.00053.
27. Kopp, F.; Mendell, J.T. Functional Classification and Experimental Dissection of Long Noncoding RNAs. *Cell* **2018**, *172*, 393–407, doi:10.1016/j.cell.2018.01.011.
28. Tong, C.; Yin, Y. Localization of RNAs in the Nucleus: *Cis* - and *Trans* - Regulation. *RNA Biol.* **2021**, *18*, 2073–2086, doi:10.1080/15476286.2021.1894025.
29. Kuang, S.; Pollard, K.S. Exploring the Roles of RNAs in Chromatin Architecture Using Deep Learning. *Nat. Commun.* **2024**, *15*, 6373, doi:10.1038/s41467-024-50573-w.

30. Hashemi, M.; Moosavi, M.S.; Abed, H.M.; Dehghani, M.; Aalipour, M.; Heydari, E.A.; Behroozaghdam, M.; Entezari, M.; Salimimoghadam, S.; Gunduz, E.S.; et al. Long Non-Coding RNA (lncRNA) H19 in Human Cancer: From Proliferation and Metastasis to Therapy. *Pharmacol. Res.* **2022**, *184*, 106418, doi:10.1016/j.phrs.2022.106418.
31. Yan, H.; Bu, P. Non-Coding RNA in Cancer. *Essays Biochem.* **2021**, *65*, 625–639, doi:10.1042/EBC20200032.
32. Lou, W.; Ding, B.; Fu, P. Pseudogene-Derived lncRNAs and Their miRNA Sponging Mechanism in Human Cancer. *Front. Cell Dev. Biol.* **2020**, *8*, 85, doi:10.3389/fcell.2020.00085.
33. Choi, S.-W.; Kim, H.-W.; Nam, J.-W. The Small Peptide World in Long Noncoding RNAs. *Brief. Bioinform.* **2019**, *20*, 1853–1864, doi:10.1093/bib/bby055.
34. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. *BMJ* **2021**, n71, doi:10.1136/bmj.n71.
35. DeOcesano-Pereira, C.; Machado, R.A.C.; Chudzinski-Tavassi, A.M.; Sogayar, M.C. Emerging Roles and Potential Applications of Non-Coding RNAs in Glioblastoma. *Int. J. Mol. Sci.* **2020**, *21*, 2611, doi:10.3390/ijms21072611.
36. Stackhouse, C.T.; Gillespie, G.Y.; Willey, C.D. Exploring the Roles of lncRNAs in GBM Pathophysiology and Their Therapeutic Potential. *Cells* **2020**, *9*, 2369, doi:10.3390/cells9112369.
37. Shahmir, S.; Zahmatkesh, N.; Mirzaahmadi, S.; Asaadi Tehrani, G. LncRNA CASC2 Inhibits Progression of Glioblastoma by Regulating the Expression of AKT in T98G Cell Line, Treated by TMZ and Thiosemicarbazone Complex. *Asian Pac. J. Cancer Prev.* **2023**, *24*, 1553–1560, doi:10.31557/APJCP.2023.24.5.1553.
38. Zhao, Z.; Liu, M.; Long, W.; Yuan, J.; Li, H.; Zhang, C.; Tang, G.; Jiang, W.; Yuan, X.; Wu, M.; et al. Knockdown lncRNA CRNDE Enhances Temozolomide Chemosensitivity by Regulating Autophagy in Glioblastoma. *Cancer Cell Int.* **2021**, *21*, 456, doi:10.1186/s12935-021-02153-x.
39. Xie, Y.; Cheng, Y. LINC01198 Facilitates Gliomagenesis through Activating PI3K/AKT Pathway. *RNA Biol.* **2020**, *17*, 1040–1052, doi:10.1080/15476286.2020.1755112.
40. Ni, H.; Wang, K.; Xie, P.; Zuo, J.; Liu, W.; Liu, C. LncRNA SAMMSON Knockdown Inhibits the Malignancy of Glioblastoma Cells by Inactivation of the PI3K/Akt Pathway. *Cell. Mol. Neurobiol.* **2021**, *41*, 79–90, doi:10.1007/s10571-020-00833-2.
41. Liu, L.; Liu, Z.; Liu, Q.; Wu, W.; Lin, P.; Liu, X.; Zhang, Y.; Wang, D.; Prager, B.C.; Gimple, R.C.; et al. LncRNA INHEG Promotes Glioma Stem Cell Maintenance and Tumorigenicity through Regulating rRNA 2'-O-Methylation. *Nat. Commun.* **2023**, *14*, 7526, doi:10.1038/s41467-023-43113-5.
42. Ma, B.; Yuan, Z.; Zhang, L.; Lv, P.; Yang, T.; Gao, J.; Pan, N.; Wu, Q.; Lou, J.; Han, C.; et al. Long Non-Coding RNA AC023115.3 Suppresses Chemoresistance of Glioblastoma by Reducing Autophagy. *Biochim. Biophys. Acta BBA - Mol. Cell Res.* **2017**, *1864*, 1393–1404, doi:10.1016/j.bbamcr.2017.05.008.
43. Kovalenko, T.F.; Yadav, B.; Anufrieva, K.S.; Rubtsov, Y.P.; Zatsepin, T.S.; Shcherbinina, E.Y.; Solyus, E.M.; Staroverov, D.B.; Larionova, T.D.; Latyshev, Y.A.; et al. Functions of Long Non-Coding RNA ROR in Patient-Derived Glioblastoma Cells. *Biochimie* **2022**, *200*, 131–139, doi:10.1016/j.biochi.2022.05.015.

44. Wang, R.; Li, Q.; Chu, X.; Li, N.; Liang, H.; He, F. Nanoparticles (NPs)-Meditated Si-lncRNA NONHSAT159592.1 Inhibits Glioblastoma Progression and Invasion through Targeting the ITGA3/FAK/PI3K/AKT Pathway. *Metab. Brain Dis.* **2024**, *40*, 31, doi:10.1007/s11011-024-01471-z.
45. Liu, C.; Zhang, Y.; She, X.; Fan, L.; Li, P.; Feng, J.; Fu, H.; Liu, Q.; Liu, Q.; Zhao, C.; et al. A Cytoplasmic Long Noncoding RNA LINC00470 as a New AKT Activator to Mediate Glioblastoma Cell Autophagy. *J. Hematol. Oncol.J Hematol Oncol* **2018**, *11*, 77, doi:10.1186/s13045-018-0619-z.
46. Wu, P.; Cai, J.; Chen, Q.; Han, B.; Meng, X.; Li, Y.; Li, Z.; Wang, R.; Lin, L.; Duan, C.; et al. Lnc-TALC Promotes O6-Methylguanine-DNA Methyltransferase Expression via Regulating the c-Met Pathway by Competitively Binding with miR-20b-3p. *Nat. Commun.* **2019**, *10*, 2045, doi:10.1038/s41467-019-10025-2.
47. Li, X.D.; Wang, M.J.; Zheng, J.L.; Wu, Y.H.; Wang, X.; Jiang, X.B. Long Noncoding RNA Just Proximal to X-inactive Specific Transcript Facilitates Aerobic Glycolysis and Temozolomide Chemoresistance by Promoting Stability of PDK1 mRNA in an m6A-dependent Manner in Glioblastoma Multiforme Cells. *Cancer Sci.* **2021**, *112*, 4543–4552, doi:10.1111/cas.15072.
48. Li, X.D.; Wang, M.J.; Zheng, J.L.; Wu, Y.H.; Wang, X.; Jiang, X.B. Long Noncoding RNA Just Proximal to X-inactive Specific Transcript Facilitates Aerobic Glycolysis and Temozolomide Chemoresistance by Promoting Stability of PDK1 mRNA in an m6A-dependent Manner in Glioblastoma Multiforme Cells. *Cancer Sci.* **2021**, *112*, 4543–4552, doi:10.1111/cas.15072.
49. Ye, B.; Shi, J.; Kang, H.; Oyebamiji, O.; Hill, D.; Yu, H.; Ness, S.; Ye, F.; Ping, J.; He, J.; et al. Advancing Pan-Cancer Gene Expression Survial Analysis by Inclusion of Non-Coding RNA. *RNA Biol.* **2020**, *17*, 1666–1673, doi:10.1080/15476286.2019.1679585.
50. Li, H.; Li, H.; Hao, Y.; Jiao, Y.; Li, Z.; Yue, H.; Xu, Z.; Wang, S.; Cao, Y.; Zhao, J. Differential Long Non-Coding RNA and mRNA Expression in Differentiated Human Glioblastoma Stem Cells. *Mol. Med. Rep.* **2016**, *14*, 2067–2076, doi:10.3892/mmr.2016.5505.
51. Yang, Y.; Wang, F.; Teng, H.; Zhang, C.; Zhang, Y.; Chen, P.; Li, Q.; Kan, X.; Chen, Z.; Wang, Z.; et al. Integrative Analysis of Multi-Omics Data Reveals a Pseudouridine-Related lncRNA Signature for Prediction of Glioma Prognosis and Chemoradiotherapy Sensitivity. *Comput. Biol. Med.* **2023**, *166*, 107428, doi:10.1016/j.compbiomed.2023.107428.
52. Niu, X.; Sun, J.; Meng, L.; Fang, T.; Zhang, T.; Jiang, J.; Li, H. A Five-lncRNAs Signature-Derived Risk Score Based on TCGA and CGGA for Glioblastoma: Potential Prospects for Treatment Evaluation and Prognostic Prediction. *Front. Oncol.* **2020**, *10*, 590352, doi:10.3389/fonc.2020.590352.
53. Mazor, G.; Levin, L.; Picard, D.; Ahmadov, U.; Carén, H.; Borkhardt, A.; Reifenberger, G.; Leprivier, G.; Remke, M.; Rotblat, B. The lncRNA TP73-AS1 Is Linked to Aggressiveness in Glioblastoma and Promotes Temozolomide Resistance in Glioblastoma Cancer Stem Cells. *Cell Death Dis.* **2019**, *10*, 246, doi:10.1038/s41419-019-1477-5.
54. Toraih, E.A.; El-Wazir, A.; Hussein, M.H.; Khashana, M.S.; Matter, A.; Fawzy, M.S.; Hosny, S. Expression of Long Intergenic Non-Coding RNA, Regulator of Reprogramming, and Its Prognostic Value in Patients with Glioblastoma. *Int. J. Biol. Markers* **2019**, *34*, 69–79, doi:10.1177/1724600818814459.

55. Zichittella, C.; Loria, M.; Celesia, A.; Di Liberto, D.; Corrado, C.; Alessandro, R.; Emanuele, S.; Conigliaro, A. Long Non-Coding RNA H19 Enhances the pro-Apoptotic Activity of ITF2357 (a Histone Deacetylase Inhibitor) in Colorectal Cancer Cells. *Front. Pharmacol.* **2023**, *14*, 1275833, doi:10.3389/fphar.2023.1275833.
56. Wang, W.-A.; Lai, L.-C.; Tsai, M.-H.; Lu, T.-P.; Chuang, E.Y. Development of a Prediction Model for Radiosensitivity Using the Expression Values of Genes and Long Non-Coding RNAs. *Oncotarget* **2016**, *7*, 26739–26750, doi:10.18632/oncotarget.8496.
57. Zhang, H.; Wang, J.; Xun, W.; Wang, J.; Song, W.; Wang, X. Long Non-Coding RNA PTCSC3 Inhibits Human Oral Cancer Cell Proliferation by Inducing Apoptosis and Autophagy. *Arch. Med. Sci.* **2021**, *17*, 492–499, doi:10.5114/aoms.2020.96409.
58. Cheng, L.; Yuan, M.; Li, S.; Lian, Z.; Chen, J.; Lin, W.; Zhang, J.; Zhong, S. Identification of an IFN-β-Associated Gene Signature for the Prediction of Overall Survival among Glioblastoma Patients. *Ann. Transl. Med.* **2021**, *9*, 925–925, doi:10.21037/atm-21-1986.
59. Ghafouri-Fard, S.; Safarzadeh, A.; Mahmud Hussen, B.; Akhavan-Bahabadi, M.; Taheri, M.; Sharifi, G. In Silico Characterization of Competing Endogenous RNA Network in Glioblastoma Multiforme with a Systems Biology Approach. *Front. Oncol.* **2022**, *12*, 1024567, doi:10.3389/fonc.2022.1024567.
60. Haghighi, S.S.; Ghaderian, S.M.H.; Rakhshan, A.; Motamed, N. Evaluation of the Expression of miRNAs, LncRNAs, and Their Target Gene, Caspase 3 in Glioblastoma Multiform: A Case–Control Study. *Mol. Biotechnol.* **2023**, *65*, 1444–1452, doi:10.1007/s12033-022-00632-8.
61. Jiang, L.-Y.; Wang, G.-H.; Xu, J.-J.; Li, X.-L.; Lin, X.-Y.; Fang, X.; Zhang, H.-X.; Feng, M.; Jiang, C.-M. CREB-Induced LINC00473 Promotes Chemoresistance to TMZ in Glioblastoma by Regulating O6-Methylguanine-DNA-Methyltransferase Expression via CEBPα Binding. *Neuropharmacology* **2024**, *243*, 109790, doi:10.1016/j.neuropharm.2023.109790.
62. Lan, T.; Quan, W.; Yu, D.-H.; Chen, X.; Wang, Z.-F.; Li, Z.-Q. High Expression of LncRNA HOTAIR Is a Risk Factor for Temozolomide Resistance in Glioblastoma via Activation of the miR-214/β-Catenin/MGMT Pathway. *Sci. Rep.* **2024**, *14*, 26224, doi:10.1038/s41598-024-77348-z.
63. Liao, X.; Zhang, S.; Li, X.; Qian, W.; Li, M.; Chen, S.; Wu, X.; Yu, X.; Li, Z.; Tang, M.; et al. Dynamic Structural Remodeling of LINC01956 Enhances Temozolomide Resistance in *MGMT* -Methylated Glioblastoma. *Sci. Transl. Med.* **2024**, *16*, eado1573, doi:10.1126/scitranslmed.ado1573.
64. Cao, Y.; Wang, P.; Ning, S.; Xiao, W.; Xiao, B.; Li, X. Identification of Prognostic Biomarkers in Glioblastoma Using a Long Non-Coding RNA-Mediated, Competitive Endogenous RNA Network. *Oncotarget* **2106**, *7*, 41737–41747, doi:10.18632/oncotarget.9569.
65. Luo, W.; Li, X.; Song, Z.; Zhu, X.; Zhao, S. Long Non-Coding RNA AGAP2-AS1 Exerts Oncogenic Properties in Glioblastoma by Epigenetically Silencing TFPI2 through EZH2 and LSD1. *Aging* **2019**, *11*, 3811–3823, doi:10.18632/aging.102018.
66. Xu, N.; Liu, B.; Lian, C.; Doycheva, D.M.; Fu, Z.; Liu, Y.; Zhou, J.; He, Z.; Yang, Z.; Huang, Q.; et al. Long Noncoding RNA AC003092.1 Promotes Temozolomide Chemosensitivity through miR-195/TFPI-2 Signaling Modulation in Glioblastoma. *Cell Death Dis.* **2018**, *9*, 1139, doi:10.1038/s41419-018-1183-8.

67. Guo, X.-Y.; Zhong, S.; Wang, Z.-N.; Xie, T.; Duan, H.; Zhang, J.-Y.; Zhang, G.-H.; Liang, L.; Cui, R.; Hu, H.-R.; et al. Immunogenomic Profiling Demonstrate AC003092.1 as an Immune-Related eRNA in Glioblastoma Multiforme. *Front. Genet.* **2021**, *12*, 633812, doi:10.3389/fgene.2021.633812.
68. Wang, J.; Li, B.; Wang, C.; Luo, Y.; Zhao, M.; Chen, P. Long Noncoding RNA FOXD2-AS1 Promotes Glioma Cell Cycle Progression and Proliferation through the FOXD2-AS1/miR-31/CDK1 Pathway. *J. Cell. Biochem.* **2019**, *120*, 19784–19795, doi:10.1002/jcb.29284.
69. Ling, Z.; Zhang, J.; Liu, Q. Oncogenic Forkhead Box D3 Antisense RNA 1 Promotes Cell Survival and Confers Temozolomide Resistance in Glioblastoma Cells through the miR-128-3p/WEE1 G2 Checkpoint Kinase Axis. *Bioengineered* **2022**, *13*, 6012–6023, doi:10.1080/21655979.2022.2042133.
70. Knockdown of Long Non-Coding RNA VIM-AS1 Inhibits Glioma Cell Proliferation and Migration, and Increases the Cell Apoptosis via Modulation of WEE1 Targeted by miR-105-5p.
71. Li, Z.; Zhang, J.; Zheng, H.; Li, C.; Xiong, J.; Wang, W.; Bao, H.; Jin, H.; Liang, P. Modulating lncRNA SNHG15/CDK6/miR-627 Circuit by Palbociclib, Overcomes Temozolomide Resistance and Reduces M2-Polarization of Glioma Associated Microglia in Glioblastoma Multiforme. *J. Exp. Clin. Cancer Res.* **2019**, *38*, 380, doi:10.1186/s13046-019-1371-0.
72. Liu, A.; Zhao, H.; Sun, B.; Han, X.; Zhou, D.; Cui, Z.; Ma, X.; Zhang, J.; Yuan, L. A Predictive Analysis Approach for Paediatric and Adult High-Grade Glioma: miRNAs and Network Insight. *Ann. Transl. Med.* **2020**, *8*, 242–242, doi:10.21037/atm.2020.01.12.
73. Fang, K.; Liu, P.; Dong, S.; Guo, Y.; Cui, X.; Zhu, X.; Li, X.; Jiang, L.; Liu, T.; Wu, Y. Magnetofection Based on Superparamagnetic Iron Oxide Nanoparticle-Mediated Low lncRNA HOTAIR Expression Decreases the Proliferation and Invasion of Glioma Stem Cells. *Int. J. Oncol.* **2016**, *49*, 509–518, doi:10.3892/ijo.2016.3571.
74. Zhao, J.; Jin, W.; Yi, K.; Wang, Q.; Zhou, J.; Tan, Y.; Xu, C.; Xiao, M.; Hong, B.; Xu, F.; et al. Combination LSD1 and HOTAIR-EZH2 Inhibition Disrupts Cell Cycle Processes and Induces Apoptosis in Glioblastoma Cells. *Pharmacol. Res.* **2021**, *171*, 105764, doi:10.1016/j.phrs.2021.105764.
75. Wu, A.-C.; Yang, W.-B.; Chang, K.-Y.; Lee, J.-S.; Liou, J.-P.; Su, R.-Y.; Cheng, S.M.; Hwang, D.-Y.; Kikkawa, U.; Hsu, T.-I.; et al. HDAC6 Involves in Regulating the lncRNA-microRNA-mRNA Network to Promote the Proliferation of Glioblastoma Cells. *J. Exp. Clin. Cancer Res.* **2022**, *41*, 47, doi:10.1186/s13046-022-02257-w.
76. Paul, Y.; Thomas, S.; Patil, V.; Kumar, N.; Mondal, B.; Hegde, A.S.; Arivazhagan, A.; Santosh, V.; Mahalingam, K.; Somasundaram, K. Genetic Landscape of Long Noncoding RNA (lncRNAs) in Glioblastoma: Identification of Complex lncRNA Regulatory Networks and Clinically Relevant lncRNAs in Glioblastoma. *Oncotarget* **2018**, *9*, 29548–29564, doi:10.18632/oncotarget.25434.
77. Huang, W.; Liu, J.; Yan, J.; Huang, Z.; Zhang, X.; Mao, Y.; Huang, X. LncRNA LINC00470 Promotes Proliferation through Association with NF45/NF90 Complex in Hepatocellular Carcinoma. *Hum. Cell* **2020**, *33*, 131–139, doi:10.1007/s13577-019-00288-8.
78. Saha, S.; Zhang, Y.; Wilson, B.; Abounader, R.; Dutta, A. The Tumor-Suppressive Long Noncoding RNA DRAIC Inhibits Protein Translation and Induces Autophagy by Activating AMPK. *J. Cell Sci.* **2021**, *134*, jcs259306, doi:10.1242/jcs.259306.

79. Han, N.; Yang, L.; Zhang, X.; Zhou, Y.; Chen, R.; Yu, Y.; Dong, Z.; Zhang, M. LncRNA MATN1-AS1 Prevents Glioblastoma Cell from Proliferation and Invasion via RELA Regulation and MAPK Signaling Pathway. *Ann. Transl. Med.* **2019**, *7*, 784–784, doi:10.21037/atm.2019.11.36.
80. Xiao, F.; Zhu, H.; Xiong, Y.; Guo, Y.; Zhang, Z.; Zeng, J.; Xiao, Y.; Liao, B.; Shang, X.; Zhao, S.; et al. Positive Feedback Loop of C-Myc/XTP6/NDH2/NF-κB to Promote Malignant Progression in Glioblastoma. *J. Exp. Clin. Cancer Res.* **2024**, *43*, 187, doi:10.1186/s13046-024-03109-5.
81. Toker, J.; Iorgulescu, J.B.; Ling, A.L.; Villa, G.R.; Gadet, J.A.M.A.; Parida, L.; Getz, G.; Wu, C.J.; Reardon, D.A.; Chiocca, E.A.; et al. Clinical Importance of the lncRNA *NEAT1* in Cancer Patients Treated with Immune Checkpoint Inhibitors. *Clin. Cancer Res.* **2023**, *29*, 2226–2238, doi:10.1158/1078-0432.CCR-22-3714.
82. Jafari, S.; Saboori, M.; Ghasemi, S. LINC01366 and LINC01433 in Glioblastoma Multiforme: A Potential Role at the Intersection of Inflammation and Angiogenesis. *Int. J. Mol. Cell. Med.* **2024**, *13*, doi:10.22088/IJMCM.BUMS.13.2.160.
83. Wang, H.; Li, L.; Yin, L. Silencing LncRNA LOXL1-AS1 Attenuates Mesenchymal Characteristics of Glioblastoma via NF-κB Pathway. *Biochem. Biophys. Res. Commun.* **2018**, *500*, 518–524, doi:10.1016/j.bbrc.2018.04.133.
84. Liu, D.; Wan, Y.; Qu, N.; Fu, Q.; Liang, C.; Zeng, L.; Yang, Y. LncRNA-FAM66C Was Identified as a Key Regulator for Modulating Tumor Microenvironment and Hypoxia-Related Pathways in Glioblastoma. *Front. Public Health* **2022**, *10*, 898270, doi:10.3389/fpubh.2022.898270.
85. Song, C.; Zhu, L.; Gu, J.; Wang, T.; Shi, L.; Li, C.; Chen, L.; Xie, S.; Lu, Y. A Necroptosis-Related lncRNA Signature Was Identified to Predict the Prognosis and Immune Microenvironment of IDH-Wild-Type GBM. *Front. Oncol.* **2022**, *12*, 1024208, doi:10.3389/fonc.2022.1024208.
86. Xu, D.; Cao, M.; Wang, B.; Bi, X.; Zhang, H.; Wu, D.; Zhang, C.; Xu, J.; Xu, Z.; Zheng, D.; et al. Epigenetically Regulated lncRNAs Dissect the Intratumoural Heterogeneity and Facilitate Immune Evasion of Glioblastomas. *Theranostics* **2023**, *13*, 1490–1505, doi:10.7150/thno.79874.
87. Fan, Y.; Gao, Z.; Xu, J.; Wang, H.; Guo, Q.; Li, B.; Li, M.; Xu, H.; Qi, Y.; Zhao, S.; et al. SPI1-Mediated MIR222HG Transcription Promotes Proneural-to-Mesenchymal Transition of Glioma Stem Cells and Immunosuppressive Polarization of Macrophages. *Theranostics* **2023**, *13*, 3310–3329, doi:10.7150/thno.82590.
88. Huang, L.; Wang, Z.; Liao, C.; Zhao, Z.; Gao, H.; Huang, R.; Chen, J.; Wu, F.; Zeng, F.; Zhang, Y.; et al. PVT1 Promotes Proliferation and Macrophage Immunosuppressive Polarization through STAT1 and CX3CL1 Regulation in Glioblastoma Multiforme. *CNS Neurosci. Ther.* **2024**, *30*, e14566, doi:10.1111/cns.14566.
89. Zang, J.; Zheng, M.-H.; Cao, X.-L.; Zhang, Y.-Z.; Zhang, Y.-F.; Gao, X.-Y.; Cao, Y.; Shi, M.; Han, H.; Liang, L. Adenovirus Infection Promotes the Formation of Glioma Stem Cells from Glioblastoma Cells through the TLR9/NEAT1/STAT3 Pathway. *Cell Commun. Signal.* **2020**, *18*, 135, doi:10.1186/s12964-020-00598-7.
90. Binder, S.; Zipfel, I.; Müller, C.; Wiedemann, K.; Schimmelpfennig, C.; Pfeifer, G.; Reiche, K.; Hauschildt, S.; Lehmann, J.; Köhl, U.; et al. The Noncoding RNA LINC00152 Conveys Contradicting Effects in Different Glioblastoma Cells. *Sci. Rep.* **2021**, *11*, 18499, doi:10.1038/s41598-021-97533-8.

91. Yuan, S.; Yan, Q.; Zhao, Z.; Zhang, J.; Zhang, H.; Yin, H.; Yuan, Z. STAT3-Mediated Upregulation of LINC00520 Contributed to Temozolomide Chemoresistance in Glioblastoma by Interacting with RNA-Binding Protein LIN28B. *Cancer Cell Int.* **2022**, *22*, 248, doi:10.1186/s12935-022-02659-y.
92. Hu, Y.; Ye, S.; Li, Q.; Yin, T.; Wu, J.; He, J. Quantitative Proteomics Analysis Indicates That Upregulation of lncRNA HULC Promotes Pathogenesis of Glioblastoma Cells. *OncoTargets Ther.* **2020**, *Volume 13*, 5927–5938, doi:10.2147/OTT.S252915.
93. Ji, J.; Zhao, L.; Zhao, X.; Li, Q.; An, Y.; Li, L.; Li, D. Genome-wide DNA Methylation Regulation Analysis of Long Non-coding RNAs in Glioblastoma. *Int. J. Mol. Med.* **2020**, doi:10.3892/ijmm.2020.4579.
94. Stackhouse, C.T.; Anderson, J.C.; Yue, Z.; Nguyen, T.; Eustace, N.J.; Langford, C.P.; Wang, J.; Rowland, J.R.; Xing, C.; Mikhail, F.M.; et al. An in Vivo Model of Glioblastoma Radiation Resistance Identifies Long Noncoding RNAs and Targetable Kinases. *JCI Insight* **2022**, *7*, e148717, doi:10.1172/jci.insight.148717.
95. Chen, L.; Gong, X.; Huang, M. YY1-Activated Long Noncoding RNA SNHG5 Promotes Glioblastoma Cell Proliferation Through P38/MAPK Signaling Pathway. *Cancer Biother. Radiopharm.* **2019**, *34*, 589–596, doi:10.1089/cbr.2019.2779.
96. Li, L.; Li, Z.; Meng, X.; Wang, X.; Song, D.; Liu, Y.; Xu, T.; Qin, J.; Sun, N.; Tian, K.; et al. Histone Lactylation-Derived LINC01127 Promotes the Self-Renewal of Glioblastoma Stem Cells via the Cis-Regulating the MAP4K4 to Activate JNK Pathway. *Cancer Lett.* **2023**, *579*, 216467, doi:10.1016/j.canlet.2023.216467.
97. Liu, R.; Gao, Z.; Li, Q.; Fu, Q.; Han, D.; Wang, J.; Li, J.; Guo, Y.; Shi, Y. Integrated Analysis of ceRNA Network to Reveal Potential Prognostic Biomarkers for Glioblastoma. *Front. Genet.* **2022**, *12*, 803257, doi:10.3389/fgene.2021.803257.
98. Tang, C.; Wang, Y.; Zhang, L.; Wang, J.; Wang, W.; Han, X.; Mu, C.; Gao, D. Identification of Novel LncRNA Targeting Smad2/PKCα Signal Pathway to Negatively Regulate Malignant Progression of Glioblastoma. *J. Cell. Physiol.* **2020**, *235*, 3835–3848, doi:10.1002/jcp.29278.
99. Krusnauskas, R.; Stakaitis, R.; Steponaitis, G.; Almstrup, K.; Vaitkiene, P. Identification and Comparison of m6A Modifications in Glioblastoma Non-Coding RNAs with MeRIP-Seq and Nanopore dRNA-Seq. *Epigenetics* **2023**, *18*, 2163365, doi:10.1080/15592294.2022.2163365.
100. Xie, P.; Yan, H.; Gao, Y.; Li, X.; Zhou, D.-B.; Liu, Z.-Q. Construction of m6A-Related lncRNA Prognostic Signature Model and Immunomodulatory Effect in Glioblastoma Multiforme. *Front. Oncol.* **2022**, *12*, 920926, doi:10.3389/fonc.2022.920926.
101. Du, B.; Zhang, Z.; Jia, L.; Zhang, H.; Zhang, S.; Wang, H.; Cheng, Z. Micropeptide AF127577.4-ORF Hidden in a lncRNA Diminishes Glioblastoma Cell Proliferation via the Modulation of ERK2/METTL3 Interaction. *Sci. Rep.* **2024**, *14*, 12090, doi:10.1038/s41598-024-62710-y.
102. Wu, L.; Zhu, X.; Song, Z.; Guo, M.; Liang, J.; Yan, D. FGD5-AS1 Facilitates Glioblastoma Progression by Activation of Wnt/β-Catenin Signaling via Regulating miR-129-5p/HNRNPK Axis. *Life Sci.* **2020**, *256*, 117998, doi:10.1016/j.lfs.2020.117998.
103. Yadav, B.; Yadav, P.; Yadav, S.; Pandey, A.K. Role of Long Noncoding RNAs in the Regulation of Alternative Splicing in Glioblastoma. *Drug Discov. Today* **2024**, *29*, 104140, doi:10.1016/j.drudis.2024.104140.

104. Gao, W.-Z.; Guo, L.-M.; Xu, T.-Q.; Yin, Y.-H.; Jia, F. Identification of a Multidimensional Transcriptome Signature for Survival Prediction of Postoperative Glioblastoma Multiforme Patients. *J. Transl. Med.* **2018**, *16*, 368, doi:10.1186/s12967-018-1744-8.
105. Xiao, Y.; Zhu, Z.; Li, J.; Yao, J.; Jiang, H.; Ran, R.; Li, X.; Li, Z. Expression and Prognostic Value of Long Non-Coding RNA H19 in Glioma via Integrated Bioinformatics Analyses. *Aging* **2020**, *12*, 3407–3430, doi:10.18632/aging.102819.
106. Zhang, K.; Sun, X.; Zhou, X.; Han, L.; Chen, L.; Shi, Z.; Zhang, A.; Ye, M.; Wang, Q.; Liu, C.; et al. Long Non-Coding RNA HOTAIR Promotes Glioblastoma Cell Cycle Progression in an EZH2 Dependent Manner. *Oncotarget* **2015**, *6*, 537–546, doi:10.18632/oncotarget.2681.
107. Janaki Ramaiah, M.; Divyapriya, K.; Kartik Kumar, S.; Rajesh, Y.B.R.D. Drug-Induced Modifications and Modulations of microRNAs and Long Non-Coding RNAs for Future Therapy against Glioblastoma Multiforme. *Gene* **2020**, *723*, 144126, doi:10.1016/j.gene.2019.144126.
108. Cai, X.; Qian, M.; Zhang, K.; Li, Y.; Chang, B.; Chen, M. Profiling and Bioinformatics Analyses of Hypoxia-Induced Differential Expression of Long Non-Coding RNA in Glioblastoma Multiforme Cells. *Biochem. Genet.* **2024**, *62*, 3052–3070, doi:10.1007/s10528-023-10597-1.
109. Zhang, Y.; Hudson, K.; Abounader, R. Unraveling the Hypoxic Puzzle: LncRNA LUCAT1 Drives Glioblastoma in Cooperation with HIF1α. *Neuro-Oncol.* **2024**, *26*, 1402–1404, doi:10.1093/neuonc/noae096.
110. Yao, Z.; Zhang, Q.; Guo, F.; Guo, S.; Yang, B.; Liu, B.; Li, P.; Li, J.; Guan, S.; Liu, X. Long Noncoding RNA PCED1B-AS1 Promotes the Warburg Effect and Tumorigenesis by Upregulating HIF-1α in Glioblastoma. *Cell Transplant.* **2020**, *29*, 096368972090677, doi:10.1177/0963689720906777.
111. Wang, S.; Guo, X.; Lv, W.; Li, Y.; Zhang, L.; Dong, C.; Zhang, J.; Cheng, G. LncRNA RPSAP52 Upregulates TGF-Β1 to Increase Cancer Cell Stemness and Predict Postoperative Survival in Glioblastoma. *Cancer Manag. Res.* **2020**, *Volume 12*, 2541–2547, doi:10.2147/CMAR.S227496.
112. Lin, J.; Lin, N.; Zhao, W. Identification and Validation of a Six-lncRNA Prognostic Signature with Its ceRNA Networks and Candidate Drugs in Lower-Grade Gliomas. *Genomics* **2020**, *112*, 2990–3002, doi:10.1016/j.ygeno.2020.05.016.
113. Chen, Q.; Cai, J.; Wang, Q.; Wang, Y.; Liu, M.; Yang, J.; Zhou, J.; Kang, C.; Li, M.; Jiang, C. Long Noncoding RNA *NEAT1* , Regulated by the EGFR Pathway, Contributes to Glioblastoma Progression Through the WNT/ **β** -Catenin Pathway by Scaffolding EZH2. *Clin. Cancer Res.* **2018**, *24*, 684–695, doi:10.1158/1078-0432.CCR-17-0605.
114. Malakootian, M.; Mirzadeh Azad, F.; Fouani, Y.; Taheri Bajgan, E.; Saberi, H.; Mowla, S.J. Anti-Differentiation Non-Coding RNA, ANCR, Is Differentially Expressed in Different Types of Brain Tumors. *J. Neurooncol.* **2018**, *138*, 261–270, doi:10.1007/s11060-018-2809-5.
115. Yang, E.; Hong, B.; Wang, Y.; Wang, Q.; Zhao, J.; Cui, X.; Wu, Y.; Yang, S.; Su, D.; Liu, X.; et al. EPIC-0628 Abrogates HOTAIR/EZH2 Interaction and Enhances the Temozolomide Efficacy via Promoting ATF3 Expression and Inhibiting DNA Damage Repair in Glioblastoma. *Cancer Lett.* **2024**, *588*, 216812, doi:10.1016/j.canlet.2024.216812.

116. Xie, H.; Shi, S.; Chen, Q.; Chen, Z. LncRNA TRG-AS1 Promotes Glioblastoma Cell Proliferation by Competitively Binding with miR-877-5p to Regulate SUZ12 Expression. *Pathol. - Res. Pract.* **2019**, *215*, 152476, doi:10.1016/j.prp.2019.152476.
117. Kraus, T.F.J.; Greiner, A.; Guibourt, V.; Lisec, K.; Kretzschmar, H.A. Identification of Stably Expressed lncRNAs as Valid Endogenous Controls for Profiling of Human Glioma. *J. Cancer* **2015**, *6*, 111–119, doi:10.7150/jca.10867.
118. Lin, L.; Lin, D.; Jin, L.; Wang, J.; Lin, Z.; Zhang, S.; Lin, G. LncRNA HOXA-AS2 Promotes Temozolomide Resistance in Glioblastoma by Regulated miR-302a-3p/IGF1 Axis. *Genet. Res.* **2022**, *2022*, 1–8, doi:10.1155/2022/3941952.
119. Le Boiteux, E.; Guichet, P.-O.; Masliantsev, K.; Montibus, B.; Vaurs-Barriere, C.; Gonthier-Gueret, C.; Chautard, E.; Verrelle, P.; Karayan-Tapon, L.; Fogli, A.; et al. The Long Non-Coding RNA HOXA-AS2 Promotes Proliferation of Glioma Stem Cells and Modulates Their Inflammation Pathway Mainly through Post-Transcriptional Regulation. *Int. J. Mol. Sci.* **2022**, *23*, 4743, doi:10.3390/ijms23094743.
120. Ho, K.; Shih, C.; Liu, A.; Chen, K. Hypoxia-inducible lncRNA MIR210HG Interacting with OCT1 Is Involved in Glioblastoma Multiforme Malignancy. *Cancer Sci.* **2022**, *113*, 540–552, doi:10.1111/cas.15240.
121. He, Z.; You, C.; Zhao, D. Long Non-Coding RNA UCA1/miR-182/PFKFB2 Axis Modulates Glioblastoma-Associated Stromal Cells-Mediated Glycolysis and Invasion of Glioma Cells. *Biochem. Biophys. Res. Commun.* **2018**, *500*, 569–576, doi:10.1016/j.bbrc.2018.04.091.
122. Liu, H.; Qin, S.; Liu, C.; Jiang, L.; Li, C.; Yang, J.; Zhang, S.; Yan, Z.; Liu, X.; Yang, J.; et al. m6A Reader IGF2BP2-Stabilized CASC9 Accelerates Glioblastoma Aerobic Glycolysis by Enhancing HK2 mRNA Stability. *Cell Death Discov.* **2021**, *7*, 292, doi:10.1038/s41420-021-00674-y.
123. Meng, M.; Yang, L.; Zhou, H.; Cheng, Q.; Peng, R.; Wang, Z.; Liang, X.; Wen, J.; Nie, J.; Hu, Z.; et al. LINC00978 Regulates Metabolic Rewiring to Promote the Malignancy of Glioblastoma through AKR1B1. *Cancer Lett.* **2023**, *567*, 216277, doi:10.1016/j.canlet.2023.216277.
124. Sun, J.; He, D.; Fu, Y.; Zhang, R.; Guo, H.; Wang, Z.; Wang, Y.; Gao, T.; Wei, Y.; Guo, Y.; et al. A Novel lncRNA ARST Represses Glioma Progression by Inhibiting ALDOA-Mediated Actin Cytoskeleton Integrity. *J. Exp. Clin. Cancer Res.* **2021**, *40*, 187, doi:10.1186/s13046-021-01977-9.
125. Hao, S.; Gao, M.; Li, Q.; Shu, L.; Wang, P.; Hao, G. Machine Learning Predicts Cuproptosis-Related lncRNAs and Survival in Glioma Patients. *Sci. Rep.* **2024**, *14*, 22323, doi:10.1038/s41598-024-72664-w.
126. Zhu, W.; Zhao, H.; Xu, F.; Huang, B.; Dai, X.; Sun, J.; Nyalali, A.M.K.; Zhang, K.; Ni, S. The Lipid-Lowering Drug Fenofibrate Combined with Si-HOTAIR Can Effectively Inhibit the Proliferation of Gliomas. *BMC Cancer* **2021**, *21*, 664, doi:10.1186/s12885-021-08417-z.
127. Liu, R.; Wang, J.; Zhang, L.; Wang, S.; Li, X.; Liu, Y.; Yu, H. GLIDR-Mediated Regulation of Tumor Malignancy and Cisplatin Resistance in Non-Small Cell Lung Cancer via the miR-342-5p/PPARGC1A Axis. *BMC Cancer* **2024**, *24*, 1126, doi:10.1186/s12885-024-12845-y.
128. Ji, X.; Liu, Z.; Gao, J.; Bing, X.; He, D.; Liu, W.; Wang, Y.; Wei, Y.; Yin, X.; Zhang, F.; et al. N6-Methyladenosine-Modified lncRNA LINREP Promotes Glioblastoma Progression

by Recruiting the PTBP1/HuR Complex. *Cell Death Differ.* **2023**, *30*, 54–68, doi:10.1038/s41418-022-01045-5.
129. Yan, Y.; Xu, Z.; Chen, X.; Wang, X.; Zeng, S.; Zhao, Z.; Qian, L.; Li, Z.; Wei, J.; Huo, L.; 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.* **2019**, *7*, 217, doi:10.3389/fcell.2019.00217.
130. Xu, C.; Qi, R.; Ping, Y.; Li, J.; Zhao, H.; Wang, L.; Du, M.Y.; Xiao, Y.; Li, X. Systemically Identifying and Prioritizing Risk lncRNAs through Integration of Pan-Cancer Phenotype Associations. *Oncotarget* **2017**, *8*, 12041–12051, doi:10.18632/oncotarget.14510.
131. Wang, J.; Quan, Y.; Lv, J.; Dong, Q.; Gong, S. LncRNA IDH1-AS1 Suppresses Cell Proliferation and Tumor Growth in Glioma. *Biochem. Cell Biol.* **2020**, *98*, 556–564, doi:10.1139/bcb-2019-0465.
132. Zeng, Z.-M.; Chen, Y.-Y.; Wen, X.-C.; Geng, X.-C.; Zhu, Y.-X.; Hao, L.-C.; Dong, Z.-S.; Yang, J.-F.; Wang, T.-T.; Zhang, R.-B.; et al. Whole-Transcriptome Sequencing with ceRNA Regulation Network Construction and Verification in Glioblastoma. *Am. J. Transl. Res.* **2023**, *15*, 4291–4313.
133. Li, Y.; Wang, Z.; Wang, Y.; Zhao, Z.; Zhang, J.; Lu, J.; Xu, J.; Li, X. Identification and Characterization of lncRNA Mediated Transcriptional Dysregulation Dictates lncRNA Roles in Glioblastoma. *Oncotarget* **2016**, *7*, 45027–45041, doi:10.18632/oncotarget.7801.
134. Zhu, X.; Jiang, L.; Yang, H.; Chen, T.; Wu, X.; Lv, K. Analyzing the lncRNA, miRNA, and mRNA-Associated ceRNA Networks to Reveal Potential Prognostic Biomarkers for Glioblastoma Multiforme. *Cancer Cell Int.* **2020**, *20*, 393, doi:10.1186/s12935-020-01488-1.
135. Yu, K.; Yang, H.; Lv, Q.; Wang, L.; Tan, Z.; Zhang, Z.; Ji, Y.; Lin, Q.; Chen, J.; He, W.; et al. Construction of a Competitive Endogenous RNA Network and Analysis of Potential Regulatory Axis Targets in Glioblastoma. *Cancer Cell Int.* **2021**, *21*, 102, doi:10.1186/s12935-021-01789-z.
136. Enciso-Mora, V.; Hosking, F.J.; Kinnersley, B.; Wang, Y.; Shete, S.; Zelenika, D.; Broderick, P.; Idbaih, A.; Delattre, J.-Y.; Hoang-Xuan, K.; et al. Deciphering the 8q24.21 Association for Glioma. *Hum. Mol. Genet.* **2013**, *22*, 2293–2302, doi:10.1093/hmg/ddt063.
137. Xu, X.; Zhong, Z.; Shao, Y.; Yi, Y. Prognostic Value of MEG3 and Its Correlation With Immune Infiltrates in Gliomas. *Front. Genet.* **2021**, *12*, 679097, doi:10.3389/fgene.2021.679097.
138. Xu, W.; Hu, G.-Q.; Da Costa, C.; Tang, J.-H.; Li, Q.-R.; Du, L.; Pan, Y.-W.; Lv, S.-Q. Long Noncoding RNA UBE2R2-AS1 Promotes Glioma Cell Apoptosis via Targeting the miR-877-3p/TLR4 Axis. *OncoTargets Ther.* **2019**, *Volume 12*, 3467–3480, doi:10.2147/OTT.S201732.
139. Hong, F.; Gong, Z.; Zhang, X.; Ma, P.; Yin, Y.; Wang, H. Identification of Biomarkers and ceRNA Network in Glioblastoma through Bioinformatic Analysis and Evaluation of Potential Prognostic Values. *Ann. Transl. Med.* **2021**, *9*, 1561–1561, doi:10.21037/atm-21-4925.
140. Zhang, Y.; Liao, G.; Bai, J.; Zhang, X.; Xu, L.; Deng, C.; Yan, M.; Xie, A.; Luo, T.; Long, Z.; et al. Identifying Cancer Driver lncRNAs Bridged by Functional Effectors through Integrating Multi-Omics Data in Human Cancers. *Mol. Ther. - Nucleic Acids* **2019**, *17*, 362–373, doi:10.1016/j.omtn.2019.05.030.
141. Yi, K.; Cui, X.; Liu, X.; Wang, Y.; Zhao, J.; Yang, S.; Xu, C.; Yang, E.; Xiao, M.; Hong, B.; et al. PTRF/Cavin-1 as a Novel RNA-Binding Protein Expedites the NF-κB/PD-L1 Axis

by Stabilizing lncRNA NEAT1, Contributing to Tumorigenesis and Immune Evasion in Glioblastoma. *Front. Immunol.* **2022**, *12*, 802795, doi:10.3389/fimmu.2021.802795.
142. Chen, W.; Li, Q.; Zhang, G.; Wang, H.; Zhu, Z.; Chen, L. LncRNA HOXA-AS3 Promotes the Malignancy of Glioblastoma through Regulating miR-455-5p/USP3 Axis. *J. Cell. Mol. Med.* **2020**, *24*, 11755–11767, doi:10.1111/jcmm.15788.
143. Hong, F.; Gong, Z.; Chen, C.; Hua, T.; Huang, Q.; Liu, Y.; Ma, P.; Zhang, X.; Wang, H.; Chen, J. UBDP1 Pseudogene and UBD Network Competitively Bind miR-6072 to Promote Glioma Progression. *Int. J. Oncol.* **2024**, *64*, 29, doi:10.3892/ijo.2024.5617.
144. Yang, X.; Niu, S.; Liu, J.; Fang, J.; Wu, Z.; Ling, S.; Di, G.; Jiang, X. Identification of an Epithelial-Mesenchymal Transition-Related lncRNA Prognostic Signature for Patients with Glioblastoma. *Sci. Rep.* **2021**, *11*, 23694, doi:10.1038/s41598-021-03213-y.
145. Li, L.; Zhou, A.; Wei, Y.; Liu, F.; Li, P.; Fang, R.; Ma, L.; Zhang, S.; Wang, L.; Liu, J.; et al. Critical Role of lncEPAT in Coupling Dysregulated EGFR Pathway and Histone H2A Deubiquitination during Glioblastoma Tumorigenesis. *Sci. Adv.* **2022**, *8*, eabn2571, doi:10.1126/sciadv.abn2571.
146. Gao, X.-Y.; Zang, J.; Zheng, M.-H.; Zhang, Y.-F.; Yue, K.-Y.; Cao, X.-L.; Cao, Y.; Li, X.-X.; Han, H.; Jiang, X.-F.; et al. Temozolomide Treatment Induces HMGB1 to Promote the Formation of Glioma Stem Cells via the TLR2/NEAT1/Wnt Pathway in Glioblastoma. *Front. Cell Dev. Biol.* **2021**, *9*, 620883, doi:10.3389/fcell.2021.620883.
147. Han, M.; Wang, S.; Fritah, S.; Wang, X.; Zhou, W.; Yang, N.; Ni, S.; Huang, B.; Chen, A.; Li, G.; et al. Interfering with Long Non-Coding RNA MIR22HG Processing Inhibits Glioblastoma Progression through Suppression of Wnt/β-Catenin Signalling. *Brain* **2020**, *143*, 512–530, doi:10.1093/brain/awz406.
148. Fazi, B.; Garbo, S.; Toschi, N.; Mangiola, A.; Lombari, M.; Sicari, D.; Battistelli, C.; Galardi, S.; Michienzi, A.; Trevisi, G.; et al. The lncRNA H19 Positively Affects the Tumorigenic Properties of Glioblastoma Cells and Contributes to NKD1 Repression through the Recruitment of EZH2 on Its Promoter. *Oncotarget* **2018**, *9*, 15512–15525, doi:10.18632/oncotarget.24496.
149. Liang, Q.; Guan, G.; Li, X.; Wei, C.; Wu, J.; Cheng, P.; Wu, A.; Cheng, W. Profiling Pro-Neural to Mesenchymal Transition Identifies a lncRNA Signature in Glioma. *J. Transl. Med.* **2020**, *18*, 378, doi:10.1186/s12967-020-02552-0.
150. Fan, Y.; Gao, Z.; Xu, J.; Wang, H.; Guo, Q.; Xue, H.; Zhao, R.; Guo, X.; Li, G. Identification and Validation of SNHG Gene Signature to Predict Malignant Behaviors and Therapeutic Responses in Glioblastoma. *Front. Immunol.* **2022**, *13*, 986615, doi:10.3389/fimmu.2022.986615.
151. Chen, H.; Hou, G.; Yang, J.; Chen, W.; Guo, L.; Mao, Q.; Ge, J.; Zhang, X. SOX9-activated PXN-AS1 Promotes the Tumorigenesis of Glioblastoma by EZH2-mediated Methylation of DKK1. *J. Cell. Mol. Med.* **2020**, *24*, 6070–6082, doi:10.1111/jcmm.15189.
152. Li, W.; Jiang, P.; Sun, X.; Xu, S.; Ma, X.; Zhan, R. Suppressing H19 Modulates Tumorigenicity and Stemness in U251 and U87MG Glioma Cells. *Cell. Mol. Neurobiol.* **2016**, *36*, 1219–1227, doi:10.1007/s10571-015-0320-5.
153. Jiang, X.; Yan, Y.; Hu, M.; Chen, X.; Wang, Y.; Dai, Y.; Wu, D.; Wang, Y.; Zhuang, Z.; Xia, H. Increased Level of H19 Long Noncoding RNA Promotes Invasion, Angiogenesis, and Stemness of Glioblastoma Cells. *J. Neurosurg.* **2016**, *124*, 129–136, doi:10.3171/2014.12.JNS1426.

154. Chen, Q.; Wang, W.; Wu, Z.; Chen, S.; Chen, X.; Zhuang, S.; Song, G.; Lv, Y.; Lin, Y. Over-Expression of lncRNA TMEM161B-AS1 Promotes the Malignant Biological Behavior of Glioma Cells and the Resistance to Temozolomide via up-Regulating the Expression of Multiple Ferroptosis-Related Genes by Sponging Hsa-miR-27a-3p. *Cell Death Discov.* **2021**, *7*, 311, doi:10.1038/s41420-021-00709-4.
155. Pokorná, M.; Kútna, V.; Ovsepian, S.V.; Matěj, R.; Černá, M.; O'Leary, V.B. Biomolecules to Biomarkers? U87MG Marker Evaluation on the Path towards Glioblastoma Multiforme Pathogenesis. *Pharmaceutics* **2024**, *16*, 123, doi:10.3390/pharmaceutics16010123.
156. Zhang, D.; Zhou, H.; Liu, J.; Mao, J. Long Noncoding RNA ASB16-AS1 Promotes Proliferation, Migration, and Invasion in Glioma Cells. *BioMed Res. Int.* **2019**, *2019*, 1–10, doi:10.1155/2019/5437531.
157. Li, H.; Yuan, X.; Yan, D.; Li, D.; Guan, F.; Dong, Y.; Wang, H.; Liu, X.; Yang, B. Long Non-Coding RNA MALAT1 Decreases the Sensitivity of Resistant Glioblastoma Cell Lines to Temozolomide. *Cell. Physiol. Biochem.* **2017**, *42*, 1192–1201, doi:10.1159/000478917.
158. Shree, B.; Sengar, S.; Tripathi, S.; Sharma, V. LINC01711 Promotes Transforming Growth Factor-Beta (TGF-β) Induced Invasion in Glioblastoma Multiforme (GBM) by Acting as a Competing Endogenous RNA for miR-34a and Promoting ZEB1 Expression. *Neurosci. Lett.* **2023**, *792*, 136937, doi:10.1016/j.neulet.2022.136937.
159. DGCR5 Suppresses the EMT of Pediatric Primary Glioblastoma Multiforme Cell and Serves as a Prognostic Biomarker.
160. Movahedpour, A.; Khatami, S.H.; Khorsand, M.; Salehi, M.; Savardashtaki, A.; Mirmajidi, S.H.; Negahdari, B.; Khanjani, N.; Naeli, P.; Vakili, O.; et al. Exosomal Noncoding RNAs: Key Players in Glioblastoma Drug Resistance. *Mol. Cell. Biochem.* **2021**, *476*, 4081–4092, doi:10.1007/s11010-021-04221-2.
161. Tsung, K.; Liu, K.Q.; Han, J.S.; Deshpande, K.; Doan, T.; Loh, Y.-H.E.; Ding, L.; Yang, W.; Neman, J.; Dou, Y.; et al. CRISPRi Screen of Long Non-Coding RNAs Identifies LINC03045 Regulating Glioblastoma Invasion. *PLOS Genet.* **2024**, *20*, e1011314, doi:10.1371/journal.pgen.1011314.
162. Wang, Z.; Wang, L.; Liang, Z.; Xi, Y. Long Non-Coding RNA BCAR4 Promotes Growth, Invasion and Tumorigenicity by Targeting miR-2276 to Upregulate MMP7 Expression in Glioma. *OncoTargets Ther.* **2019**, *Volume 12*, 10963–10973, doi:10.2147/OTT.S226026.
163. Wu, W.; Yu, T.; Wu, Y.; Tian, W.; Zhang, J.; Wang, Y. The miR155HG/miR-185/ANXA2 Loop Contributes to Glioblastoma Growth and Progression. *J. Exp. Clin. Cancer Res.* **2019**, *38*, 133, doi:10.1186/s13046-019-1132-0.
164. Li, J.; Ji, X.; Wang, H. Targeting Long Noncoding RNA HMMR-AS1 Suppresses and Radiosensitizes Glioblastoma. *Neoplasia* **2018**, *20*, 456–466, doi:10.1016/j.neo.2018.02.010.
165. Hao, Y.; Li, X.; Chen, H.; Huo, H.; Liu, Z.; Chai, E. Over-Expression of Long Noncoding RNA HOTAIRM1 Promotes Cell Proliferation and Invasion in Human Glioblastoma by up-Regulating SP1 via Sponging miR-137. *NeuroReport* **2020**, *31*, 109–117, doi:10.1097/WNR.0000000000001380.
166. Lin, H.; Zuo, D.; He, J.; Ji, T.; Wang, J.; Jiang, T. Long Noncoding RNA WEE2-AS1 Plays an Oncogenic Role in Glioblastoma by Functioning as a Molecular Sponge for MicroRNA-520f-3p. *Oncol. Res. Featur. Preclin. Clin. Cancer Ther.* **2020**, *28*, 591–603, doi:10.3727/096504020X15982623243955.

167. Wu, X.; Wan, Q.; Wang, J.; Hou, P.; Zhang, Q.; Wang, Q.; Lu, X. Epigenetic Activation of lncRNA MIR155HG Mediated by Promoter Hypomethylation and SP1 Is Correlated with Immune Infiltration in Glioma. *OncoTargets Ther.* **2022**, *Volume 15*, 219–235, doi:10.2147/OTT.S349078.
168. Chen, X.; Pan, C.; Xu, C.; Sun, Y.; Geng, Y.; Kong, L.; Xiao, X.; Zhao, Z.; Zhou, W.; Huang, L.; et al. Identification of Survival-associated Key Genes and Long Non-coding RNAs in Glioblastoma Multiforme by Weighted Gene Co-expression Network Analysis. *Int. J. Mol. Med.* **2019**, doi:10.3892/ijmm.2019.4101.
169. Mazor, G.; Smirnov, D.; Ben David, H.; Khrameeva, E.; Toiber, D.; Rotblat, B. TP73-AS1 Is Induced by YY1 during TMZ Treatment and Highly Expressed in the Aging Brain. *Aging* **2021**, *13*, 14843–14861, doi:10.18632/aging.203182.
170. Witusik-Perkowska, M.; Jaskólski, D.J.; Liberski, P.P.; Szemraj, J. If Artificial In Vitro Microenvironment Can Influence Tumor Drug Resistance Network via Modulation of lncRNA Expression?—Comparative Analysis of Glioblastoma-Derived Cell Culture Models and Initial Tumors In Vivo. *Cell. Mol. Neurobiol.* **2022**, *42*, 1005–1020, doi:10.1007/s10571-020-00991-3.
171. Zhong, X.; Cai, Y. Long Non-Coding RNA (lncRNA) HOXD-AS2 Promotes Glioblastoma Cell Proliferation, Migration and Invasion by Regulating the miR-3681-5p/MALT1 Signaling Pathway. *Bioengineered* **2021**, *12*, 9113–9127, doi:10.1080/21655979.2021.1977104.
172. Ahmadov, U.; Picard, D.; Bartl, J.; Silginer, M.; Trajkovic-Arsic, M.; Qin, N.; Blümel, L.; Wolter, M.; Lim, J.K.M.; Pauck, D.; et al. The Long Non-Coding RNA HOTAIRM1 Promotes Tumor Aggressiveness and Radiotherapy Resistance in Glioblastoma. *Cell Death Dis.* **2021**, *12*, 885, doi:10.1038/s41419-021-04146-0.
173. Liu, S.; Mitra, R.; Zhao, M.-M.; Fan, W.; Eischen, C.M.; Yin, F.; Zhao, Z. The Potential Roles of Long Noncoding RNAs (lncRNA) in Glioblastoma Development. *Mol. Cancer Ther.* **2016**, *15*, 2977–2986, doi:10.1158/1535-7163.MCT-16-0320.
174. Zhang, X.; Li, R. lncRNA MAFG-AS1 Enhances Radioresistance of Glioblastoma Cells via miR-642a-5p/Notch1 Axis. *Acta Neurobiol. Exp. (Warsz.)* **2022**, *82*, 315–326, doi:10.55782/ane-2022-030.
175. Luo, L.; Zhang, Y.; He, H.; Chen, C.; Zhang, B.; Cai, M. LncRNA FEZF1-AS1 Sponges miR-34a to Upregulate Notch-1 in Glioblastoma. *Cancer Manag. Res.* **2020**, *Volume 12*, 1827–1833, doi:10.2147/CMAR.S240531.
176. Wu, J.; Wang, N.; Yang, Y.; Jiang, G.; Zhan, H.; Li, F. LINC01152 Upregulates MAML2 Expression to Modulate the Progression of Glioblastoma Multiforme via Notch Signaling Pathway. *Cell Death Dis.* **2021**, *12*, 115, doi:10.1038/s41419-020-03163-9.
177. Shahcheraghi, S.H.; Roshani Asl, E.; Lotfi, M.; Ayatollahi, J.; Khaleghinejad, S.H.; Aljabali, A.A.A.; Bakshi, H.A.; El-Tanani, M.; Charbe, N.B.; Serrano-Aroca, Á.; et al. Non-Coding RNAs as Key Regulators of the Notch Signaling Pathway inGlioblastoma: Diagnostic, Prognostic, and Therapeutic Targets. *CNS Neurol. Disord. - Drug Targets* **2024**, *23*, 1203–1216, doi:10.2174/0118715273277458231213063147.
178. Yao, Z.; Zhang, Q.; Guo, F.; Guo, S.; Yang, B.; Liu, B.; Li, P.; Li, J.; Guan, S.; Liu, X. Long Noncoding RNA PCED1B-AS1 Promotes the Warburg Effect and Tumorigenesis by Upregulating HIF-1α in Glioblastoma. *Cell Transplant.* **2020**, *29*, 096368972090677, doi:10.1177/0963689720906777.

179. Huang, H.; Shah, H.; Hao, J.; Lin, J.; Prayson, R.A.; Xie, L.; Bao, S.; Chakraborty, A.A.; Jankowsky, E.; Zhao, J.; et al. Long Non-Coding RNA Lung Cancer-Associated Transcript-1 Promotes Glioblastoma Progression by Enhancing Hypoxia-Inducible Factor 1 **Alpha** Activity. *Neuro-Oncol.* **2024**, *26*, 1388–1401, doi:10.1093/neuonc/noae036.
180. Cai, X.; Qian, M.; Zhang, K.; Li, Y.; Chang, B.; Chen, M. Profiling and Bioinformatics Analyses of Hypoxia-Induced Differential Expression of Long Non-Coding RNA in Glioblastoma Multiforme Cells. *Biochem. Genet.* **2024**, *62*, 3052–3070, doi:10.1007/s10528-023-10597-1.
181. Tantai, J.; Hu, D.; Yang, Y.; Geng, J. Combined Identification of Long Non-Coding RNA XIST and HIF1A-AS1 in Serum as an Effective Screening for Non-Small Cell Lung Cancer.
182. Li, Y.-P.; Liu, Y.; Xiao, L.-M.; Chen, L.-K.; Tao, E.-X.; Zeng, E.-M.; Xu, C.-H. Induction of Cancer Cell Stemness in Glioma through Glycolysis and the Long Noncoding RNA HULC-Activated FOXM1/AGR2/HIF-1α Axis. *Lab. Invest.* **2022**, *102*, 691–701, doi:10.1038/s41374-021-00664-9.
183. Pan, T.; Xie, D.-K.; Li, J.; Qiang, Y.-J.; Fan, S.-Y.; Wang, T.-T.; Han, Y.-Y.; Zang, J.; Yang, Y.; Zhao, J.-L.; et al. Glioma-Stem-Cell-Derived Exosomes Remodeled Glioma-Associated Macrophage via NEAT1/miR-125a/STAT3 Pathway. *Cancers* **2024**, *16*, 2500, doi:10.3390/cancers16142500.
184. Su, R.; Cao, S.; Ma, J.; Liu, Y.; Liu, X.; Zheng, J.; Chen, J.; Liu, L.; Cai, H.; Li, Z.; et al. Knockdown of SOX2OT Inhibits the Malignant Biological Behaviors of Glioblastoma Stem Cells via Up-Regulating the Expression of miR-194-5p and miR-122. *Mol. Cancer* **2017**, *16*, 171, doi:10.1186/s12943-017-0737-1.
185. Liu, B.; Zhou, J.; Wang, C.; Chi, Y.; Wei, Q.; Fu, Z.; Lian, C.; Huang, Q.; Liao, C.; Yang, Z.; et al. LncRNA SOX2OT Promotes Temozolomide Resistance by Elevating SOX2 Expression via ALKBH5-Mediated Epigenetic Regulation in Glioblastoma. *Cell Death Dis.* **2020**, *11*, 384, doi:10.1038/s41419-020-2540-y.
186. Amirmahani, F.; Vallian, S.; Asadi, M.H. The LncRNA MIAT Is Identified as a Regulator of Stemness-Associated Transcript in Glioma. *Mol. Biol. Rep.* **2023**, *50*, 517–530, doi:10.1007/s11033-022-07962-5.
187. Xavier-Magalhães, A.; Gonçalves, C.S.; Fogli, A.; Lourenço, T.; Pojo, M.; Pereira, B.; Rocha, M.; Lopes, M.C.; Crespo, I.; Rebelo, O.; 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* **2018**, *9*, 15740–15756, doi:10.18632/oncotarget.24597.
188. Shi, T.; Guo, D.; Xu, H.; Su, G.; Chen, J.; Zhao, Z.; Shi, J.; Wedemeyer, M.; Attenello, F.; Zhang, L.; et al. HOTAIRM1, an Enhancer lncRNA, Promotes Glioma Proliferation by Regulating Long-Range Chromatin Interactions within HOXA Cluster Genes. *Mol. Biol. Rep.* **2020**, *47*, 2723–2733, doi:10.1007/s11033-020-05371-0.
189. Li, Q.; Dong, C.; Cui, J.; Wang, Y.; Hong, X. Over-Expressed lncRNA HOTAIRM1 Promotes Tumor Growth and Invasion through up-Regulating HOXA1 and Sequestering G9a/EZH2/Dnmts Away from the HOXA1 Gene in Glioblastoma Multiforme. *J. Exp. Clin. Cancer Res.* **2018**, *37*, 265, doi:10.1186/s13046-018-0941-x.
190. Xia, H.; Liu, Y.; Wang, Z.; Zhang, W.; Qi, M.; Qi, B.; Jiang, X. Long Noncoding RNA HOTAIRM1 Maintains Tumorigenicity of Glioblastoma Stem-Like Cells Through

Regulation of HOX Gene Expression. *Neurotherapeutics* **2020**, *17*, 754–764, doi:10.1007/s13311-019-00799-0.
191. Li, Y.; Ma, K.; Xie, Q.; Zhang, X.; Zhang, X.; Chen, K.; Kong, L.; Qian, R. Identification of HOXD10 as a Marker of Poor Prognosis in Glioblastoma Multiforme. *OncoTargets Ther.* **2021**, *Volume 14*, 5183–5195, doi:10.2147/OTT.S336225.
192. Wang, X.; Sun, Y.; Xu, T.; Qian, K.; Huang, B.; Zhang, K.; Song, Z.; Qian, T.; Shi, J.; Li, L. HOXB13 Promotes Proliferation, Migration, and Invasion of Glioblastoma through Transcriptional Upregulation of lncRNA HOXC-AS3. *J. Cell. Biochem.* **2019**, *120*, 15527–15537, doi:10.1002/jcb.28819.
193. Waters, E.; Pucci, P.; Rahman, R.; Yatsyshyna, A.P.; Porter, H.; Hirst, M.; Gromnicova, R.; Kraev, I.; Mongiardini, V.; Grimaldi, B.; et al. REST-Dependent Glioma Progression Occurs Independently of the Repression of the Long Non-Coding RNA HAR1A. *PLOS ONE* **2024**, *19*, e0312237, doi:10.1371/journal.pone.0312237.
194. Han, J.; Yu, X.; Wang, S.; Wang, Y.; Liu, Q.; Xu, H.; Wang, X. IGF2BP2 Induces U251 Glioblastoma Cell Chemoresistance by Inhibiting FOXO1-Mediated PID1 Expression Through Stabilizing lncRNA DANCR. *Front. Cell Dev. Biol.* **2022**, *9*, 659228, doi:10.3389/fcell.2021.659228.
195. Gao, Z.; Xu, J.; Fan, Y.; Qi, Y.; Wang, S.; Zhao, S.; Guo, X.; Xue, H.; Deng, L.; Zhao, R.; et al. PDIA3P1 Promotes Temozolomide Resistance in Glioblastoma by Inhibiting C/EBPβ Degradation to Facilitate Proneural-to-Mesenchymal Transition. *J. Exp. Clin. Cancer Res.* **2022**, *41*, 223, doi:10.1186/s13046-022-02431-0.
196. Zhang, L.; Cao, Y.; Wei, M.; Jiang, X.; Jia, D. Long Noncoding RNA-RNCR3 Overexpression Deleteriously Affects the Growth of Glioblastoma Cells through miR-185-5p/Krüppel-like Factor 16 Axis. *J. Cell. Biochem.* **2018**, *119*, 9081–9089, doi:10.1002/jcb.27167.
197. Shou, J.; Gao, H.; Cheng, S.; Wang, B.; Guan, H. LncRNA HOXA-AS2 Promotes Glioblastoma Carcinogenesis by Targeting miR-885-5p/RBBP4 Axis. *Cancer Cell Int.* **2021**, *21*, 39, doi:10.1186/s12935-020-01690-1.
198. Wang, D.; Chen, Q.; Liu, J.; Liao, Y.; Jiang, Q. Silencing of lncRNA CHRM3-AS2 Expression Exerts Anti-Tumour Effects Against Glioma via Targeting microRNA-370-5p/KLF4. *Front. Oncol.* **2022**, *12*, 856381, doi:10.3389/fonc.2022.856381.
199. Guo, S.; King, P.; Liang, E.; Guo, A.A.; Liu, M. LncRNA HOTAIR Sponges miR-301a-3p to Promote Glioblastoma Proliferation and Invasion through Upregulating FOSL1. *Cell. Signal.* **2022**, *94*, 110306, doi:10.1016/j.cellsig.2022.110306.
200. Wang, J.-B.; Liu, F.-H.; Chen, J.-H.; Ge, H.-T.; Mu, L.-Y.; Bao, H.-B.; Lin, Z.-G. Identifying Survival-Associated Modules from the Dysregulated Triplet Network in Glioblastoma Multiforme. *J. Cancer Res. Clin. Oncol.* **2017**, *143*, 661–671, doi:10.1007/s00432-016-2332-z.
201. Long, S.; Wu, B.; Yang, L.; Wang, L.; Wang, B.; Yan, Y.; Jiang, J.; Yang, B.; Zhou, Q.; Shi, M.; et al. Novel Tumor Necrosis Factor-Related Long Non-Coding RNAs Signature for Risk Stratification and Prognosis in Glioblastoma. *Front. Neurol.* **2023**, *14*, 1054686, doi:10.3389/fneur.2023.1054686.
202. Ji, Y.; Gu, Y.; Hong, S.; Yu, B.; Zhang, J.; Liu, J. Comprehensive Analysis of lncRNA-TF Crosstalks and Identification of Prognostic Regulatory Feedback Loops of Glioblastoma Using lncRNA/TF-mediated ceRNA Network. *J. Cell. Biochem.* **2020**, *121*, 755–767, doi:10.1002/jcb.29321.

203. Long, S.; Wu, B.; Yang, L.; Wang, L.; Wang, B.; Yan, Y.; Jiang, J.; Yang, B.; Zhou, Q.; Shi, M.; et al. Novel Tumor Necrosis Factor-Related Long Non-Coding RNAs Signature for Risk Stratification and Prognosis in Glioblastoma. *Front. Neurol.* **2023**, *14*, 1054686, doi:10.3389/fneur.2023.1054686.
204. Vazifehmand, R.; Ali, D.S.; Othman, Z.; Chau, D.-M.; Stanslas, J.; Shafa, M.; Sekawi, Z. The Evaluation Expression of Non-Coding RNAs in Response to HSV-G47Δ Oncolytic Virus Infection in Glioblastoma Multiforme Cancer Stem Cells. *J. Neurovirol.* **2022**, *28*, 566–582, doi:10.1007/s13365-022-01089-w.
205. Zhang, S.; Guo, S.; Liang, C.; Lian, M. Long Intergenic Noncoding RNA 00021 Promotes Glioblastoma Temozolomide Resistance by Epigenetically Silencing P21 through Notch Pathway. *IUBMB Life* **2020**, *72*, 1747–1756, doi:10.1002/iub.2301.
206. Leisegang, M.S.; Fork, C.; Josipovic, I.; Richter, F.M.; Preussner, J.; Hu, J.; Miller, M.J.; Epah, J.; Hofmann, P.; Günther, S.; et al. Long Noncoding RNA MANTIS Facilitates Endothelial Angiogenic Function. *Circulation* **2017**, *136*, 65–79, doi:10.1161/CIRCULATIONAHA.116.026991.
207. Jiang, L.; Yang, H.; Chen, T.; Zhu, X.; Ye, J.; Lv, K. Identification of HMG-Box Family Establishes the Significance of SOX6 in the Malignant Progression of Glioblastoma. *Aging* **2020**, *12*, 8084–8106, doi:10.18632/aging.103127.
208. Torres-Bayona, S.; Aldaz, P.; Auzmendi-Iriarte, J.; Saenz-Antoñanzas, A.; Garcia, I.; Arrazola, M.; Gerovska, D.; Undabeitia, J.; Querejeta, A.; Egaña, L.; et al. PR-LncRNA Signature Regulates Glioma Cell Activity through Expression of SOX Factors. *Sci. Rep.* **2018**, *8*, 12746, doi:10.1038/s41598-018-30836-5.
209. Angelucci, C.; D'Alessio, A.; Lama, G.; Binda, E.; Mangiola, A.; Vescovi, A.L.; Proietti, G.; Masuelli, L.; Bei, R.; Fazi, B.; et al. Cancer Stem Cells from Peritumoral Tissue of Glioblastoma Multiforme: The Possible Missing Link between Tumor Development and Progression. *Oncotarget* **2018**, *9*, 28116–28130, doi:10.18632/oncotarget.25565.
210. Porto, F.W.; Daulatabad, S.V.; Janga, S.C. Long Non-Coding RNA Expression Levels Modulate Cell-Type-Specific Splicing Patterns by Altering Their Interaction Landscape with RNA-Binding Proteins. *Genes* **2019**, *10*, 593, doi:10.3390/genes10080593.
211. Wang, H.; Li, L.; Yin, L. Silencing LncRNA LOXL1-AS1 Attenuates Mesenchymal Characteristics of Glioblastoma via NF-κB Pathway. *Biochem. Biophys. Res. Commun.* **2018**, *500*, 518–524, doi:10.1016/j.bbrc.2018.04.133.
212. Zeng, H.; Xu, N.; Liu, Y.; Liu, B.; Yang, Z.; Fu, Z.; Lian, C.; Guo, H. Genomic Profiling of Long Non-Coding RNA and mRNA Expression Associated with Acquired Temozolomide Resistance in Glioblastoma Cells. *Int. J. Oncol.* **2017**, *51*, 445–455, doi:10.3892/ijo.2017.4033.
213. Zhao, J.; Yang, S.; Lv, C.; Liu, Y. Cancer-Associated Fibroblasts Suppressed Ferroptosis in Glioblastoma via Upregulating lncRNA DLEU1. *Am. J. Physiol.-Cell Physiol.* **2023**, *324*, C1039–C1052, doi:10.1152/ajpcell.00454.2022.
214. Zhu, K.; Miao, C.; Tian, Y.; Qin, Z.; Xue, J.; Xia, J.; Zhu, S.; Xu, A.; Yang, J.; Wang, Z. lncRNA MIR4435-2HG Promoted Clear Cell Renal Cell Carcinoma Malignant Progression via miR-513a-5p/KLF6 Axis. *J. Cell. Mol. Med.* **2020**, *24*, 10013–10026, doi:10.1111/jcmm.15609.
215. Xu, H.; Zhang, B.; Yang, Y.; Li, Z.; Zhao, P.; Wu, W.; Zhang, H.; Mao, J. LncRNA MIR4435-2HG Potentiates the Proliferation and Invasion of Glioblastoma Cells via

Modulating miR-1224-5p/TGFBR2 Axis. *J. Cell. Mol. Med.* **2020**, *24*, 6362–6372, doi:10.1111/jcmm.15280.
216. Bomsztyk, K.; Mar, D.; Denisenko, O.; Powell, S.; Vishnoi, M.; Yin, Z.; Delegard, J.; Hadley, C.; Tandon, N.; Patel, A.J.; et al. Analysis of DNA Methylation in Gliomas: Assessment of Preanalytical Variables. *Lab. Invest.* **2024**, *104*, 102160, doi:10.1016/j.labinv.2024.102160.
217. Lu, Y.; Guo, G.; Hong, R.; Chen, X.; Sun, Y.; Liu, F.; Zhang, Z.; Jin, X.; Dong, J.; Yu, K.; et al. LncRNA HAS2-AS1 Promotes Glioblastoma Proliferation by Sponging miR-137. *Front. Oncol.* **2021**, *11*, 634893, doi:10.3389/fonc.2021.634893.
218. Cai, H.; Yu, Y.; Ni, X.; Li, C.; Hu, Y.; Wang, J.; Chen, F.; Xi, S.; Chen, Z. LncRNA LINC00998 Inhibits the Malignant Glioma Phenotype via the CBX3-Mediated c-Met/Akt/mTOR Axis. *Cell Death Dis.* **2020**, *11*, 1032, doi:10.1038/s41419-020-03247-6.
219. Liang, J.; Xie, J.; He, J.; Li, Y.; Wei, D.; Zhou, R.; Wei, G.; Liu, X.; Chen, Q.; Li, D. Inhibiting LNCRNA NEAT1 Increases Glioblastoma Response to TMZ by Reducing Connexin 43 Expression. *Cancer Rep.* **2024**, *7*, e70031, doi:10.1002/cnr2.70031.
220. Mamivand, A.; Bayat, S.; Maghrouni, A.; Shabani, S.; Khoshnevisan, A.; Saffar, H.; Tabrizi, M. Data Mining of Bulk and Single-Cell RNA Sequencing Introduces OBI1-AS1 as an Astrocyte Marker with Possible Role in Glioma Recurrence and Progression. *Clin. Epigenetics* **2022**, *14*, 35, doi:10.1186/s13148-022-01260-4.
221. Ren, S.; Xu, Y. AC016405.3, a Novel Long Noncoding RNA, Acts as a Tumor Suppressor through Modulation of TET2 by microRNA-19a-5p Sponging in Glioblastoma. *Cancer Sci.* **2019**, *110*, 1621–1632, doi:10.1111/cas.14002.
222. Fu, Q.; Li, S.; Zhou, Q.; Yalikun, K.; Yisireyili, D.; Xia, M. Low LINC00599 Expression Is a Poor Prognostic Factor in Glioma. *Biosci. Rep.* **2019**, *39*, BSR20190232, doi:10.1042/BSR20190232.
223. Wang, X.; Tian, W.; Wu, L.; Wei, Z.; Li, W.; Xu, Y.; Li, Y. LncRNA SNHG4 Regulates miR-138/c-Met Axis to Promote the Proliferation of Glioblastoma Cells. *NeuroReport* **2020**, *31*, 657–662, doi:10.1097/WNR.0000000000001469.
224. Dong, N.; Qi, W.; Wu, L.; Li, J.; Zhang, X.; Wu, H.; Zhang, W.; Jiang, J.; Zhang, S.; Fu, W.; et al. LINC00606 Promotes Glioblastoma Progression through Sponge miR-486-3p and Interaction with ATP11B. *J. Exp. Clin. Cancer Res.* **2024**, *43*, 139, doi:10.1186/s13046-024-03058-z.
225. Gao, W.; Li, H.; Liu, Y.; Zhang, Y.; Zhao, H.; Liu, F. Long Non-coding RNA FLVCR1-AS1 Promotes Glioma Cell Proliferation and Invasion by Negatively Regulating miR-30b-3p. *Mol. Med. Rep.* **2020**, *22*, 723–732, doi:10.3892/mmr.2020.11149.
226. Ren, J.; Yang, Y.; Xue, J.; Xi, Z.; Hu, L.; Pan, S.-J.; Sun, Q. Long Noncoding RNA SNHG7 Promotes the Progression and Growth of Glioblastoma via Inhibition of miR-5095. *Biochem. Biophys. Res. Commun.* **2018**, *496*, 712–718, doi:10.1016/j.bbrc.2018.01.109.
227. Brodie, S.; Lee, H.K.; Jiang, W.; Cazacu, S.; Xiang, C.; Poisson, L.M.; Datta, I.; Kalkanis, S.; Ginsberg, D.; Brodie, C. The Novel Long Non-Coding RNA TALNEC2, Regulates Tumor Cell Growth and the Stemness and Radiation Response of Glioma Stem Cells. *Oncotarget* **2017**, *8*, 31785–31801, doi:10.18632/oncotarget.15991.
228. Gong, X.; Huang, M.-Y. Tumor-Suppressive Function of lncRNA-MEG3 in Glioma Cells by Regulating miR-6088/SMARCB1 Axis. *BioMed Res. Int.* **2020**, *2020*, 4309161, doi:10.1155/2020/4309161.

229. Xie, P.; Li, X.; Chen, R.; Liu, Y.; Liu, D.; Liu, W.; Cui, G.; Xu, J. Upregulation of HOTAIRM1 Increases Migration and Invasion by Glioblastoma Cells. *Aging* **2021**, *13*, 2348–2364, doi:10.18632/aging.202263.
230. Zhang, J.; Chen, G.; Gao, Y.; Liang, H. HOTAIR/miR-125 Axis-mediated Hexokinase 2 Expression Promotes Chemoresistance in Human Glioblastoma. *J. Cell. Mol. Med.* **2020**, *24*, 5707–5717, doi:10.1111/jcmm.15233.
231. Yuan, Z.; Yang, Z.; Li, W.; Wu, A.; Su, Z.; Jiang, B. Expression of Concern Issued: Exosome-Mediated Transfer of Long Noncoding RNA HOTAIR Regulates Temozolomide Resistance by miR-519a-3p/RRM1 Axis in Glioblastoma. *Cancer Biother. Radiopharm.* **2020**, cbr.2019.3499, doi:10.1089/cbr.2019.3499.
232. Nie, E.; Jin, X.; Miao, F.; Yu, T.; Zhi, T.; Shi, Z.; Wang, Y.; Zhang, J.; Xie, M.; You, Y. TGF-B1 Modulates Temozolomide Resistance in Glioblastoma via Altered microRNA Processing and Elevated MGMT. *Neuro-Oncol.* **2021**, *23*, 435–446, doi:10.1093/neuonc/noaa198.
233. Zhao, R.; Li, B.; Zhang, S.; He, Z.; Pan, Z.; Li, X.; Guo, Q.; Qiu, W.; Qi, Y.; Zhao, S.; et al. The N6-Methyladenosine-Modified Pseudogene HSPA7 Correlates with the Tumor Microenvironment and Predicts the Response to Immune Checkpoint Therapy in Glioblastoma 2020.
234. Dong, Z.-Q.; Guo, Z.-Y.; Xie, J. The lncRNA EGFR-AS1 Is Linked to Migration, Invasion and Apoptosis in Glioma Cells by Targeting miR-133b/RACK1. *Biomed. Pharmacother.* **2019**, *118*, 109292, doi:10.1016/j.biopha.2019.109292.
235. Tang, W.; Wang, D.; Shao, L.; Liu, X.; Zheng, J.; Xue, Y.; Ruan, X.; Yang, C.; Liu, L.; Ma, J.; et al. LINC00680 and TTN-AS1 Stabilized by EIF4A3 Promoted Malignant Biological Behaviors of Glioblastoma Cells. *Mol. Ther. - Nucleic Acids* **2020**, *19*, 905–921, doi:10.1016/j.omtn.2019.10.043.
236. Fu, T.; Yang, Y.; Mu, Z.; Sun, R.; Li, X.; Dong, J. Silencing lncRNA LINC01410 Suppresses Cell Viability yet Promotes Apoptosis and Sensitivity to Temozolomide in Glioblastoma Cells by Inactivating PTEN/AKT Pathway via Targeting miR-370-3p. *Immunopharmacol. Immunotoxicol.* **2021**, *43*, 680–692, doi:10.1080/08923973.2021.1966031.
237. Shu, G.; Su, H.; Wang, Z.; Lai, S.; Wang, Y.; Liu, X.; Dai, L.; Bi, Y.; Chen, W.; Huang, W.; et al. LINC00680 Enhances Hepatocellular Carcinoma Stemness Behavior and Chemoresistance by Sponging miR-568 to Upregulate AKT3. *J. Exp. Clin. Cancer Res.* **2021**, *40*, 45, doi:10.1186/s13046-021-01854-5.
238. Wan, Y.; Liang, F.; Wei, M.; Liu, Y. RETRACTED ARTICLE: Long Non-Coding RNA LINC00525 Regulates the Proliferation and Epithelial to Mesenchymal Transition of Human Glioma Cells by Sponging miR-338-3p. *AMB Express* **2020**, *10*, 156, doi:10.1186/s13568-020-01094-4.
239. Fawzy, M.S.; Ellawindy, A.; Hussein, M.H.; Khashana, M.S.; Darwish, M.K.; Abdel-Daim, M.M.; Toraih, E.A. Long Noncoding RNA H19, and Not microRNA miR-326, Is over-Expressed and Predicts Survival in Glioblastoma. *Biochem. Cell Biol.* **2018**, *96*, 832–839, doi:10.1139/bcb-2018-0122.
240. Bazrgar, M.; Mirmotalebisohi, S.A.; Ahmadi, M.; Azimi, P.; Dargahi, L.; Zali, H.; Ahmadiani, A. Comprehensive Analysis of L Nc RNA -associated Ce RNA Network Reveals Novel Potential Prognostic Regulatory Axes in Glioblastoma Multiforme. *J. Cell. Mol. Med.* **2024**, *28*, e18392, doi:10.1111/jcmm.18392.

241. Gu, J.; Ye, Y.; Sunil, R.; Zhan, W.; Yu, R. Downregulation of lncRNA SATB2-AS1 Facilitates Glioma Cell Proliferation by Sponging miR-671-5p. *Exp. Ther. Med.* **2023**, *26*, 503, doi:10.3892/etm.2023.12202.
242. Song, Y.; Chen, B.; Jiao, H.; Yi, L. Long Noncoding RNA UNC5B-AS1 Suppresses Cell Proliferation by Sponging miR-24-3p in Glioblastoma Multiforme. *BMC Med. Genomics* **2024**, *17*, 83, doi:10.1186/s12920-024-01851-5.
243. Ruiz Esparza-Garrido, R.; Rodríguez-Corona, J.M.; López-Aguilar, J.E.; Rodríguez-Florido, M.A.; Velázquez-Wong, A.C.; Viedma-Rodríguez, R.; Salamanca-Gómez, F.; Velázquez-Flores, M.Á. Differentially Expressed Long Non-Coding RNAs Were Predicted to Be Involved in the Control of Signaling Pathways in Pediatric Astrocytoma. *Mol. Neurobiol.* **2017**, *54*, 6598–6608, doi:10.1007/s12035-016-0123-9.
244. Xu, J.; Hou, X.; Pang, L.; Sun, S.; He, S.; Yang, Y.; Liu, K.; Xu, L.; Yin, W.; Xu, C.; et al. Identification of Dysregulated Competitive Endogenous RNA Networks Driven by Copy Number Variations in Malignant Gliomas. *Front. Genet.* **2019**, *10*, 1055, doi:10.3389/fgene.2019.01055.
245. Zhang, L.; Wang, H.; Xu, M.; Chen, F.; Li, W.; Hu, H.; Yuan, Q.; Su, Y.; Liu, X.; Wuri, J.; et al. Long Noncoding RNA HAS2-AS1 Promotes Tumor Progression in Glioblastoma via Functioning as a Competing Endogenous RNA. *J. Cell. Biochem.* **2020**, *121*, 661–671, doi:10.1002/jcb.29313.
246. Zhang, L.; Cao, Y.; Wei, M.; Jiang, X.; Jia, D. Long Noncoding RNA-RNCR3 Overexpression Deleteriously Affects the Growth of Glioblastoma Cells through miR-185-5p/Krüppel-like Factor 16 Axis. *J. Cell. Biochem.* **2018**, *119*, 9081–9089, doi:10.1002/jcb.27167.
247. Gao, Y.; Liu, J.; Mao, X.; He, Z.; Zhu, T.; Wang, Z.; Li, X.; Yin, J.; Zhang, W.; Zhou, H.; et al. LncRNA FOXD1-AS1 Acts as a Potential Oncogenic Biomarker in Glioma. *CNS Neurosci. Ther.* **2020**, *26*, 66–75, doi:10.1111/cns.13152.
248. Nizar, R.; Cazacu, S.; Xiang, C.; Krasner, M.; Barbiro-Michaely, E.; Gerber, D.; Schwartz, J.; Fried, I.; Yuval, S.; Brodie, A.; et al. Propofol Inhibits Glioma Stem Cell Growth and Migration and Their Interaction with Microglia via BDNF-AS and Extracellular Vesicles. *Cells* **2023**, *12*, 1921, doi:10.3390/cells12151921.
249. Buccarelli, M.; Lulli, V.; Giuliani, A.; Signore, M.; Martini, M.; D'Alessandris, Q.G.; Giannetti, S.; Novelli, A.; Ilari, R.; Giurato, G.; et al. Deregulated Expression of the Imprinted *DLK1-DIO3* Region in Glioblastoma Stemlike Cells: Tumor Suppressor Role of lncRNA MEG3. *Neuro-Oncol.* **2020**, *22*, 1771–1784, doi:10.1093/neuonc/noaa127.
250. Liu, Y.; Xu, N.; Liu, B.; Huang, Y.; Zeng, H.; Yang, Z.; He, Z.; Guo, H. Long Noncoding RNA RP11-838N2.4 Enhances the Cytotoxic Effects of Temozolomide by Inhibiting the Functions of miR-10a in Glioblastoma Cell Lines. *Oncotarget* **2016**, *7*, 43835–43851, doi:10.18632/oncotarget.9699.
251. Pang, L.; Hu, J.; Li, F.; Yuan, H.; Yan, M.; Liao, G.; Xu, L.; Pang, B.; Ping, Y.; Xiao, Y.; et al. Discovering Rare Genes Contributing to Cancer Stemness and Invasive Potential by GBM Single-Cell Transcriptional Analysis. *Cancers* **2019**, *11*, 2025, doi:10.3390/cancers11122025.
252. Zhou, M.; Zhang, Z.; Zhao, H.; Bao, S.; Cheng, L.; Sun, J. An Immune-Related Six-lncRNA Signature to Improve Prognosis Prediction of Glioblastoma Multiforme. *Mol. Neurobiol.* **2017**, doi:10.1007/s12035-017-0572-9.

253. Zheng, J.; Su, Z.; Kong, Y.; Lin, Q.; Liu, H.; Wang, Y.; Wang, J. LncRNAs Predicted to Interfere With the Gene Regulation Activity of miR-637 and miR-196a-5p in GBM. *Front. Oncol.* **2020**, *10*, 303, doi:10.3389/fonc.2020.00303.
254. Chen, G.-Y.; Zhang, Z.-S.; Chen, Y.; Li, Y. Long Non-coding RNA SNHG9 Inhibits Ovarian Cancer Progression by Sponging microRNA-214-5p. *Oncol. Lett.* **2020**, *21*, 80, doi:10.3892/ol.2020.12341.
255. Sun, X.; Qian, Y.; Wang, X.; Cao, R.; Zhang, J.; Chen, W.; Fang, M. LncRNA TRG-AS1 Stimulates Hepatocellular Carcinoma Progression by Sponging miR-4500 to Modulate BACH1. *Cancer Cell Int.* **2020**, *20*, 367, doi:10.1186/s12935-020-01440-3.
256. Huang, K.; Yue, X.; Zheng, Y.; Zhang, Z.; Cheng, M.; Li, L.; Chen, Z.; Yang, Z.; Bian, E.; Zhao, B. Development and Validation of an Mesenchymal-Related Long Non-Coding RNA Prognostic Model in Glioma. *Front. Oncol.* **2021**, *11*, 726745, doi:10.3389/fonc.2021.726745.
257. Li, W.; Cui, Y.; Ma, W.; Wang, M.; Cai, Y.; Jiang, Y. LncRNA RBPMS-AS1 Promotes NRGN Transcription to Enhance the Radiosensitivity of Glioblastoma through the microRNA-301a-3p/CAMTA1 Axis. *Transl. Oncol.* **2022**, *15*, 101282, doi:10.1016/j.tranon.2021.101282.
258. Su, Y.-K.; Lin, J.W.; Shih, J.-W.; Chuang, H.-Y.; Fong, I.-H.; Yeh, C.-T.; Lin, C.-M. Targeting BC200/miR218-5p Signaling Axis for Overcoming Temozolomide Resistance and Suppressing Glioma Stemness. *Cells* **2020**, *9*, 1859, doi:10.3390/cells9081859.
259. Zhao, C.; Gao, Y.; Guo, R.; Li, H.; Yang, B. Microarray Expression Profiles and Bioinformatics Analysis of mRNAs, lncRNAs, and circRNAs in the Secondary Temozolomide-Resistant Glioblastoma. *Invest. New Drugs* **2020**, *38*, 1227–1235, doi:10.1007/s10637-019-00884-3.
260. Zhou, Y.; Dai, W.; Wang, H.; Pan, H.; Wang, Q. Long Non-Coding RNA CASP5 Promotes the Malignant Phenotypes of Human Glioblastoma Multiforme. *Biochem. Biophys. Res. Commun.* **2018**, *500*, 966–972, doi:10.1016/j.bbrc.2018.04.217.
261. Shi, W.; Ding, W.; Zhao, Z.; Wang, R.; Wang, F.; Tang, Y.; Zhu, J.; Su, C.; Zhao, X.; Liu, L. Peroxidase Is a Novel Potential Marker in Glioblastoma through Bioinformatics Method and Experimental Validation. *Front. Genet.* **2022**, *13*, 990344, doi:10.3389/fgene.2022.990344.
262. Zhang, L.; Wang, H.; Xu, M.; Chen, F.; Li, W.; Hu, H.; Yuan, Q.; Su, Y.; Liu, X.; Wuri, J.; et al. Long Noncoding RNA HAS2-AS1 Promotes Tumor Progression in Glioblastoma via Functioning as a Competing Endogenous RNA. *J. Cell. Biochem.* **2020**, *121*, 661–671, doi:10.1002/jcb.29313.
263. Huang, Y.; Deng, S.; Jiang, Q.; Shi, J. LncRNA RARA-AS1 Could Serve as a Novel Prognostic Biomarker in Pan-Cancer and Promote Proliferation and Migration in Glioblastoma. *Sci. Rep.* **2023**, *13*, 17376, doi:10.1038/s41598-023-44677-4.
264. Wang, Z.; Ji, X.; Gao, L.; Guo, X.; Lian, W.; Deng, K.; Xing, B. Comprehensive In Silico Analysis of a Novel Serum Exosome-Derived Competitive Endogenous RNA Network for Constructing a Prognostic Model for Glioblastoma. *Front. Oncol.* **2021**, *11*, 553594, doi:10.3389/fonc.2021.553594.
265. Cai, T.; Liu, Y.; Xiao, J. Long Noncoding RNA MALAT 1 Knockdown Reverses Chemoresistance to Temozolomide via Promoting Micro RNA -101 in Glioblastoma. *Cancer Med.* **2018**, *7*, 1404–1415, doi:10.1002/cam4.1384.

266. Zhang, L.; Wang, H.; Xu, M.; Chen, F.; Li, W.; Hu, H.; Yuan, Q.; Su, Y.; Liu, X.; Wuri, J.; et al. Long Noncoding RNA HAS2-AS1 Promotes Tumor Progression in Glioblastoma via Functioning as a Competing Endogenous RNA. *J. Cell. Biochem.* **2020**, *121*, 661–671, doi:10.1002/jcb.29313.
267. Cardoso, A.M.; Morais, C.M.; Rebelo, O.; Tão, H.; Barbosa, M.; Pedroso De Lima, M.C.; Jurado, A.S. Downregulation of Long Non-Protein Coding RNA MVIH Impairs Glioblastoma Cell Proliferation and Invasion through an miR-302a-Dependent Mechanism. *Hum. Mol. Genet.* **2021**, *30*, 46–64, doi:10.1093/hmg/ddab009.
268. Yi, T.; Song, Y.; Zuo, L.; Wang, S.; Miao, J. LINC00470 Stimulates Methylation of PTEN to Facilitate the Progression of Endometrial Cancer by Recruiting DNMT3a Through MYC. *Front. Oncol.* **2021**, *11*, 646217, doi:10.3389/fonc.2021.646217.
269. Cardenosa-Rubio, M.C.; Graybill, R.M.; Bailey, R.C. Combining Asymmetric PCR-Based Enzymatic Amplification with Silicon Photonic Microring Resonators for the Detection of lncRNAs from Low Input Human RNA Samples. *The Analyst* **2018**, *143*, 1210–1216, doi:10.1039/C7AN02045G.
270. Porto, F.W.; Daulatabad, S.V.; Janga, S.C. Long Non-Coding RNA Expression Levels Modulate Cell-Type-Specific Splicing Patterns by Altering Their Interaction Landscape with RNA-Binding Proteins. *Genes* **2019**, *10*, 593, doi:10.3390/genes10080593.
271. Bi, C.-L.; Liu, J.-F.; Zhang, M.-Y.; Lan, S.; Yang, Z.-Y.; Fang, J.-S. LncRNA NEAT1 Promotes Malignant Phenotypes and TMZ Resistance in Glioblastoma Stem Cells by Regulating Let-7g-5p/MAP3K1 Axis. *Biosci. Rep.* **2020**, *40*, BSR20201111, doi:10.1042/BSR20201111.
272. Pokorná, M.; Hudec, M.; Juříčková, I.; Vácha, M.; Polívková, Z.; Kútna, V.; Pala, J.; Ovsepian, S.V.; Černá, M.; O'Leary, V.B. All-Trans Retinoic Acid Fosters the Multifarious U87MG Cell Line as a Model of Glioblastoma. *Brain Sci.* **2021**, *11*, 812, doi:10.3390/brainsci11060812.
273. Wang, J.; Qin, C.; Zhong, C.; Wen, Y.; Ke, S.; Liao, B. Long Non-Coding RNA CASC2 Targeting miR-18a Suppresses Glioblastoma Cell Growth, Metastasis and EMT in Vitro and in Vivo. *J. Biosci.* **2020**, *45*, 107, doi:10.1007/s12038-020-00077-8.
274. Shang, C.; Tang, W.; Pan, C.; Hu, X.; Hong, Y. Long Non-Coding RNA TUSC7 Inhibits Temozolomide Resistance by Targeting miR-10a in Glioblastoma. *Cancer Chemother. Pharmacol.* **2018**, *81*, 671–678, doi:10.1007/s00280-018-3522-y.
275. He, D.; Xin, T.; Pang, B.; Sun, J.; Liu, Z.H.; Qin, Z.; Ji, X.S.; Yang, F.; Wei, Y.B.; Wang, Z.X.; et al. A Novel lncRNA MDHDH Suppresses Glioblastoma Multiforme by Acting as a Scaffold for MDH2 and PSMA1 to Regulate NAD+ Metabolism and Autophagy. *J. Exp. Clin. Cancer Res.* **2022**, *41*, 349, doi:10.1186/s13046-022-02543-7.
276. Huang, C.; Shao, T.; Duan, F.; Li, R.; Luo, M.; Huang, Q.; Wang, Y.; Luo, Z. Lncrna Foxd3-As1 Contributes to Glioblastoma Progression via Sponging Mir-3918 to Upregulate Ccnd1. *Turk. Neurosurg.* **2023**, doi:10.5137/1019-5149.JTN.38366-22.2.
277. Shen, J.; Hodges, T.R.; Song, R.; Gong, Y.; Calin, G.A.; Heimberger, A.B.; Zhao, H. Serum HOTAIR and GAS5 Levels as Predictors of Survival in Patients with Glioblastoma. *Mol. Carcinog.* **2018**, *57*, 137–141, doi:10.1002/mc.22739.
278. Wan, W.; Hou, Y.; Wang, K.; Cheng, Y.; Pu, X.; Ye, X. The LXR-623-Induced Long Non-Coding RNA LINC01125 Suppresses the Proliferation of Breast Cancer Cells via PTEN/AKT/P53 Signaling Pathway. *Cell Death Dis.* **2019**, *10*, 248, doi:10.1038/s41419-019-1440-5.

279. Chen, S.; Li, W.; Guo, A. LOXL1-AS1 Predicts Poor Prognosis and Promotes Cell Proliferation, Migration, and Invasion in Osteosarcoma. *Biosci. Rep.* **2019**, *39*, BSR20190447, doi:10.1042/BSR20190447.
280. Peng, Q.; Li, R.; Li, Y.; Xu, X.; Ni, W.; Lin, H.; Ning, L. Prediction of a Competing Endogenous RNA Co-expression Network as a Prognostic Marker in Glioblastoma. *J. Cell. Mol. Med.* **2020**, *24*, 13346–13355, doi:10.1111/jcmm.15957.
281. Zhou, L.; Huang, X.; Zhang, Y.; Wang, J.; Li, H.; Huang, H. PSMG3-AS1 Enhances Glioma Resistance to Temozolomide via Stabilizing c-Myc in the Nucleus. *Brain Behav.* **2022**, *12*, e2531, doi:10.1002/brb3.2531.
282. Zhu, H.; Chen, Z.; Shen, L.; Tang, T.; Yang, M.; Zheng, X. Long Noncoding RNA LINC-PINT Suppresses Cell Proliferation, Invasion, and EMT by Blocking Wnt/β-Catenin Signaling in Glioblastoma. *Front. Pharmacol.* **2021**, *11*, 586653, doi:10.3389/fphar.2020.586653.
283. Voce, D.J.; Bernal, G.M.; Wu, L.; Crawley, C.D.; Zhang, W.; Mansour, N.M.; Cahill, K.E.; Szymura, S.J.; Uppal, A.; Raleigh, D.R.; et al. Temozolomide Treatment Induces lncRNA MALAT1 in an NF-κB and P53 Codependent Manner in Glioblastoma. *Cancer Res.* **2019**, *79*, 2536–2548, doi:10.1158/0008-5472.CAN-18-2170.
284. Dodangeh, F.; Sadeghi, Z.; Maleki, P.; Raheb, J. Long Non-Coding RNA SOX2-OT Enhances Cancer Biological Traits via Sponging to Tumor Suppressor miR-122-3p and miR-194-5p in Non-Small Cell Lung Carcinoma. *Sci. Rep.* **2023**, *13*, 12371, doi:10.1038/s41598-023-39000-0.
285. Wang, H.; Liu, D.; Yang, J. Prognostic Risk Model Construction and Molecular Marker Identification in Glioblastoma Multiforme Based on mRNA/microRNA/Long Non-Coding RNA Analysis Using Random Survival Forest Method. *Neoplasma* **2019**, *66*, 459–469, doi:10.4149/neo_2018_181008N746.
286. Liao, K.; Lin, Y.; Gao, W.; Xiao, Z.; Medina, R.; Dmitriev, P.; Cui, J.; Zhuang, Z.; Zhao, X.; Qiu, Y.; et al. Blocking lncRNA MALAT1/miR-199a/ZHX1 Axis Inhibits Glioblastoma Proliferation and Progression. *Mol. Ther. Nucleic Acids* **2019**, *18*, 388–399, doi:10.1016/j.omtn.2019.09.005.
287. Balci, T.; Yilmaz Susluer, S.; Kayabasi, C.; Ozmen Yelken, B.; Biray Avci, C.; Gunduz, C. Analysis of Dysregulated Long Non-Coding RNA Expressions in Glioblastoma Cells. *Gene* **2016**, *590*, 120–122, doi:10.1016/j.gene.2016.06.024.
288. Lv, D.; Wang, X.; Dong, J.; Zhuang, Y.; Huang, S.; Ma, B.; Chen, P.; Li, X.; Zhang, B.; Li, Z.; et al. Systematic Characterization of lncRNAs' Cell-to-Cell Expression Heterogeneity in Glioblastoma Cells. *Oncotarget* **2016**, *7*, 18403–18414, doi:10.18632/oncotarget.7580.
289. Wang, Y.; Xie, T.; Liu, H.; Yu, X. LncRNA HLA-F-AS1 Enhances the Migration, Invasion and Apoptosis of Glioblastoma Cells by Targeting lncRNA MEG3. *Cancer Manag. Res.* **2021**, *Volume 13*, 9139–9145, doi:10.2147/CMAR.S322351.
290. Pang, B.; Quan, F.; Ping, Y.; Hu, J.; Lan, Y.; Pang, L. Dissecting the Invasion-Associated Long Non-Coding RNAs Using Single-Cell RNA-Seq Data of Glioblastoma. *Front. Genet.* **2021**, *11*, 633455, doi:10.3389/fgene.2020.633455.
291. Liu, Q.; Qi, C.; Li, G.; Su, W. Prediction of the Outcome for Patients with Glioblastoma with lncRNA Expression Profiles. *BioMed Res. Int.* **2019**, *2019*, 1–10, doi:10.1155/2019/5076467.

292. Hazra, R.; Utama, R.; Naik, P.; Dobin, A.; Spector, D.L. Identification of Glioblastoma Stem Cell-Associated lncRNAs Using Single-Cell RNA Sequencing Datasets. *Stem Cell Rep.* **2023**, *18*, 2056–2070, doi:10.1016/j.stemcr.2023.10.004.
293. Guo, H.; Wu, L.; Yang, Q.; Ye, M.; Zhu, X. Functional Linc-POU3F3 Is Overexpressed and Contributes to Tumorigenesis in Glioma. *Gene* **2015**, *554*, 114–119, doi:10.1016/j.gene.2014.10.038.
294. Li, D.; Lu, J.; Li, H.; Qi, S.; Yu, L. Identification of a Long Noncoding RNA Signature to Predict Outcomes of Glioblastoma. *Mol. Med. Rep.* **2019**, doi:10.3892/mmr.2019.10184.
295. Zhao, R.; Sa, X.; Ouyang, N.; Zhang, H.; Yang, J.; Pan, J.; Gu, J.; Zhou, Y. A Pan-Cancer Analysis of Transcriptome and Survival Reveals Prognostic Differentially Expressed LncRNAs and Predicts Novel Drugs for Glioblastoma Multiforme Therapy. *Front. Genet.* **2021**, *12*, 723725, doi:10.3389/fgene.2021.723725.
296. Jin, Z.; Li, H.; Long, Y.; Liu, R.; Ni, X. MicroRNA-1269 Is Downregulated in Glioblastoma and Its Maturation Is Regulated by Long Non-Coding RNA SLC16A1 Antisense RNA 1. *Bioengineered* **2022**, *13*, 12749–12759, doi:10.1080/21655979.2022.2070581.
297. Zhang, Z.; Yin, J.; Lu, C.; Wei, Y.; Zeng, A.; You, Y. Exosomal Transfer of Long Non-Coding RNA SBF2-AS1 Enhances Chemoresistance to Temozolomide in Glioblastoma. *J. Exp. Clin. Cancer Res.* **2019**, *38*, 166, doi:10.1186/s13046-019-1139-6.
298. Jiang, G.; Dong, H.; Dong, Y.; Yang, X. Long Non-coding RNA Unigene56159 Promotes Glioblastoma Multiforme Cell Proliferation and Invasion through Negatively Regulating microRNA-194-5p. *Mol. Med. Rep.* **2019**, doi:10.3892/mmr.2019.10852.
299. Wang, Y.; Wang, S.; Wang, H.; Zhao, D.; Zhang, H.; Liu, H.; Cui, J.; Wang, K. Knockdown of Long Non-Coding RNA LINC00941 Suppressed Cell Proliferation, Colony-Formation, and Migration of Human Glioblastoma Cell Lines. *Folia Neuropathol.* **2023**, *61*, 209–216, doi:10.5114/fn.2023.126894.
300. Guo, K.; Fang, L.; Li, M.; Li, A.; Liu, N. Long Non-Coding RNA KTN1-AS1 Targets miR-505 to Promote Glioblastoma Progression. *Behav. Neurol.* **2023**, *2023*, 1–11, doi:10.1155/2023/4190849.
301. Li, D.; Hu, J.; Li, S.; Zhou, C.; Feng, M.; Li, L.; Gao, Y.; Chen, X.; Wu, X.; Cao, Y.; et al. LINC01393, a Novel Long Non-Coding RNA, Promotes the Cell Proliferation, Migration and Invasion through MiR-128-3p/NUSAP1 Axis in Glioblastoma. *Int. J. Mol. Sci.* **2023**, *24*, 5878, doi:10.3390/ijms24065878.
302. Liu, K.; Deng, Y.; Yang, Y.; Wang, H.; Zhou, P. MicorRNA-195 Links Long Non-Coding RNA SEMA3B Antisense RNA 1 (Head to Head) and Cyclin D1 to Regulate the Proliferation of Glioblastoma Cells. *Bioengineered* **2022**, *13*, 8798–8805, doi:10.1080/21655979.2022.2052646.
303. Gong, M.; Wang, X.; Mu, L.; Wang, Y.; Pan, J.; Yuan, X.; Zhou, H.; Xing, J.; Wang, R.; Sun, J.; et al. Steroid Receptor Coactivator-1 Enhances the Stemness of Glioblastoma by Activating Long Noncoding RNA XIST/miR-152/KLF4 Pathway. *Cancer Sci.* **2021**, *112*, 604–618, doi:10.1111/cas.14685.
304. Villa, G.R.; Chiocca, E.A. The Role of Long Noncoding Ribonucleic Acids in Glioblastoma: What the Neurosurgeon Should Know. *Neurosurgery* **2023**, *92*, 1104–1111, doi:10.1227/neu.0000000000002449.
305. Li, X.; Chen, R.; Ren, C.; Huang, A.; Ding, W.; Wang, H. Systematic Analysis of the Long Noncoding RNA (lncRNA)-miRNA-mRNA Competing Endogenous RNA Network to

Identify Prognostic Biomarkers and the Potential Regulatory Axis in Glioblastoma Multiforme. *Transl. Cancer Res.* **2021**, *10*, 4739–4755, doi:10.21037/tcr-21-1162.
306. Wu, Z. MiR-195 Connects lncRNA RUNX1-IT1 and Cyclin D1 to Regulate the Proliferation of Glioblastoma Cells. *Int. J. Neurosci.* **2023**, *133*, 13–18, doi:10.1080/00207454.2021.1881090.
307. Shi, J.; Wang, Y.-J.; Sun, C.-R.; Qin, B.; Zhang, Y.; Chen, G. Long Noncoding RNA lncHERG Promotes Cell Proliferation, Migration and Invasion in Glioblastoma. *Oncotarget* **2017**, *8*, 108031–108041, doi:10.18632/oncotarget.22446.
308. Long, Y.; Li, H.; Jin, Z.; Zhang, X. LncRNA SLC16A1-AS1 Is Upregulated in Glioblastoma and Promotes Cancer Cell Proliferation by Regulating miR-149 Methylation. *Cancer Manag. Res.* **2021**, *Volume 13*, 1215–1223, doi:10.2147/CMAR.S264613.
309. Liu, X.; Chen, R.; Liu, L. SP1–DLEU1–miR-4429 Feedback Loop Promotes Cell Proliferative and Anti-Apoptotic Abilities in Human Glioblastoma. *Biosci. Rep.* **2019**, *39*, BSR20190994, doi:10.1042/BSR20190994.
310. Zhong, C.; Yu, Q.; Peng, Y.; Zhou, S.; Liu, Z.; Deng, Y.; Guo, L.; Zhao, S.; Chen, G. Novel LncRNA OXCT1-AS1 Indicates Poor Prognosis and Contributes to Tumorigenesis by Regulating miR-195/CDC25A Axis in Glioblastoma. *J. Exp. Clin. Cancer Res.* **2021**, *40*, 123, doi:10.1186/s13046-021-01928-4.
311. Kraus, T.F.J.; Langwieder, C.K.; Hölzl, D.; Hutarew, G.; Schlicker, H.U.; Alinger-Scharinger, B.; Schwartz, C.; Sotlar, K. Dissecting the Methylomes of EGFR-Amplified Glioblastoma Reveals Altered DNA Replication and Packaging, and Chromatin and Gene Silencing Pathways. *Cancers* **2023**, *15*, 3525, doi:10.3390/cancers15133525.
312. Luo, X.; Tu, T.; Zhong, Y.; Xu, S.; Chen, X.; Chen, L.; Yang, F. ceRNA Network Analysis Shows That lncRNA CRNDE Promotes Progression of Glioblastoma Through Sponge Mir-9-5p. *Front. Genet.* **2021**, *12*, 617350, doi:10.3389/fgene.2021.617350.
313. Li, S.; Wang, Y.; Cao, Q.; Li, H.; Zhao, Z.; Wei, B.; Yuan, H.; Chen, Z.; Yang, S. GLIDR Promotes the Aggressiveness Progression of Prostate Cancer Cells by Sponging miR-128–3p. *Pathol. - Res. Pract.* **2023**, *242*, 154343, doi:10.1016/j.prp.2023.154343.
314. Zhao, H.; Li, J.; Yan, X.; Bian, X. LncRNA MAFG-AS1 Suppresses the Maturation of miR-34a to Promote Glioblastoma Cell Proliferation. *Cancer Manag. Res.* **2021**, *Volume 13*, 3493–3501, doi:10.2147/CMAR.S274615.
315. Hu, T.; Wang, F.; Han, G. LncRNA PSMB8-AS1 Acts as ceRNA of miR-22-3p to Regulate DDIT4 Expression in Glioblastoma. *Neurosci. Lett.* **2020**, *728*, 134896, doi:10.1016/j.neulet.2020.134896.
316. Mu, Y.; Tang, Q.; Feng, H.; Zhu, L.; Wang, Y. lncRNA KTN1-AS1 Promotes Glioma Cell Proliferation and Invasion by Negatively Regulating miR-505-3p. *Oncol. Rep.* **2020**, *44*, 2645–2655, doi:10.3892/or.2020.7821.
317. Jiang, J.; Wang, X.; Lu, J. PWRN1 Suppressed Cancer Cell Proliferation and Migration in Glioblastoma by Inversely Regulating Hsa-miR-21-5p. *Cancer Manag. Res.* **2020**, *Volume 12*, 5313–5322, doi:10.2147/CMAR.S250166.
318. Wang, X.; Yu, X.; Xu, H.; Wei, K.; Wang, S.; Wang, Y.; Han, J. Serum-Derived Extracellular Vesicles Facilitate Temozolomide Resistance in Glioblastoma through a HOTAIR-Dependent Mechanism. *Cell Death Dis.* **2022**, *13*, 344, doi:10.1038/s41419-022-04699-8.

319. Wang, G.; Lin, X.; Han, H.; Zhang, H.; Li, X.; Feng, M.; Jiang, C. lncRNA H19 Promotes Glioblastoma Multiforme Development by Activating Autophagy by Sponging miR-491-5p. *Bioengineered* **2022**, *13*, 11440–11455, doi:10.1080/21655979.2022.2065947.
320. Sun, J.; Wang, L. HOXA-AS2 Enhances GBM Cell Malignancy by Suppressing miR-2116-3p Thereby Upregulating SERPINA3. *BMC Cancer* **2022**, *22*, 366, doi:10.1186/s12885-022-09462-y.
321. Yuan, Y.; Jiaoming, L.; Xiang, W.; Yanhui, L.; Shu, J.; Maling, G.; Qing, M. Analyzing the Interactions of mRNAs, miRNAs, lncRNAs and circRNAs to Predict Competing Endogenous RNA Networks in Glioblastoma. *J. Neurooncol.* **2018**, *137*, 493–502, doi:10.1007/s11060-018-2757-0.
322. Hu, S.; Yao, Y.; Hu, X.; Zhu, Y. LncRNA DCST1-AS1 Downregulates miR-29b through Methylation in Glioblastoma (GBM) to Promote Cancer Cell Proliferation. *Clin. Transl. Oncol.* **2020**, *22*, 2230–2235, doi:10.1007/s12094-020-02363-1.
323. Yu, Q.; Li, X.; Feng, T. GLIDR Promotes the Progression of Glioma by Regulating the miR-4677-3p/MAGI2 Axis. *Exp. Cell Res.* **2021**, *406*, 112726, doi:10.1016/j.yexcr.2021.112726.
324. Reon, B.J.; Takao Real Karia, B.; Kiran, M.; Dutta, A. *LINC00152* Promotes Invasion through a 3′-Hairpin Structure and Associates with Prognosis in Glioblastoma. *Mol. Cancer Res.* **2018**, *16*, 1470–1482, doi:10.1158/1541-7786.MCR-18-0322.
325. Shao, L.; He, Q.; Liu, Y.; Liu, X.; Zheng, J.; Ma, J.; Liu, L.; Li, H.; Li, Z.; Xue, Y. UPF1 Regulates the Malignant Biological Behaviors of Glioblastoma Cells via Enhancing the Stability of Linc-00313. *Cell Death Dis.* **2019**, *10*, 629, doi:10.1038/s41419-019-1845-1.
326. Lu, Y.; Tian, M.; Liu, J.; Wang, K. LINC00511 Facilitates Temozolomide Resistance of Glioblastoma Cells via Sponging miR-126-5p and Activating Wnt/Β-catenin Signaling. *J. Biochem. Mol. Toxicol.* **2021**, *35*, e22848, doi:10.1002/jbt.22848.
327. Gao, Y.; Xu, Y.; Wang, J.; Yang, X.; Wen, L.; Feng, J. lncRNA MNX1-AS1 Promotes Glioblastoma Progression Through Inhibition of miR-4443. *Oncol. Res. Featur. Preclin. Clin. Cancer Ther.* **2019**, *27*, 341–347, doi:10.3727/096504018X15228909735079.
328. Wang, G.; Li, Z.; Tian, N.; Han, L.; Fu, Y.; Guo, Z.; Tian, Y. miR-148b-3p Inhibits Malignant Biological Behaviors of Human Glioma Cells Induced by High HOTAIR Expression. *Oncol. Lett.* **2016**, *12*, 879–886, doi:10.3892/ol.2016.4743.
329. Peng, G.; Su, J.; Xiao, S.; Liu, Q. LINC00152 Acts as a Potential Marker in Gliomas and Promotes Tumor Proliferation and Invasion through the LINC00152/miR-107/RAB10 Axis. *J. Neurooncol.* **2021**, *154*, 285–299, doi:10.1007/s11060-021-03836-1.
330. Oliver, L.; Landais, Y.; Gratas, C.; Cartron, P.-F.; Paris, F.; Heymann, D.; Vallette, F.M.; Serandour, A. Transcriptional Landscape of the Interaction of Human Mesenchymal Stem Cells with Glioblastoma in Bioprinted Co-Cultures. *Stem Cell Res. Ther.* **2024**, *15*, 424, doi:10.1186/s13287-024-04022-6.
331. Lu, H.; Chen, Y.; Yu, Y.; Liao, X.; Liang, H.; Liang, L.; Mo, P.; Huang, X.; Ding, S.; Liu, C.; et al. Gene Expression Profile Identifies LncRNA AL355974.3 As a Potential Glioma Biomarker. *Curr. Med. Sci.* **2024**, *44*, 1047–1057, doi:10.1007/s11596-024-2899-6.
332. Lan, L.; Liang, Z.; Zhao, Y.; Mo, Y. LncRNA MCM3AP-AS1 Inhibits Cell Proliferation in Cervical Squamous Cell Carcinoma by down-Regulating miRNA-93. *Biosci. Rep.* **2020**, *40*, BSR20193794, doi:10.1042/BSR20193794.
333. Wang, D.; Cao, X.; Han, Y.; Yu, D. LncRNA SNHG9 Is Downregulated in Non-Small Cell Lung Cancer and Suppressed miR-21 Through Methylation to Promote Cell

Proliferation. *Cancer Manag. Res.* **2020**, *Volume 12*, 7941–7948, doi:10.2147/CMAR.S253052.
334. Cao, S.; Zheng, J.; Liu, X.; Liu, Y.; Ruan, X.; Ma, J.; Liu, L.; Wang, D.; Yang, C.; Cai, H.; et al. FXR1 Promotes the Malignant Biological Behavior of Glioma Cells via Stabilizing MIR17HG. *J. Exp. Clin. Cancer Res.* **2019**, *38*, 37, doi:10.1186/s13046-018-0991-0.
335. Li, X.; Zhang, J.; Zhang, M.; Qi, X.; Wang, S.; Teng, J. Construction and Comprehensive Analysis of a Competitive Endogenous RNA Network to Reveal Potential Biomarkers for the Malignant Differentiation of Glioma. *Medicine (Baltimore)* **2021**, *100*, e27248, doi:10.1097/MD.0000000000027248.
336. Chen, H.-H.; Zong, J.; Wang, S.-J. LncRNA GAPLINC Promotes the Growth and Metastasis of Glioblastoma by Sponging miR-331-3p. *Eur. Rev. Med. Pharmacol. Sci.* **2019**, *23*, 262–270, doi:10.26355/eurrev_201901_16772.
337. Qi, J.; Pan, L.; Yu, Z.; Ni, W. The lncRNA RP3-439F8.1 Promotes GBM Cell Proliferation and Progression by Sponging miR-139-5p to Upregulate NR5A2. *Pathol. - Res. Pract.* **2021**, *223*, 153319, doi:10.1016/j.prp.2020.153319.
338. Kim, S.-S.; Harford, J.B.; Moghe, M.; Rait, A.; Pirollo, K.F.; Chang, E.H. Targeted Nanocomplex Carrying siRNA against MALAT1 Sensitizes Glioblastoma to Temozolomide. *Nucleic Acids Res.* **2018**, *46*, 1424–1440, doi:10.1093/nar/gkx1221.
339. Zhang, L.; Wang, Q.; Wang, F.; Zhang, X.; Zhang, L.; Tang, Y.; Wang, S. LncRNA LINC01446 Promotes Glioblastoma Progression by Modulating miR-489-3p/TPT1 Axis. *Biochem. Biophys. Res. Commun.* **2018**, *503*, 1484–1490, doi:10.1016/j.bbrc.2018.07.067.
340. Zhang, X.; Niu, W.; Mu, M.; Hu, S.; Niu, C. Long Non-Coding RNA LPP-AS2 Promotes Glioma Tumorigenesis via miR-7-5p/EGFR/PI3K/AKT/c-MYC Feedback Loop. *J. Exp. Clin. Cancer Res.* **2020**, *39*, 196, doi:10.1186/s13046-020-01695-8.
341. Okamoto, R.; Toya, K.; Ogino, Y.; Sato, A. Downregulation of Long Noncoding RNA *TP73-AS1* Expression Confers Resistance to Temozolomide in Human Glioblastoma Cells. *Nucleosides Nucleotides Nucleic Acids* **2024**, *43*, 86–98, doi:10.1080/15257770.2023.2234960.
342. Zhang, X.-Q.; Sun, S.; Lam, K.-F.; Kiang, K.M.-Y.; Pu, J.K.-S.; Ho, A.S.-W.; Lui, W.-M.; Fung, C.-F.; Wong, T.-S.; Leung, G.K.-K. A Long Non-Coding RNA Signature in Glioblastoma Multiforme Predicts Survival. *Neurobiol. Dis.* **2013**, *58*, 123–131, doi:10.1016/j.nbd.2013.05.011.
343. Sakurai, K.; Ito, H. Multifaced Roles of the Long Non-Coding RNA DRAIC in Cancer Progression. *Life Sci.* **2024**, *343*, 122544, doi:10.1016/j.lfs.2024.122544.
344. Fattahi, M.; Alamdari-palangi, V.; Rahimi Jaberi, K.; Ehtiati, S.; Ojaghi, S.; Rahimi-Jaberi, A.; Samavarchi Tehrani, S.; Dang, P.; Movahedpour, A.; Hossein Khatami, S. Exosomal Long Non-Coding RNAs in Glioblastoma. *Clin. Chim. Acta* **2024**, *553*, 117705, doi:10.1016/j.cca.2023.117705.
345. Wang, W.; Liu, W. Integration of Gene Interaction Information into a Reweighted Random Survival Forest Approach for Accurate Survival Prediction and Survival Biomarker Discovery. *Sci. Rep.* **2018**, *8*, 13202, doi:10.1038/s41598-018-31497-0.
346. Luo, Q.; Yang, Z.; Deng, R.; Pang, X.; Han, X.; Liu, X.; Du, J.; Tian, Y.; Wu, J.; Tang, C. Comprehensive Analysis of Prognosis of Patients with GBM Based on 4 m6A-Related lncRNAs and Immune Cell Infiltration. *Heliyon* **2023**, *9*, e12838, doi:10.1016/j.heliyon.2023.e12838.

347. Mohammad, A.-A.; Rahbar, A.; Lui, W.-O.; Davoudi, B.; Catrina, A.; Stragliotto, G.; Mellbin, L.; Hamsten, A.; Rydén, L.; Yaiw, K.-C.; et al. Detection of Circulating Hcmv-miR-UL112-3p in Patients with Glioblastoma, Rheumatoid Arthritis, Diabetes Mellitus and Healthy Controls. *PLoS ONE* **2014**, *9*, e113740, doi:10.1371/journal.pone.0113740.
348. Zhang, Y.; Feng, J.; Fu, H.; Liu, C.; Yu, Z.; Sun, Y.; She, X.; Li, P.; Zhao, C.; Liu, Y.; et al. Coagulation Factor X Regulated by CASC2c Recruited Macrophages and Induced M2 Polarization in Glioblastoma Multiforme. *Front. Immunol.* **2018**, *9*, 1557, doi:10.3389/fimmu.2018.01557.
349. Huang, Y.; Liu, L.; Fang, M.; Yan, W. In Silico Analysis Identifies Upregulated lncRNA DLGAP1-AS1 Which Is Correlated to Poor Prognosis and Promotes Cell Proliferation in Glioblastoma. *Comput. Math. Methods Med.* **2022**, *2022*, 1–14, doi:10.1155/2022/5038124.
350. Choudhary, S.; Burns, S.C.; Mirsafian, H.; Li, W.; Vo, D.T.; Qiao, M.; Lei, X.; Smith, A.D.; Penalva, L.O. Genomic Analyses of Early Responses to Radiation in Glioblastoma Reveal New Alterations at Transcription, Splicing, and Translation Levels. *Sci. Rep.* **2020**, *10*, 8979, doi:10.1038/s41598-020-65638-1.
351. Engström, P.G.; Tommei, D.; Stricker, S.H.; Ender, C.; Pollard, S.M.; Bertone, P. Digital Transcriptome Profiling of Normal and Glioblastoma-Derived Neural Stem Cells Identifies Genes Associated with Patient Survival. *Genome Med.* **2012**, *4*, 76, doi:10.1186/gm377.
352. Reon, B.J.; Anaya, J.; Zhang, Y.; Mandell, J.; Purow, B.; Abounader, R.; Dutta, A. Expression of lncRNAs in Low-Grade Gliomas and Glioblastoma Multiforme: An In Silico Analysis. *PLOS Med.* **2016**, *13*, e1002192, doi:10.1371/journal.pmed.1002192.
353. Attenello, F.J.; Tsung, K.; Bishara, I.; Loh, Y.E.; Chen, T.C. *In Vivo* CRISPR Screening for Novel Noncoding RNA Functional Targets in Glioblastoma Models. *J. Neurosci. Res.* **2021**, *99*, 2029–2045, doi:10.1002/jnr.24850.
354. Amer, R.G.; Ezz El Arab, L.R.; Abd El Ghany, D.; Saad, A.S.; Bahie-Eldin, N.; Swellam, M. Prognostic Utility of lncRNAs (LINC00565 and LINC00641) as Molecular Markers in Glioblastoma Multiforme (GBM). *J. Neurooncol.* **2022**, *158*, 435–444, doi:10.1007/s11060-022-04030-7.
355. He, Y.; Wang, L.; Tang, J.; Han, Z. Genome-Wide Identification and Analysis of the Methylation of lncRNAs and Prognostic Implications in the Glioma. *Front. Oncol.* **2021**, *10*, 607047, doi:10.3389/fonc.2020.607047.
356. Jana, S.; Mondal, M.; Mahale, S.; Gupta, B.; Prasasvi, K.R.; Kandasami, L.; Jha, N.; Chowdhury, A.; Santosh, V.; Kanduri, C.; et al. PITAR, a DNA Damage-Inducible Cancer/Testis Long Noncoding RNA, Inactivates P53 by Binding and Stabilizing TRIM28 mRNA. *eLife* **2024**, *12*, RP88256, doi:10.7554/eLife.88256.
357. Yan, Y.; Zhang, L.; Jiang, Y.; Xu, T.; Mei, Q.; Wang, H.; Qin, R.; Zou, Y.; Hu, G.; Chen, J.; et al. LncRNA and mRNA Interaction Study Based on Transcriptome Profiles Reveals Potential Core Genes in the Pathogenesis of Human Glioblastoma Multiforme. *J. Cancer Res. Clin. Oncol.* **2015**, *141*, 827–838, doi:10.1007/s00432-014-1861-6.
358. Ou-Yang, L.; Huang, J.; Zhang, X.-F.; Li, Y.-R.; Sun, Y.; He, S.; Zhu, Z. LncRNA-Disease Association Prediction Using Two-Side Sparse Self-Representation. *Front. Genet.* **2019**, *10*, 476, doi:10.3389/fgene.2019.00476.
359. Ruan, M.; Liu, J.; Ren, X.; Li, C.; Zhao, A.Z.; Li, L.; Yang, H.; Dai, Y.; Wang, Y. Whole Transcriptome Sequencing Analyses of DHA Treated Glioblastoma Cells. *J. Neurol. Sci.* **2019**, *396*, 247–253, doi:10.1016/j.jns.2018.11.027.

360. Chen, G.; Cao, Y.; Zhang, L.; Ma, H.; Shen, C.; Zhao, J. Analysis of Long Non-Coding RNA Expression Profiles Identifies Novel lncRNA Biomarkers in the Tumorigenesis and Malignant Progression of Gliomas. *Oncotarget* **2017**, *8*, 67744–67753, doi:10.18632/oncotarget.18832.
361. Li, Y.; Guo, D. Identification of Novel lncRNA Markers in Glioblastoma Multiforme and Their Clinical Significance: A Study Based on Multiple Sequencing Data. *OncoTargets Ther.* **2020**, *Volume 13*, 1087–1098, doi:10.2147/OTT.S235951.
362. Wang, N.; Li, J.; Xin, Q.; Xu, N. USP30-AS1 Contributes to Mitochondrial Quality Control in Glioblastoma Cells. *Biochem. Biophys. Res. Commun.* **2021**, *581*, 31–37, doi:10.1016/j.bbrc.2021.10.006.
363. Poursheikhani, A.; Mosallaei, M.; Heidari, M.F.; Rajaeinejad, M.; Chamanara, M.; Zoshk, M.Y.; Aslani, P.; Hazrati, E.; Mohammadimehr, M.; Behroozi, J. Long Non-Coding RNA CRNDE, LINC00957, and AC072061.1 as a Promising Diagnostic and Prognostic Biomarker in Glioblastoma Multiforme. *Iran. J. Public Health* **2024**, doi:10.18502/ijph.v53i9.16462.
364. Li, X.; Sun, L.; Wang, X.; Wang, N.; Xu, K.; Jiang, X.; Xu, S. A Five Immune-Related lncRNA Signature as a Prognostic Target for Glioblastoma. *Front. Mol. Biosci.* **2021**, *8*, 632837, doi:10.3389/fmolb.2021.632837.
365. Li, M.; Long, S.; Hu, J.; Wang, Z.; Geng, C.; Ou, S. Systematic Identification of lncRNA-Based Prognostic Biomarkers for Glioblastoma. *Aging* **2019**, *11*, 9405–9423, doi:10.18632/aging.102393.
366. Zhang, J.; Liu, L.; Li, J.; Le, T.D. LncmiRSRN: Identification and Analysis of Long Non-Coding RNA Related miRNA Sponge Regulatory Network in Human Cancer. *Bioinformatics* **2018**, *34*, 4232–4240, doi:10.1093/bioinformatics/bty525.
367. Li, X.; Meng, Y. Immune-Related lncRNA Risk Signatures Predict Survival of IDH Wild-Type and MGMT Promoter Unmethylated Glioblastoma. *BioMed Res. Int.* **2020**, *2020*, 1971284, doi:10.1155/2020/1971284.
368. Zhang, Z.; Ren, P.; Cao, Y.; Wang, T.; Huang, G.; Li, Y.; Zhou, S.; Yang, W.; Yang, L.; Liu, G.; et al. HOXD-AS2-STAT3 Feedback Loop Attenuates Sensitivity to Temozolomide in Glioblastoma. *CNS Neurosci. Ther.* **2023**, *29*, 3430–3445, doi:10.1111/cns.14277.
369. Pancholi, S.; Tripathi, A.; Bhan, A.; Acharya, M.M.; Pillai, P. Emerging Concepts on the Role of Extracellular Vesicles and Its Cargo Contents in Glioblastoma-Microglial Crosstalk. *Mol. Neurobiol.* **2022**, *59*, 2822–2837, doi:10.1007/s12035-022-02752-3.
370. Hongzhen, Z.; Yanyu, L.; Xuexiang, L.; Meiyu, D.; Xiaoli, C.; Yun, G.; Jingfan, C.; Shengming, D. The Diagnostic and Prognostic Significance of Long Non-Coding RNA CRNDE in Pan-Cancer Based on TCGA, GEO and Comprehensive Meta–Analysis. *Pathol. - Res. Pract.* **2019**, *215*, 256–264, doi:10.1016/j.prp.2018.11.008.
371. Isaev, K.; Jiang, L.; Wu, S.; Lee, C.A.; Watters, V.; Fort, V.; Tsai, R.; Coutinho, F.J.; Hussein, S.M.I.; Zhang, J.; et al. Pan-Cancer Analysis of Non-Coding Transcripts Reveals the Prognostic Onco-lncRNA HOXA10-AS in Gliomas. *Cell Rep.* **2021**, *37*, 109873, doi:10.1016/j.celrep.2021.109873.
372. Vecera, M.; Sana, J.; Oppelt, J.; Tichy, B.; Alena, K.; Lipina, R.; Smrcka, M.; Jancalek, R.; Hermanova, M.; Kren, L.; et al. Testing of Library Preparation Methods for Transcriptome Sequencing of Real Life Glioblastoma and Brain Tissue Specimens: A Comparative Study with Special Focus on Long Non-Coding RNAs. *PLOS ONE* **2019**, *14*, e0211978, doi:10.1371/journal.pone.0211978.

373. Zheng, C.; Wei, Y.; Zhang, Q.; Sun, M.; Wang, Y.; Hou, J.; Zhang, P.; Lv, X.; Su, D.; Jiang, Y.; et al. Multiomics Analyses Reveal *DARS1-AS1* /YBX1–Controlled Posttranscriptional Circuits Promoting Glioblastoma Tumorigenesis/Radioresistance. *Sci. Adv.* **2023**, *9*, eadf3984, doi:10.1126/sciadv.adf3984.
374. Zou, Z.; Zhang, M.; Xu, S.; Zhang, Y.; Zhang, J.; Li, Z.; Zhu, X. Computational Identification of Long Non-Coding RNAs Associated with Graphene Therapy in Glioblastoma Multiforme. *Brain Commun.* **2023**, *6*, fcad293, doi:10.1093/braincomms/fcad293.
375. Long, S.; Li, G. Comprehensive Analysis of a Long Non-coding RNA-mediated Competitive Endogenous RNA Network in Glioblastoma Multiforme. *Exp. Ther. Med.* **2019**, doi:10.3892/etm.2019.7647.
376. Zhang, M.; Zhao, K.; Xu, X.; Yang, Y.; Yan, S.; Wei, P.; Liu, H.; Xu, J.; Xiao, F.; Zhou, H.; et al. A Peptide Encoded by Circular Form of LINC-PINT Suppresses Oncogenic Transcriptional Elongation in Glioblastoma. *Nat. Commun.* **2018**, *9*, 4475, doi:10.1038/s41467-018-06862-2.
377. Lu, C.; Wei, Y.; Wang, X.; Zhang, Z.; Yin, J.; Li, W.; Chen, L.; Lyu, X.; Shi, Z.; Yan, W.; et al. DNA-Methylation-Mediated Activating of lncRNA SNHG12 Promotes Temozolomide Resistance in Glioblastoma. *Mol. Cancer* **2020**, *19*, 28, doi:10.1186/s12943-020-1137-5.
378. Dymova, M.A.; Vasileva, N.S.; Kuligina, E.V.; Savinovskaya, Y.I.; Zinchenko, N.D.; Ageenko, A.B.; Mishinov, S.V.; Stepanov, G.A.; Richter, V.A.; Semenov, D.V. MicroRNA and mRNA Expression Changes in Glioblastoma Cells Cultivated under Conditions of Neurosphere Formation. *Curr. Issues Mol. Biol.* **2022**, *44*, 5294–5311, doi:10.3390/cimb44110360.

Appendix

Table 1 Detail information of list of articles involved with PI3K/AKT/mTOR pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[278] (30867411)	LINC01125	PTEN, AKT, p53	Suppresses proliferation of breast cancer cells via the PTEN/AKT/p53 signaling pathway.	Upregulated	PTEN/AKT /p53 signaling axis.	Tumor suppressor	LXR-623	LXR-623 upregulates the expression of the lncRNA LINC01125, which in turn suppresses the proliferation of breast cancer cells via the PTEN/AKT/p53 signaling pathway	Human, female mice	N/A	RT-qPCR
[6] (30837348)	LINC00657	PTEN	Inhibit GBM progression by acting as a molecular sponge for miR-190a-3p, thereby regulating PTEN expression.	Downregulated	miR-190a-3p/PTEN axis	Tumor suppressor	N/A	N/A	N/A	N/A	RT-qPCR
[268] (34249684)	LINC00470	PTEN	Stimulates PTEN methylation to facilitate the progression of endometrial cancer by recruiting DNMT3a through MYC	Upregulated	MYC/DNMT3a pathway	Tumor growth	5-aza-2'-deoxycytidine (5-Aza-CdR)	Expression of PTEN, which was otherwise reduced by LINC00470	Human, mice	103	qRT-PCR
[39] (32378450)	LINC01198	PIK3CA, PTEN	Facilitates glioma genesis through activating the PI3K/AKT pathway	Upregulated	PI3K/AKT signaling pathway	Oncogene	SC79	AKT activator used to rescue the effects of LINC01198 suppression	Human, mice	N/A	qRT-PCR
[40] (32236901)	SAMMSON.	PI3K/Akt pathway	Inhibits the malignancy of cells by inactivating the PI3K/Akt pathway.	Upregulated	PI3K/Akt signaling pathway	Oncogene	740Y-P	Activates the PI3K/Akt pathway, counteracting the effects of SAMMSON knockdown.	Human	19	qRT-PCR
[37] (37247274)	CASC2	AKT	Inhibits the progression of GBM by regulating the expression of the AKT gene	Upregulated	PI3K/Akt/ mTOR signaling pathway	Tumor suppressor	TMZ	Expression of CASC2 was increased after treatment with TMZ and Thiosemicarbazone complexes	Human cell lines	N/A	qRT-PCR
[38] (34454479)	CRNDE	PI3K/Akt /mTOR pathway	Enhances TMZ chemoresistance by regulating autophagy	Upregulated	PI3K/Akt/ mTOR signaling pathway	Tumor growth	TMZ	Upregulation of CRNDE, which is associated with chemoresistance.	Human	58	qRT-PCR
[251] (31888172)	CRNDE	mTOR	Promotes glioma cell growth and invasion through mTOR signaling	N/A	Cancer stemness and invasion.	Oncogene	N/A	N/A	Human	5	Single-cell RNA sequencing

											(scRNA-seq)
[44] (39570470)	NONHSAT159592.1	AKT, ITGA3	inhibits progression and invasion by targeting the ITGA3/FAK/PI3K/AKT pathway	downregulated	ITGA3/FAK/PI3K/AKT signaling pathway	Oncogene	Nanoparticles (NPs)	GBM cell proliferation, invasion, and EMT progression	Human, mice	N/A	qRT-PCR
[45] (29866190)	LINC00470	AKT	Activates AKT, promotes GBM autophagy	Upregulated	PI3K-AKT signaling pathway	Oncogene	N/A	N/A	Human	N/A	RIP, RNA pulldown
[52] (33392085)	LNC01545, WDR11-AS1, NDUFA6-DT, FRY-AS1, and TBX5-AS1	PI3K-Akt, VEGFA-VEGFR2, TGF-beta, Notch, and T-Cell pathways	Associated with survival in GBM patients and are involved in pathways related to oncogenesis and tumor progression	Upregulated & downregulated	PI3K-Akt signaling pathway	Oncogene	N/A	N/A	Human	167	RNA seq
[279]	LOXL1-AS1	PI3K/Akt pathway	Promotes cell proliferation, migration, and invasion in osteosarcoma by regulating the PI3K-AKT pathway	Upregulated	PI3K-AKT signaling pathway	Oncogene	N/A	N/A	Human	96	qRT-PCR
[280] (33047898)	NORAD and XIST	LYZ, PIK3AP1	Affects immune activities and tumor microenvironment variations in GBM	N/a	PI3K/AKT pathway	tumor microenvironment and immune activities	N/A	N/A	Human (M-108, F-59)	167	qRT-PCR
[50] (27432080)	ENSG00000261924.1	RPTOR	Regulating target mRNAs and interacting with various transcription factors.	Upregulated	network of llncRNAs and mRNAs	Tumor suppressor	N/A	N/A	Human	N/A	RT-qPCR
[42] (28499919)	AC023115.3	GSK3β	Suppress chemoresistance in GBM by reducing autophagy. Creasing the chemosensitivity of glioma	Upregulated	miR-26a-GSK3β-Mcl1 pathway	Tumor suppressor	Cisplatin	Upregulates the lncRNA AC023115.3, which in turn promotes cisplatin-induced apoptosis by inhibiting autophagy in cells.	N/A	N/A	qRT-PCR
[7] (34470587)	PITPNA-AS1	EGFR	Stimulates cell proliferation and suppresses cell apoptosis in GBM by targeting the miR-223-3p/EGFR axis and activating the PI3K/AKT signaling pathway	Upregulated	miR-223-3p/EGFR axis and activation of the PI3K/AKT signaling pathway	Tumor growth	N/A	N/A	Human	N/A	RT-qPCR
[43] (35654242)	Linc-RoR	EGFR, Oct4, Sox2, and p53	promote GBM progression by increasing cancer stem cell populations and regulating mitosis.	upregulated	EGFR signaling pathways	Tumor growth	N/A	N/A	N/A	23	qRT-PCR

[41] (37980347)	INHEG	EGFR, IGF1R, CDK6, and PDGFRB	Promote GSC maintenance and tumorigenicity by regulating rrna 2'-O-methylation.	Upregulated	2'-O-methylation and the INHEG/NOP58/snoRNP pathway	Tumor growth	N/A	N/A	Human	2	qRT-PCR, RNA sequencing
[49] (31607216)	MALAT-1, HOTAIR, MVIH, BLACAT1, and NET1.	EGFR, IGF1R, CDK6, and PDGFRB	Serve as prognostic biomarkers for cancer survival, demonstrating their potential to predict patient outcomes across various cancer types.	Upregulated	N/A	N/A	N/A	N/A	Human	N/A	RNA sequencing
[51] (37748218)	DNAJC27-AS1	IDH1, EGFR, PTEN	Predict glioma prognosis and chemoradiotherapy sensitivity through a pseudouridine-related lncrna signature.	Upregulated	pseudouridine-related lncRNAs	Tumor growth, Tumor suppressor, Repair	mitoxantrone	Effective for the low-risk group of glioma patients, but the paper does not specify its direct effect on lncrnas.	Human	N/A	qRT-PCR
[46] (31053733)	TALC	c-Met	Promotes O6-methylguanine-DNA methyltransferase (MGMT) expression by regulating the c-Met pathway through competitive binding with mir-20b-3p	Upregulated	c-Met/Stat3/p300 axis	Oncogene	TMZ	Upregulates the expression of lnc-TALC, which promotes TMZ resistance in GBM cells.	Human, mice	57	qRT-PCR, lncRNA microarray
[281] (35380741)	PSMG3-AS1	c-Myc	Enhances glioma resistance to TMZ by stabilizing c-Myc in the nucleus	Upregulated	c-Myc protein in the nucleus	Oncogene	TMZ	Mediates resistance to TMZ; knockdown of PSMG3-AS1 increases sensitivity to TMZ, while overexpression induces resistance	Human	N/A	qRT-PCR
[10] (36988488)	LINC02283	PDGFRA	Enhances PDGF receptor A-mediated signaling and drives GBM tumorigenesis	Upregulated	AKT and ERK pathways	Growth and repair	TMZ	Interaction leads to increased PDGFRA signaling, which in turn drives tumorigenesis and contributes to the malignancy of cells	Human	N/A	
[48] (34390075)	JPX (just proximal to X-inactive specific transcript)	PDK1	Promotes GBM progression and TMZ chemoresistance by stabilizing PDK1 mrna in an m6a-dependent manner.	Upregulated	FTO/PDK1 axis	Oncogene	TMZ	Promotes the stability of the long non-coding RNA (lncrna) JPX, which in turn enhances GBM progression and chemoresistance.	Human	50	RT-qPCR

Table 2 Detail information of list of articles involved with p53 pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[53] (30867410)	TP73-AS1	TP73-AS1	Promotes TMZ resistance in cancer stem cells	Upregulated	Regulation of metabolism-related genes and ALDH1A1 expression	Oncogene	TMZ	Downregulation of TP73-AS1 leads to increased sensitivity to TMZ in gCSC	Human	N/A	qRT-PCR
[54] (30852975)	LINC-ROR	p53	Upregulated in GBM and is associated with poor disease progression-free and overall survival	upregulated	P53 pathway	Oncogene	N/A	N/A	Human (M-75%, F-24.6%)	N/A	qRT-PCR
[55] (37841928)	H19	TP53	Enhance the pro-apoptotic activity of ITF2357 in colorectal cancer cells by stabilizing TP53 and its transcriptional targets, NOXA and PUMA.	upregulated	TP53 and its transcriptional targets, NOXA and PUMA	Tumor growth and therapy resistance	ITF2357 (givinostat)	Upregulates the lncRNA H19, enhancing its pro-apoptotic activity in colorectal cancer cells.	N/A	N/A	qRT-PCR
[56] (27050376)	TP53TG1	TP53	Radiosensitivity and modulates the expression of TP53	upregulated	P53 signaling pathway.	Tumor suppressor	N/A	N/A	Human	N/A	microarray analysis
[57] (33747284)	PTCSC3	Bax	Inhibits human oral cancer cell proliferation by inducing apoptosis and autophagy	downregulated	Long non-coding RNA PTCSC3	Tumor suppressor	N/A	N/A	Human	N/A	RT-qPCR

Table 3 Detail information of list of articles involved with cell cycle regulation/DNA damage pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[68] (31347720)	FOXD2-AS1	CDK1	Promotes glioma cell cycle progression and proliferation through the FOXD2-AS1/mir-31/CDK1 pathway	Upregulated	FOXD2-AS1/miR-31/CDK1 pathway.	Tumor growth	N/A	N/A	Human	30	qRT-PCR
[74] (34246782)	HOTAIR	CDKN1A, BBC3	Cell cycle progression and can be used as an independent predictor	Upregulated	HOTAIR/EZH2 and HOTAIR/LSD1 pathways.	Tumor growth	AC1Q3QWB (AQB) and GSK-LSD1	Combination of AQB and GSK-LSD1 disrupts the interaction between HOTAIR and EZH2, and inhibits the LSD1 domain,	Human, mice	N/A	Agilent Human ceRNA Microarray

								leading to cell cycle arrest and apoptosis in cells			
[76] (30038703)	ANRIL	CDKN2A, CDKN2B	Regulation of cell proliferation and colony growth	Upregulated & downregulated	INK4b/ARF/INK4a locus.	Tumor growth	N/A	N/A	Human	19	RT-qPCR
[73] (2727775)	HOTAIR	PDCD4, CCND1, CDK4	Regulates gene expression by recruiting chromatin-modifying complexes, affecting the transcription of specific genes.	Downregulated	HOTAIR/EZH2/LSD1 pathway.	Tumor growth	Superparamagnetic iron oxide nanoparticles (SPIONs)	Facilitated the downregulation of HOTAIR expression, which in turn increased the expression of PDCD4 and reduced the expression of CCND1 and CDK4.	Human, mice	N/A	qRT-PCR
[71] (31462285)	SNHG-15	CDK6	Promotes GBM and TMZ resistance by regulating CDK6 and mir-627-5p.	Upregulated	SNHG15/miR-627/CDK6 signaling network	Tumor suppressor	TMZ	TMZ resistance is mediated by SNHG15, while Palbociclib treatment reduces SNHG15 levels and increases sensitivity to TMZ	Human, mouse	40	qRT-PCR
[72] (32309389)	HOXA-AS3, H19, and LINC00152	CDK6, CA12, NRP1	Involved in the progression and poor prognosis of glioma by regulating mirna and promoting tumor progression	Upregulated & regulated	PI3K/AKT and ECM-receptor interaction.	Tumor growth, Tumor suppressor, Repair	N/A	N/A	Human	455	microarray analysis
[69] (35191808)	FOXD3-AS1	WEE1	Promotes cell survival and confers TMZ resistance in GBM cells	Upregulated	miR-128-3p/WEE1 G2 checkpoint kinase axis	Oncogene	TMZ	Higher FOXD3-AS1 expression compared to parental cells. Overexpression of FOXD3-AS1 increased TMZ tolerance in TMZ-sensitive cells, whereas depletion of FOXD3-AS1 sensitized TMZ-resistant cells to TMZ treatment	Human glioma cell	N/A	qRT-PCR
[70] (32633376)	VIM-AS1	WEE1	To regulate glioma cell proliferation, migration, and apoptosis via the VIM-AS1/mir-105-5p/WEE1 signaling pathway.	Upregulated	miR-105-5p/WEE1 signaling axis	Tumor suppressor	N/A	N/A	Human, mice	24	qRT-PCR
[75] (35109908)	LINC00461	TOP2A, BCL2, ITGB3	Promotes the proliferation of GBM cells	Upregulated	HDAC6/RBP/LINC00461 axis	Oncogene	Azaindolylsulfonamide (MPT0B291)	decreases the expression of LINC00461, leading to cell-cycle arrest and suppression of GBM cell proliferation	Human, mice	N/A	RT-qPCR
[58] (34350240)	AC093278.2, AC004067.1, LINC01116,	PRDX1, SEC61B,	Independent prognostic factors for the overall survival of GBM patients	Upregulated & downregulated	IFN-β-associated	Oncogene	β-interferon	IFN-β sensitizes glioma cells that harbor the unmethylated MGMT	Human	50	qRT-PCR

	and AC017104.1	XRCC5, BCL2L2			gene signature		(IFN-β)	promoter and are resistant to TMZ			
[59] (36313669)	CRNDE and XIST	TOP2A, RRM2	Enhances GBM progression by sponging mir-9-5p	Upregulated	lncRNA-miRNA-mRNA competitive endogenous RNA (ceRNA) network	Oncogene	N/A	N/A	Human	34	microarray analysis
[60] (36637626)	LINC01605 and FAS-AS1.	Caspace 3	Involved in apoptosis regulation by increasing the proliferation of cancer cells and preventing their apoptosis	Upregulated & downregulated	apoptosis regulatory network	Tumor growth and repair	N/A	N/A	Human	100	qRT-PCR
[61] (37981063)	LINC00473.	MGMT, CEBPα	Promotes chemoresistance to TMZ in GBM by regulating MGMT expression via cebpα binding.	Upregulated	CREB/LINC00473/CEBPα/MGMT pathway	Oncogene	TMZ	Associated with elevated levels of LINC00473, which promotes chemoresistance by upregulating MGMT expression.	Human, mice (12)	N/A	qRT-PCR
[8] (35219686)	UCA1	MGMT	Modulates glioma cell sensitivity to TMZ through MGMT-related DNA damage pathways	Upregulated	lncRNA UCA1/miR-182-5p/MGMT axis	Oncogene	TMZ	UCA1 knockdown enhances the efficacy of TMZ in affecting glioma cell viability, apoptosis, MGMT protein level, and DNA damage markers.	Human (M-9, F-8), mice	17	qRT-PCR
[62] (39482401)	HOTAIR	MGMT	Associated with TMZ resistance in GBM by activating the mir-214/β-catenin/MGMT pathway	Upregulated	HOTAIR/miR-214/β-catenin/MGMT pathway	Oncogene	TMZ	Methotrexate enhances TMZ sensitivity in TMZ-resistant cells by reducing the expression of HOTAIR and β-catenin	Human	N/A	qRT-PCR
[63] (39356744)	LINC01956	MGMT	Involved in the structural remodeling of RNA, which enhances TMZ resistance in MGMT-methylated GBM	Upregulated	CHK1/DDX46/LINC01956/MGMT pathway	Oncogene	TMZ	Activates a CHK1/DDX46 axis that contributes to the unwinding of the stem-loop structures of LINC01956	Animal	N/A	qRT-PCR
[64] (27229531)	MCM3MP-AS	MCM3AP, MATR3, XPO1, and ZCCHC14	Competitive ceRNA that regulates gene expression and is associated with GBM prognosis.	Upregulated	MCM3AP-AS/MIR17HG ceRNA module	Tumor growth	N/A	N/A	Human (M-262, F-160)	422	qRT-PCR
[65] (31186379)	AGAP2-AS1	TFPI2	Promotes progression by epigenetically silencing TFPI2 expression through interactions with EZH2 and LSD1.	Upregulated	EZH2 and LSD1	Tumor suppressor	N/A	N/A	Human	58	qRT-PCR

[66] (30442884)	AC003092.1	TFPI2	Enhances TMZ chemosensitivity in GBM by modulating the mir-195/TFPI-2 signaling pathway.	Downregulated	miR-195/TFPI-2 signaling axis	Tumor suppressor	TMZ	Upregulating its expression	Human (M-59, F-49), mice	108	qRT-PCR
[67] (33815468)	AC003092.1	TFPI2	Immune-related enhancer RNA (erna) that plays a critical role in the occurrence and development of glioma	Upregulated	miR-195/TFPI2 signaling axis	Tumor growth	TMZ	Inhibiting the function of mir-195, promoting TMZ-induced apoptosis	Human	161	RT-qPCR

Table 4 Detail information of list of articles involved with NF-κB Signaling pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[77] (31612313)	LINC00470.	Cyclin E1, NF90	Promotes hepatocellular carcinoma (HCC) cell proliferation by stabilizing cyclin E1 mrna through association with the NF45/NF90 complex	Upregulated	NF45/NF90 complex	Oncogene	N/A	N/A	Human	80	qRT-PCR
[9] (33130316)	LINC01057	NF-κB	Promotes mesenchymal differentiation by activating NF-κb signaling in GBM	Upregulated	NF-κB signaling pathway	Oncogene	TNF-α	Enhances the effect of LINC01057 on mesenchymal differentiation	Human, animals' model	12	qRT-PCR
[78] (34746949)	DRAIC	NF-κB	Inhibits protein translation and induces autophagy by activating AMPK.	Downregulated	NF-κB inhibition and AMPK activation	Tumor suppressor	N/A	N/A	Human	N/A	qRT-PCR
[86] (37056564)	CD109-AS1 and LINC02447	immune evasion markers, glioma	To act as novel immunoreactive biomarkers for glioma, facilitating immune evasion and contributing to glioma progression	Upregulated	immune regulation and epigenetic mechanisms that facilitate immune evasion	immune evasion biomarkers	N/A	N/A	Human	551	qRT-PCR
[81] (7053197)	NEAT1	interferon-gamma (IFNγ)	Predict treatment outcomes to immune checkpoint inhibitors in cancer by regulating interferon-gamma signaling and inflammatory pathways	Upregulated	interferon-gamma (IFNγ) signaling	immune modulator	N/A	N/A	Human	27	qRT-PCR

[80] (38965580)		IκBα	Promote the malignant progression of GBM	Upregulated	NF-κB signaling pathway	Oncogene	JSH-23	Targets the NF-κB signaling pathway. It effectively inhibits the continuous activation of this pathway induced by the lncRNA XTP6	Human, mice	12	RNA in situ hybridization (RNA-ISH)
[79] (32042800)	MATN1-AS1	RELA	Inhibits GBM cell proliferation and invasion through inhibition of RELA via E2F6 and suppression of the MAPK signaling pathway	Downregulated	MATN1-AS1/RELA/MAPK signaling axis	Tumor suppressor	TMZ	N/A	Human, mice	75	RT-qPCR
[82] (39184824)	LINC01366 and LINC01433	RELA	Involved in inflammation and angiogenesis in GBM	Upregulated	RELA/LINC01366/LINC01433 axis	Oncogene	N/A	N/A	Human (M-17, F-8)	25	qRT-PCR
[84] (35874989)	FAM66C	RELA, FOS, STAT3, NFKB1, CEBPB, ETS1, SP1, USF2, ETS2, and SMAD	Key regulator for modulating tumor microenvironment and hypoxia-related pathways in GBM	Upregulated	EMT, angiogenesis, and hypoxia signaling	Oncogene	N/A	N/A	Human	369	RNA seq
[211] (29678575)	LOXL1-AS1	RELB	Regulator of the NF-kb signaling pathway. It represses RELB directly, resulting in increased marker genes of the proneural subtype and decreased those of the mesenchymal subtype	Upregulated	LOXL1-AS1–NF-κB–RELB axis	Tumor growth	TMZ	N/A	Human	N/A	qRT-PCR
[4] (34277786)	AC122129.1, AC017104.1, AL357992.1, LINC01736, AP003481.1, AC098613.1, and PSMB8-AS1	PYCARD	Involved in glioma cell proliferation, migration, and chemoresistance	Upregulated	PYCARD-related signaling pathway network	Tumor growth, immune modulation and pro-tumorigenic factor	TMZ	Affects the expression of PYCARD and its related lncrnas, promoting glioma cell proliferation and migration	Human	144	qRT-PCR
[85] (36601479)	RP11-131L12.4	RIPK3	Crucial role in necroptosis suppression	Upregulated	RP11-131L12.4-mediated necroptosis pathway	Tumor growth	TMZ	Did not show significant differences in its levels between the high-risk and low-risk groups	Human	128	qRT-PCR

Table 5 Detail information of list of articles involved with JAK/STAT signaling pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[87] (37351164)	MIR222HG	SOCS3	Promotes the mesenchymal transition and radio resistance in GSC	Upregulated	SPI1-mediated MIR222HG transcription network	Oncogenes	PLX-4720	Acts on mesenchymal GSC to enhance radiosensitivity.	Human	12	RNA sequencing, RNA pulldown, mass spectrometry, RIP, ChIP, luciferase reporter assays, and Co-IP were performed.
[88] (38287522)	PVT1	STAT1 and CX3CL1	Promote GBM progression by enhancing cell proliferation and macrophage immunosuppressive polarization through the regulation of STAT1 and CX3CL1	Upregulated	STAT1 regulation and CX3CL1-mediated macrophage recruitment and M2 polarization	Oncogene	N/A	NA	Human, mice	325	RT-qPCR
[89] (32843056)	NEAT1	STAT3	NEAT1 is involved in promoting the formation of GSC through the TLR9/NEAT1/STAT3 pathway	Upregulated	TLR9/MYD88/STAT3 signaling axis	Oncogene	Static	Inhibits the STAT3 signaling pathway, which in turn reduces the expression of stemness-related transcription factors and impairs the formation of GSC	Human, mice	N/A	RT-qPCR
[90] (34531451)	N/A	STAT3	N/A	Upregulated	STAT3 signaling	Oncogene, therapy resistance	N/A	N/A	N/A	N/A	N/A
[91] (35945579)	LINC00520	STAT3, LIN28B	Contributes to TMZ chemoresistance in GBM by interacting with RNA-binding protein LIN28B	Upregulated	RNA-binding protein LIN28B to inhibit autophagy and reduce DNA damage	Oncogene	TMZ	Upregulates LINC00520, which in turn contributes to TMZ chemoresistance by interacting with LIN28B	Human, mice	N/A	qRT-PCR

Table 6 Detail information of list of articles involved with MAPK signaling pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[271]	NEAT1	MAP3K1	Promotes malignant phenotypes and TMZ resistance in GSC by regulating the let-7g-5p/MAP3K1 axis	Upregulated	NEAT1/let-7g-5p/MAP3K1 axis	Oncogene	TMZ	Silencing NEAT1 enhances the sensitivity of GBM stem cells to TMZ and inhibits their malignant phenotypes	Human	22	qRT-PCR
[93] (32319552)	SNHG16, SNHG7, SNHG18, SNHG9	MAPK1 and E2F7	Promote TMZ resistance in GBM cells by acting as a molecular sponge for mir-129-5p, leading to the upregulation of MAPK1 and E2F7.	Upregulated	methylation-mediated	Oncogene	TMZ	Promotes the upregulation of lncrna SNHG12 in GBM cells, leading to TMZ resistance.	Human, mice	N/A	RNA-Sequencing
[94] (35852875)	CASC19/PCAT2	MAP2K6	Involved in the regulation of DNA damage repair pathways	Upregulated	DNA damage repair pathways	Radio resistance and tumor progression	sitravatinib and brigatinib	Target kinases that are associated with the differential expression of lncrnas, including CASC19/PCAT2	GBM patient-derived xenograft models	8	RNA seq
[95] (31657621)	SNHG5	p38/MAPK	Promotes GBM cell proliferation through the p38/MAPK signaling pathway.	Upregulated	YY1/SNHG5/p38-MAPK axis	Oncogene	TNF-α, SB203580	TNF-α counteracted the inhibitory effect of SNHG5 knockdown on the p38/MAPK pathway, while SB203580 abrogated the GBM cell proliferation promoted by SNHG5 overexpression.	Human	N/A	qRT-PCR
[96] (38084701)	LINC01127	MAP4K4	Promotes the self-renewal of GSC via cis regulating the MAP4K4 to activate the JNK pathway	Upregulated	MAP4K4/JNK/NF-κB axis	Oncogene	SP600125	Impeded the orthotopic tumor growth in GBM xenografts, indicating that it affects the LINC01127-mediated axis	Animal	N/A	qRT-PCR, RIP-PCR, and ChIP-PCR
[97] (35237295)	LOXL1-AS1	MAPK	Associated with patient survival and has a functional inhibitory effect on the proliferation of GBM cells	Upregulated	MAPK signaling and cell apoptosis	Oncogene, Tumor growth	GSK2256098	A novel oral focal adhesion kinase (FAK) inhibitor, demonstrates growth inhibition in GBM cell	Human	154	qRT-PCR
[98]	TCONS_00020456.	Smad2/PKCα	Negatively regulates the malignant progression of GBM by targeting the Smad2/pkcα signaling pathway.	Downregulated	Smad2/PKCα signaling pathway	Tumor suppressor	N/A	N/A	Human, mice	148	qRT-PCR
[92] (32606802)	HULC	RRAS	Promotes GBM cell proliferation, invasion, and migration by regulating RRAS expression	Upregulated	Ras signaling pathway	Oncogene	N/A	N/A	Human cell lines	N/A	qRT-PCR

Table 7 Detail information of list of articles involved with m6A methylation regulation pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[99] (36597408)	MIR1915HG, THAP9-AS1, MALAT1, NORAD1, and NEAT1	m6A	GBM progression and potential as therapeutic targets.	Upregulated	m6A	Tumor growth	N/A	N/A	Human	N/A	MeRIP-seq (methylated RNA immunoprecipitation and sequencing) and Nanopore dRNA-seq (direct RNA sequencing).
[100] (35719945)	m6A-related lncRNAs: AC005229.3, SOX21-AS1, AL133523.1, and AC004847.1	m6A related genes	Predicting and assessing the survival of GBM patients	Upregulated & regulated	m6A	Tumor growth	Doxorubicin and Methotrexate, and AZD8055, BI.2536, GW843682X, and Vorinostat	Drugs have higher IC50 values in patients in the high-risk group, indicating reduced sensitivity to these drugs	Human	N/A	RNA sequencing data and LASSO regression analysis
[101] (38802444)	AF127577.4	METTL3	Encodes a micro peptide, AF127577.4-ORF, which suppresses GBM cell proliferation by diminishing METTL3 protein stability	Downregulated	ERK2/METTL3 interaction network	Tumor suppressor	ERK inhibitor	The ERK inhibitor SCH772984 reduces the phosphorylated ERK (p-ERK) level and downregulates METTL3 protein expression, which is influenced by the micro peptide encoded by lncRNA AF127577.4	Human	N/A	RT-qPCR
[102] (32585241)	FGD5-AS1	HNRNPK	Promotes GBM progression by regulating the mir-129-5p/HNRNPK axis	Upregulated	miR-129-5p/HNRNPK axis, activating the Wnt/β-catenin	Oncogene	N/A	N/A	Human, mice	64	qRT-PCR

					signaling pathway						
[103]	MALAT1, TUG1, CRNDE	SRSF1	Regulating alternative splicing, which affects cancer invasion, metastasis, apoptosis, therapeutic resistance, and tumor development.	Upregulated / downregulated	tumorigenesis, invasion, angiogenesis, and abnormal metabolism	Tumor suppressor, oncogene	TMZ	Affects the lncRNA networks by causing dysregulation, which leads to resistance in GBM treatment.	Human	N/A	qRT-PCR

Table 8 Details of list of articles involved with TGF-β / MYC signaling pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[111] (32368136)	AC021739.2, AL031722.1, AL354740.1, FGD5-AS1, LINC00844, and NEAT1	TGF-β1	Upregulates TGF-β1 to increase cancer cell stemness and predict postoperative survival in GBM	Upregulated	TGF-β signaling pathway	Oncogene	N/A	N/A	Human (M-30, F-20)	50	qRT-PCR
[112] (32447005)	NEAT1	TGF-β	Involved in the prognosis of lower-grade gliomas (LGG) and are part of the cerna networks that regulate tumor proliferation and metastasis	Upregulated & downregulated	AK-STAT signaling pathway, TGF-β signaling pathway	Tumor progression	irinotecan, camptothecin, mitoxantrone, azacitidine, mestranol, and enilconazole	Target the ceRNA networks involving the identified lncRNAs, potentially reversing the expression signatures associated with LGG	Human (M-280, F-226)	506	RNA seq
[113] (29138341)	ANCR	EZH2	Promotes GBM progression by scaffolding EZH2 and regulating the WNT/β-catenin pathway.	Upregulated	GFR/NEAT1/EZH2/β-catenin axis	Tumor growth	N/A	N/A	Human, mice	81	qRT-PCR
[114] (29476310)	HOTAIR	EZH2	To act as a potential diagnostic and therapeutic target in brain cancers by regulating glioma cell differentiation and apoptosis.	Upregulated	RNA ANCR	Tumor growth	N/A	N/A	Human	N/A	qRT-PCR, RNA sequencing
[106] (25428914)	HOTAIR	EZH2	Promote GBM cell cycle progression in an EZH2-dependent manner	Upregulated	HOTAIR/EZH2 axis	Tumor growth	TMZ	N/A	Human	N/A	qPCR, western blot analysis
[115] (38490327)	HOTAIR	EZH2	Regulate the progression of GBM by interacting with the protein EZH2	Upregulated	HOTAIR/EZH2/ATF3 axis	Tumor growth	EPIC-0628	Disrupts the interaction between the lncRNA HOTAIR and the protein EZH2, enhancing the efficacy of TMZ in treating GBM	Human, mice	N/A	RNA immunoprecipitation (RIP).
[107] (31589963)	HOXA6as, H19 upstream conserved 1 and 2, Zfhx2as, and BC200	PRC2	Acts as a scaffold for various epigenetic proteins, such as EZH2 and LSD1, and influences the chromatin epigenetic state at various	Upregulated	Histone acetylation and tumor growth	Tumor suppressor, oncogene, DNA repair	I-BET151, a BET bromodomain	Caused a reduction in the levels of the tumor-promoting lncRNA HOTAIR	Human	N/A	qRT-PCR

			genomic loci involved in silencing				inhibit or				
[117] (25561975)	H19	H19	Suitable as normalizers for profiling lncrna expression in various glioma types and normal brain tissue	Upregulated	Transcriptional regulation	Tumor suppressor	N/A	N/A	Human	30	qRT-PCR
[105] (32081833)	TRG-AS1	H19, TGF-beta signaling	Immune infiltration level of glioma through copy number variations, impacting the prognosis of glioma patients.	Upregulated	PI3K-Akt and TGF-beta signaling	Tumor growth	N/A	N/A	Human	352	RNA sequencing
[116] (31196742)	SUZ12	SUZ12	Promotes GBM cell proliferation by competitively binding with mir-877-5p to regulate SUZ12 expression.	Upregulated	TRG-AS1/miR-877-5p/SUZ12 axis	Tumor growth	N/A	N/A	Human	51	RT-qPCR

Table 9 Details of list of articles involved with autophagy and metabolic regulation

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[121] (29655792)	UCA1	PFKFB2	Modulates glycolysis and invasion of glioma cells in cooperation with mir-182	Upregulated	UCA1/miR-182/PFKFB2 axis	Tumor growth	Recombinant CXCL14 protein	CXCL14 upregulates UCA1 and downregulates miR-182, enhancing invasion and glycolysis in glioma	Human	N/A	qPCR, Immunoblotting
[122] (34645788)	CASC9	HK2	Promotes aerobic glycolysis in GBM by enhancing HK2 mrna stability.	Upregulated	CASC9/IGF2BP2/HK2 axis	Oncogene	N/A	N/A	Human (M-17, F-13)	30	qRT-PCR
[104] (30572911)	The lncRNAs mentioned are CTD-2140B24.6, LINC02015, AC068888.1, CERNA1, and LINC00618	GALE	Multidimensional transcriptome signature used for survival prediction in postoperative GBM	Upregulated	PCG-lncRNA signature	Oncogene	TMZ	PCG-lncRNA signature could predict the response to TMZ-chemoradiation in GBM patients after surgery	Human	233	TCGA, TANRIC, and GEO, and the detection method involved bioinformatics analysis and survival analysis
[123] (37336288)	LINC00978	AKR1B1	Promote the malignancy of GBM by regulating metabolic rewiring through AKR1B1.	Upregulated	AKR1B1 pathway	Oncogene	2-deoxyglucose (2DG)	Enhances the sensitivity of GBM cells to 2DG by upregulating the expression of the lncRNA LINC00978, which in turn positively regulates AKR1B1 expression.	Human, mice	109	qRT-PCR, RNA sequencing

[124] (34099027)	ARST	ALDOA	Represses glioma progression by inhibiting ALDOA-mediated actin cytoskeleton integrity	Downregulated	ALDOA-mediated actin cytoskeleton integrity pathway	Tumor suppressor	N/A	N/A	Human, mice	144	qRT-PCR
[125] (39333603)	ZFAS1	ATP7A, LIAS, LIPT1, CDKN2A, PDHA1, DBT	Involved in glioma development by regulating mir-1271-5p and HK2, leading to increased proliferation, invasion, and migration	Upregulated	Protein-Protein Interaction (PPI) network	Tumor suppression, oncogene and repair	anti-parasitic drug	Targets mitochondrial metabolism, which aligns with the function of cuproptosis, a form of programmed cell death related to copper accumulation within cells	Human	169	qRT-PCR
[126] (34082742)	HOTAIR	PPAR alpha	Negatively regulates the expression of pparα, which is involved in lipid metabolism and the malignant progression of gliomas.	Upregulated	HOTAIR/PPARα signaling pathway	Tumor suppressor	Fenofibrate.	Combined with si-HOTAIR, significantly inhibits the proliferation and invasion of glioma cells by upregulating pparα expression.	Human	702	qRT-PCR
[127] (39256686)	GLIDR	PPARGC1A	GLIDR promotes non-small cell lung cancer (NSCLC) progression and cisplatin resistance by sponging mir-342-5p to regulate PPARGC1A expression	Upregulated	GLIDR-mediated miR-342-5p/PPARGC1A axis	Tumor growth	Cisplatin	Reducing GLIDR expression enhances cisplatin sensitivity in resistant NSCLC and decreases the malignant characteristics of NSCLC	Human, mice	149	qRT-PCR
[128] (35871232)	LINREP	PTBP1/HuR complex	Promotes GBM progression by recruiting the PTBP1/hur complex and protecting PTBP1 from ubiquitin-proteasome degradation, which enhances PTBP1-induced alternative splicing events and contributes to cell proliferation, migration, and invasion	Upregulated	LINREP/PTBP1/HuR axis	Tumor growth	N/A	N/A	Human, animal	105	RT-qPCR
[102] (32585241)	FGD5-AS1	HNRNPK	Promotes GBM progression by regulating the mir-129-5p/HNRNPK axis and activating Wnt/β-catenin signaling	Upregulated	miR-129-5p/HNRNPK axis, activating the Wnt/β-catenin signaling pathway	Oncogene	N/A	N/A	Human, mice	64	qRT-PCR
[129] (31632968)	ADAMTS9-AS2.	FUS	Promotes TMZ resistance by upregulating the FUS/MDM2 ubiquitination axis.	Upregulated	ADAMTS9-AS2/FUS/MDM2 ubiquitination axis	Oncogene	TMZ	Associated with the overexpression of ADAMTS9-AS2, which stabilizes the FUS protein by inhibiting its MDM2-mediated K48	Human	144	qRT-PCR

								polyubiquitination and degradation.			
[125] (39333603)	ZFAS1	ATP7A, LIAS, LIPT1, CDKN2 A, PDHA1, DBT	Involved in glioma development by regulating mir-1271-5p and HK2, leading to increased proliferation, invasion, and migration	Upregulated	Protein-Protein Interaction (PPI) network	Tumor suppression, oncogene and repair	anti-parasitic drug	Targets mitochondrial metabolism, which aligns with the function of cuproptosis, a form of programmed cell death related to copper accumulation within cells	Human	169	qRT-PCR
[130] (28076842)	SNHG1	IDH1	Identified as a novel disease risk factor for disease diagnosis and prognosis in GBM	Upregulated	gene and lncRNA co-expression pan-cancer network (GLCPN)	Tumor suppressor	N/A	N/A	Human	N/A	qRT-PCR
[131] (32990028)	IDH1-AS1	IDH1	Interacts with IDH1 and inhibits cell proliferation in glioma by altering IDH1 enzymatic activities	Downregulated	lncRNA IDH1-AS1/IDH1 pathway	Tumor suppressor	N/A	N/A	Human, animal	N/A	qRT-PCR

Table 10 Details of list of articles involved with immune modulation and inflammation

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[132] (37434823)	ENST00000440016	CD22, TRIM 24	Involved in the regulation of gene expression related to GBM pathogenesis	Upregulated & downregulated	hsa-miR-296-5p and hsa-miR-874-5p	Tumor growth, prognosis	N/A	N/A	Human (M-5, F-5)	10	RT-qPCR
[133] (26943771)	HOTAIR	MXI1, CD58, PRKCE, ATF5	Modulates gene expression and is associated with GBM prognosis.	Upregulated	HOTAIR-MXI1-CD58/PRKCE	Tumor suppressor, growth, repair and progression, resistance	N/A	N/A	Human	N/A	RT-qPCR
[134] (32821246)	RP11-268F1.3, RP11-547C13.1, and RP11-90M5.4	C1s and HSD3B7	Regulate mRNA expression by sponging miRNA	Upregulated	C1s/miR-132-3p/RP11-268F1.3 axis and the HSD3B7/miR-346/RP11-547C13.1 axis	Oncogene	N/A	N/A	Human	81	qRT-PCR

[135] (33579282)	MIR155HG	C1S	ceRNA and is involved in the regulation of gene expression by sponging mir-129-5p	Upregulated	MIR155HG /miR-129-5p/C1S axis	Oncogene	N/A	N/A	Human	37	RT-qPCR
[136] (23399484)	CCDC26	CD14	Involved in glioma development by potentially affecting GSC fate determination	Upregulated	NP rs55705857	Tumor growth	N/A	N/A	Human	4147	Genotyping and imputation techniques
[137] (34220951)	MEG3	CD8 T cells, dendritic cells	Acts as a tumor suppressor and is involved in regulating immune cell infiltration in gliomas	Downregulated	MEG3-mediated immune infiltration pathway	Tumor suppressor	N/A	N/A	Human	955	Oncomine and TIMER
[138] (31123407)	UBE2R2-AS1	TLR4	Promotes glioma cell apoptosis by targeting the mir-877-3p/TLR4 axis	Downregulated	UBE2R2-AS1/miR-877-3p/TLR4 axis	Tumor suppressor	N/A	N/A	Human (M-70, F-52)	122	Microarray analysis, qRT-PCR
[139] (34790767)	IL10RB-AS1	IL10RB	Upregulated in GBM and associated with poor prognosis	Upregulated	IL10RB-AS1/hsa-miR-26a-5p/GBP1 competitive endogenous RNA (ceRNA) axis	Oncogene	N/A	N/A	Human	14	qRT-PCR
[140] (31302496)	RP11-571M6.8	PD-1, PD-L1, CTLA-4	Immunosuppressive function in GBM	Upregulated	RP11-571M6.8/PD-1/PD-L1/CTLA-4 axis	Tumor suppressor	methyl ethyl ketone (MEK) inhibitors	The lncRNA CTD-2256P15.2 responded to the sensitivity of MEK inhibitors	Human	2148	qRT-PCR
[141] (35069587)	NEAT1	PD-L1	Stabilizes the NF-kb/PD-L1 axis, contributing to tumorigenesis and immune evasion in GBM	Upregulated	NF-kB/PD-L1 axis	Oncogene	Actinomycin D.	To block mRNA synthesis, showing that PTRF resulted in significantly lower degradation of NEAT1	N/a	N/A	RT-qPCR
[142] (32918360)	HOXA-AS3	USP3	Cell proliferation, invasion, and migration by regulating the mir-455-5p/USP3 axis	Upregulated	HOXA-AS3/miR-455-5p/USP3 axis	Oncogene	N/A	N/A	Human, mice	25	qRT-PCR
[143] (38275102)	UBDP1	UBD	Promotes glioma progression by sponging mir-6072	Upregulated	UBDP1/miR-6072/UBD network	Oncogene	N/A	N/A	Human and animal (mice)	30 (15 male, 15 female)	RT-qPCR, FISH
[87] (37351164)	MIR222HG	SOCS3	Promotes the mesenchymal transition and radio resistance in GSC	Upregulated	SPI1-mediated MIR222HG	Oncogenes	PLX-4720	Acts on mesenchymal GSC to enhance radiosensitivity.	Human	12	RNA sequencing, RNA

					transcription network						pulldown, mass spectrometry,

Table 11Details of list of articles involved with Wnt/β-catenin signaling pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[144] (34880375)	AC012615.1, H19, LINC00609, LINC00634, POM121L9P, SNHG11, and USP32P3	SOX2, Wnt5α, and β-catenin.	Involved in the EMT and are associated with the prognosis of GBM	Upregulated	EMT, metastasis-related pathways, and immune activities	Tumor, growth	N/A	N/A	Human	153 patients from the TCGA-GBM cohort and 387 patients from the CGGA-GBM cohort	qRT-PCR
[282] (33505307)	LINC-PINT	Wnt/β-catenin signaling pathway	Suppresses cell proliferation, invasion, and EMT by blocking Wnt/β-catenin signaling in GBM	Downregulated	Wnt/β-catenin signaling pathway	Tumor suppressor	Lithium chloride (LiCl)	Activates the Wnt/β-catenin pathway, which counteracts the suppression effect of LINC-PINT on EMT markers	Human, mice	N/A	qRT-PCR
[145] (36197973)	lncEPAT	Wnt/β-catenin signaling pathway, miR-101/EZH2 axis	Mediates the integration of the dysregulated EGFR pathway with H2A deubiquitination in GBM	Upregulated	EGFR signaling pathways	Tumor growth	Gefitinib and PD153035.	Inhibition of the EGFR pathway by gefitinib and PD153035 decreased the expression levels of incept	Human, mouse	157	RT-qPCR
[146] (36197973)	NEAT1	Wnt/β-catenin signaling pathway	Upregulates Wnt/β-catenin signaling to promote the formation of GSC	Upregulated	TLR2/NEAT1/Wnt signaling pathway	Tumor growth	TMZ	Upregulates HMGB1, which in turn upregulates NEAT1, promoting the formation of GSC.	Human	N/A	qRT-PCR
[147] (31891366)	MIR22HG	SFRP2 and PCDH15	Promote GBM progression by activating the Wnt/β-catenin signaling pathway.	Upregulated	Wnt/β-catenin signaling pathway.	Oncogene	Silico drug design method	N/A	45 years of more	N/A	RT-qPCR
[148] (29643989)	H19	NKD1	Positively affects the tumorigenic properties of GBM cells and contributes to NKD1 repression through the recruitment of EZH2 on its promoter	Upregulated	Wnt signaling pathway	Oncogene	N/A	N/A	Human	N/A	qRT-PCR

[149] (33028341)	LINC01057, TP73-AS1, AP000695.4, LINC01503, CRNDE, OSMR-AS1, SNHG18, AC145343.2, RP11-25K21.6, and RP11-38L15.2	CD44	Involved in promoting pro-neural to mesenchymal transition (PMT) in glioma, which is associated with aggressive phenotypes and poor prognosis	Upregulated	NF-κB pathway	Tumor growth	NSC141562	Blocking the lncRNA MIR155HG axis with NSC141562 suppressed mesenchymal transition	Human	N/A	weighted gene co-expression network analysis (WGCNA), gene set enrichment analysis (GSEA)
[150] (36159816)	SNHG18	CD44	Plays a crucial role in the tumorigenesis and subtype determination of GSC	Upregulated	EGFR and ERK-MAPK signaling pathways.	Oncogene	AZD3759 (Zorifertinib)	Enhances the sensitivity of GSC to radiotherapy by affecting the subtype of GSC, potentially initiating a proneural-to-mesenchymal transition	Human, mice	12	qRT-PCR
[154] (34689169)	TMEM161B-AS1	FANCD2, CD44	Promotes the malignant biological behavior of GSC and resistance to TMZ by up-regulating the expression of multiple ferroptosis-related genes by sponging hsa-mir-27a-3p	Upregulated	TMEM161B-AS1-hsa-miR-27a-3p-FANCD2/CD44 network	Oncogene	TMZ	Resistance is mediated by the lncRNA TMEM161B-AS1, which up-regulates the expression of FANCD2 and CD44 by sponging hsa-miR-27a-3p	Human, mice	N/A	qRT-PCR
[153] (28306408)	H19	CD133	To promote invasion, angiogenesis, and stemness of GBM cells, contributing to tumorigenicity.	Upregulated	H19-mediated pathway	Oncogene	N/A	N/A	Human, mice (6)	30	RT-qPCR
[155] (38258133)	PARTICLE and GAS5	CD133, CD54	Acts as a tumor activator	Upregulated & downregulated	prominin-1, ICAM-1, PARTICLE, and GAS5	Tumor growth, tumor suppressor	All-trans retinoic acid (ATRA)	Significantly curtails the expression of PARTICLE	Human, mice	N/A	FISH, qPCR
[152] (26983719)	H19	CD133, NANOG, Oct4, Sox2	Promoting GBM malignancy and maintaining its stem cell properties	Upregulated	PI3K/Akt and p53/Rb	Tumor growth	TMZ	Increased apoptosis in H19-knockdown GBM cells	Human	N/A	qRT-PCR
[151] (32329150)	PXN-AS1	DKK1	Promotes GBM progression by epigenetically silencing DKK1 and activating the Wnt/β-catenin pathway	Upregulated	Wnt/β-catenin pathway	Oncogene	Wnt/β-catenin pathway activator (LiCl)	Counteracted the suppression of Wnt/β-catenin pathway in PXN-AS1-silenced GBM cells	Human, mice	N/A	qRT-PCR

Table 12 Details of list of articles involved with EMT pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[156] (30949502)	ASB16-AS1	EMT signaling	Promotes proliferation, migration, and invasion in glioma cells	Upregulated	ASB16-AS1/EMT signaling pathway	Oncogene	N/A	N/A	Human	normal tissue-14, LGG-29, HGG-49	qRT-PCR
[160] (34273059)	H19	ZEB1	To modulate GBM drug resistance through exosomal RNA	Upregulated	ZEB1	Oncogene	TMZ	Modulating GBM drug resistance through exosomal non-coding RNAs	Human	N/A	N/A
[157] (28668966)	MALAT1	ZEB1	Decreases the sensitivity of resistant GBM cell lines to the chemotherapeutic drug TMZ by regulating ZEB1 expression and contributing to multidrug resistance (MDR) mechanisms	Upregulated	ZEB1 expression to influence EMT	Tumor growth	TMZ	Decreases the sensitivity of resistant GBM cell lines to the chemotherapeutic drug TMZ by regulating ZEB1 expression and contributing to multidrug resistance (MDR) mechanisms	Human	N/A	Cell transfection, RNA isolation and RT-PCR, Western blot, MTT assay
[158] (36341927)	LINC01711, lncRNA-MUF	Snail, ZEB1	Promotes invasion in GBM by modulating mir/34a/Snail axis, acting as a competing endogenous RNA for mir-34a and promoting ZEB1 expression.	Upregulated	TGF-β/miR-34a/ZEB1 signaling pathway.	Oncogene	TMZ	LINC01711 depletion sensitizes glioma cells to TMZ-induced apoptosis by inhibiting ZEB1	Human glioma cell	N/A	qRT-PCR
[159] (31799672)	DGCR5	N-cadherin, E-cadherin, ZEB1,	Inhibits the proliferation, aggressiveness phenotypes, and EMT of GBM cells	Downregulated	E-cadherin and N-cadherin.	Tumor suppressor	N/A	N/A	Human, mice	36	qRT-PCR
[161] (38857306)	LINC03045	WASF3	Regulate GBM invasion by modulating the expression of WASF3.	Upregulated	WASF3-JAK/STAT pathway	Oncogene	N/A	N/A	N/A	20	CRISPR interference
[162] (31849498)	BCAR4	MMP7	Promotes growth, invasion, and tumorigenicity by targeting mir-2276 to upregulate MMP7 expression in glioma	Upregulated	BCAR4/miR-2276/MMP7 axis	Oncogene	N/A	N/A	Human, mice	30	qRT-PCR
[163] (30898167)	miR155HG	ANXA2	Sponges mir-185 to promote ANXA2 expression, contributing to GBM growth and progression.	Upregulated	miR155HG/miR-185/ANXA2 signaling loop	Oncogene	STAT3 phosphorylation.	SH-4-54 inhibitor reduces miR155HG expression by inhibiting STAT3 phosphorylation.	Human	24	qRT-PCR, FISH
[164] (34608452)	HMMR-AS1	HMMR	Regulate HMMR expression, thereby affecting GBM cell	Upregulated	HMMR-AS1	Tumor growth	N/A	N/A	Human, mice	N/A	qRT-PCR

			growth, migration, invasion, and radiosensitivity.								
[165] (31876683)	HOTAIRM1	specificity protein 1 (SP1)	Promotes cell proliferation and invasion in human GBM by up-regulating specificity protein 1 (SP1) via sponging mir-137.	Upregulated / downregulated	HOTAIRM1/miR-137/SP1 axis	Tumor suppressor	N/A	N/A	Human	21	qRT-PCR
[166] (32838835)	WEE2-AS1	SP1	Molecular sponge for microrna-520f-3p, thereby facilitating the malignancy of GBM by increasing specificity protein 1 (SP1) expression.	Upregulated	WEE2-AS1/miR-520f-3p/SP1 axis	Oncogene	N/A	N/A	Human, mice	59	qRT-PCR
[167] (35299997)	MIR155HG.	SP1	Involved in promoting glioma progression and immune infiltration.	Upregulated	MIR155HG/SP1 axis	Tumor growth	N/A	N/A	Human	N/A	qRT-PCR
[168] (30816427)	LOC541471	PLEK2	Associated with the survival time of GBM patients, and it is involved in the oxidative phosphorylation of GBM with pleckstrin-2.	Upregulated	extracellular matrix organization, oxidative phosphorylation, and tyrosine kinase receptor signaling pathways	Tumor growth, suppressor and repair	N/A	N/A	Human	N/A	weighted gene co-expression network analysis (WGCNA).
[169] (34115613)	TP73-AS1	ALDH1A1	N/A	Upregulated	TP73-AS1/YY1 axis	Oncogene	N/A	N/A	N/A	N/A	N/A
[269] (29431756)	MALAT1 and KIAA0495.	MALAT1, KIAA0495	MALAT1 acts as a tumor suppressor in GBM	Upregulated	MALAT1	Tumor suppressor	N/A	N/A	Human	N/A	qRT-PCR
[171] (34802389)	HOXD-AS2	MALT1	Promote GBM cell proliferation, migration, and invasion by regulating the mir-3681-5p/MALT1 signaling	Upregulated	miR-3681-5p/MALT1 signaling axis	Tumor growth	N/A	N/A	N/A	92	qRT-PCR
[283] (30940658)	MALAT	MALAT1	Promoting chemoresistance in GBM by regulating miRNA and inducing transformation to a mesenchymal phenotype	Upregulated	NF-κB and p53 signaling axes	Tumor growth	TMZ	Induces the expression of MALAT1 in a manner dependent on NF-κB and p53	Human, mice	34	qRT-PCR
[170] (33245508)	MALAT1, CASC2, H19, TUSC7, XIST, RP11-838N2.4, DLX6-AS1, GLIDR,	MALAT1, CASC2, H19, TUSC7	Involved in tumor resistance via various processes such as multi-drug resistance, EMT, autophagy, cell proliferation and viability, and DNA repair	Upregulated & downregulated	EMT, autophagy, cell proliferation, and DNA repair	Tumor growth, suppressor and repair	TMZ	Influences the expression of lncRNAs related to GBM resistance	Human	N/A	qRT-PCR

	MIR210HG, and SOX2-OT										
[172] (34584066)	HOTAIRM1	TGM2	Promote GBM aggressiveness and radiotherapy resistance by modulating mitochondrial function and reactive oxygen species (ROS) levels.	Upregulated	mitochondrial function and reactive oxygen species (ROS) levels.	Oncogene	N/A	N/A	N/A	N/A	qRT-PCR

Table 13 Details of list of articles involved with Notch signaling pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[173] (36009578)	RAMP2-AS1	NOTCH3	Inhibits GBM progression via NOTCH3 pathway	Downregulated	NOTCH3 signaling pathway	Tumor suppressor	N/A	N/A	Human	20 patients	RNA microarray
[177] (38279763)	Various lncRNAs	Notch, MYC, Hes1, and Hey1	Modulating the Notch signaling pathway by targeting critical mRNA expression at the post-transcriptional or transcriptional levels	Upregulated / downregulated	NOTCH3 signaling pathway	Tumor growth	arsenic trioxide (As2O3) and TMZ	Arsenic trioxide represses tumorigenesis of GBM cell lines by reducing the levels of CSLCs. TMZ's effectiveness is influenced by the expression of EFEMP1, which is related to TMZ resistance. Suppressing EFEMP1 reduces cell survival after TMZ therapy.	Human	N/A	qRT-PCR
[174] (36214714)	MAFG-AS1	notch1	Enhances radio resistance of GBM cells via the mir-642a-5p/Notch1 axis.	Upregulated / downregulated	NOTCH1 signaling pathway	Radio resistance and tumor growth	N/A	N/A	Human	N/A	qRT-PCR
[175] (32210625)	FEZF1-AS1	Notch-1, miR34a	Sponges mir-34a to upregulate Notch-1, promoting cancer cell invasion and migration in GBM	Upregulated	FEZF1-AS1/miR-34a/Notch-1 pathway	Oncogene	N/A	N/A	Human (M-38, F-22)	60	qRT-PCR
[176] (33483471)	LINC01152	MAML2	Upregulates MAML2 expression to promote tumorigenesis in GBM via the Notch signaling pathway	Upregulated	LINC01152 /miR-466/MAML2 axis	Oncogene	N/A	N/A	Human, mice	38	qRT-PCR

Table 14 Details of list of articles involved in Hypoxia-Induced pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[178] (32326742)	PCED1B-AS1	HIF	To promote the Warburg effect and tumorigenesis in GBM by upregulating HIF-1α.	Upregulated	PCED1B-AS1/HIF-1α	Oncogene	N/A	N/A	Human (M-42, F-34), mice (5)	76	qRT-PCR
[179] (38456228)	LUCAT1	HIF1α	Promotes GBM progression by enhancing Hypoxia-inducible factor 1 alpha	Upregulated	HIF1α-LUCAT1-CBP axis	Tumor progression	N/A	N/A	Human, animal	N/A	RNA-seq, qPCR, Northern blot, single

											molecule FISH, and RNA immunoprecipitation
[109] (38769725)	LUCAT1	HIF1α.	Promotes GSC maintenance under hypoxic conditions by enhancing HIF1α activity.	Upregulated	LUCAT1/HIF1α/CBP axis	Tumor progression	N/A	N/A	Human	N/A	qRT-PCR, FISH
[180] (38066404)	uc003tnq.3	HIF-1α	To regulate GBM cell proliferation, invasion, and migration under hypoxic conditions by interacting with RNA-binding proteins, TF, and miRNA	Upregulated	Hippo signaling and nucleotide-excision repair	Tumor progression	N/A	N/A	Human	N/A	qRT-PCR, RNA sequencing
[181] (26339353)	XIST and HIF1A-AS1	XIST, HIF1A-AS1	Serve as a predictive biomarker for non-small cell lung cancer (NSCLC) screening, with increased serum levels of XIST being significantly associated with NSCLC.	Upregulated	XIST and HIF1A-AS1	Tumor progression	N/A	N/A	Human (M-15, F-17)	30	qRT-PCR
[182] (35013529)	HULC	FOXM1, AGR2, and HIF-1	Promotes the progression of glioma by enhancing glycolysis and maintaining the stemness of GSC	Upregulated	HULC/FOXM1/AGR2/HIF-1α axis	Oncogene	WZB117.	Inhibits the expression of HULC, thereby reducing glycolysis and stemness of GSCs	Human (M-28, F-22)	50	qRT-PCR
[183] (39061140)	NEAT1	NEAT1	Promotes the M2 polarization of glioma-associated macrophages by repressing the expression of mir-125a, which in turn elevates the target gene STAT3	Upregulated	NEAT1/miR-125a/STAT3 pathway	GBM progression	TMZ	Induces the expression of NEAT1 in glioma cells	Human cell lines, mice	N/A	qRT-PCR

Table 15 Details of list of articles involved with Transcriptional factors

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[270] (31390792)	CCAT1, EPB41L4A-AS1, LINC00263, LINC00680, LINC00909, MIR210HG, PVT1	proteins	To modulate cell-type-specific splicing patterns by altering their interaction landscape with RNA-binding proteins	N/A	Cell-type-specific alternative splicing	Tumor growth	N/A	N/A	Human	N/A	RNA-Sequencing
[203] (37153654)	C1RL-AS1, LINC00968, MIR155HG, CPB2-AS1, LINC00906, and WDR11-AS1	protein-coding genes (PCGs)	To serve as a prognostic biomarker for GBM by constructing a TNF-related lncRNA signature that can stratify patients into different risk categories and predict their clinical outcomes	Upregulated	TNF signaling pathway via NF-κB	Tumor growth	TMZ	N/A	Human	N/A	qRT-PCR
[204] (35951174)	LEF1-AS1, MALAT1, LINC00470, TUSC7, HOTAIR, NEAT1, XIST, and H19	protein coding genes	Regulate GBM cell proliferation, invasion, and migration under hypoxic conditions.	Downregulated	HSV-G47Δ oncolytic virus targeting miRNA and lncRNA expression in hypoxic conditions	Tumor progression and resistance	HSV-G47Δ oncolytic virus	Downregulating their expression in GSC under both normoxic and hypoxic conditions	Human	N/A	qPCR
[205] (32449315)	LINC00021	p21	To promote TMZ resistance in GBM by epigenetically silencing p21 through the Notch pathway.	Upregulated	Epigenetic silencing of p21 through the Notch signaling pathway	Tumor growth	TMZ	Upregulates the expression of the lncRNA LINC00021, which in turn promotes TMZ resistance in GBM by epigenetically silencing p21 through the Notch pathway	Human, mice	N/A	RNA extraction, RT-qPCR
[184] (36273152)	SOX2OT	SOX3, TDGF-1	Regulates the biological behaviors of GSC by up-regulating the expression of mir-194-5p and mir-122	Upregulated	SOX2OT-miR-194-5p/miR-122-SOX3-TDGF-1 pathway	Oncogene	N/A	N/A	Human, mice	26	qRT-PCR
[206] (28351900)	MANTIS	SOX18, SMAD6, COUP-TF	Facilitates endothelial angiogenic function	Upregulated & upregulated	SWI/SNF chromatin-remodeling complex	Endothelial angiogenic function	N/A	N/A	Human and animal (rat, monkey)	N/A	RNA pulldown, immunoprecipitation, microarray

[207] (32388501)	SOX21-AS1	SOX6	Acts as a tumor suppressor in GBM	Upregulated	MAPT, GSK3B, FYN, and DPYSL4	Oncogene	TMZ	Affects the expression of SOX21-AS1, enhancing its tumor-suppressive effects.	Human	174	qRT-PCR
[209] (29963265)	H19	Nestin, Musashi-1, SOX2, c-MetERK 1, JNK	Involved in the progression of gliomas and promotes glioma cell invasion	Upregulated	MAPK/ERK and JNK	Tumor growth	TMZ	N/A	Human	N/A	qRT-PCR
[185] (32439916)	SOX2OT	SOX2	Promotes TMZ resistance by elevating SOX2 expression via ALKBH5-mediated epigenetic regulation in GBM	Upregulated	Wnt5a/β-catenin signaling pathway.	Tumor growth	TMZ	Increased expression of SOX2OT, which in turn upregulates SOX2 expression, enhancing TMZ resistance	Human (85 Grade IV (GBM), 5 Grade III, 13 Grade II, and 15 Grade I astrocytoma cases)	118	qRT-PCR
[208] (30143669)	PR-LncRNA	SOX1, SOX2, SOX9	Regulates glioma cell activity through the expression of SOX factors.	Downregulated	SOX factors	Tumor suppressor	N/A	N/A	Human (M-21, F-22)	43	qRT-PCR
[284] (37524903)	SOX2-OT	FOXO1, SOX2-OT	To enhance non-small cell lung carcinoma (NSCLC) malignancy by sponging tumor suppressor miRNAs, mir-122-3p and mir-194-5p, leading to dysregulation of downstream pathways.	N/A	FOXO1 and FOXA1 pathways	Oncogene	N/A	N/A	Human	2 human cell line	qRT-PCR, RNA extraction
[186] (36352177)	MIAT	Nanog, Sox2, let-7a-5p, miR-29b-3p	Identified as a regulator of stemness-associated transcript in glioma	Upregulated	Nanog/Sox2/let-7a-5p/miR-29b-3p axis	Oncogene	N/A	N/A	Human brain tumor	28	qRT-PCR
[191] (34737577)	HOTAIR and LINC01305.	HOXD8, HOXD9, HOXD11, HOXD13, HOXB3	HOTAIR is involved in promoting malignant progression and poor prognosis in glioma patients	Upregulated	HOXD10-associated ceRNA network	Tumor suppressor	TMZ	N/A	Human (M-43, F-28)	71	qRT-PCR
[188] (32180085)	HOTAIRM1	HOXA cluster genes	Promotes glioma proliferation by regulating long-range chromatin interactions within HOXA cluster genes	Upregulated	HOTAIRM1/HOXA cluster pathway	Tumor growth	N/A	N/A	Human	N/A	qRT-PCR

[216] (39426568)	HOTAIRM1	HOXA	Involved in mediating inflammatory response by binding to rela-rela homodimers and inhibiting rela's DNA binding to multiple NF-kb signaling sites	Upregulated	Epigenetic regulation	Tumor repair	TMZ	Affects the expression of HOTAIRM1, which in turn influences the methylation status of the MGMT promoter	Human	88	Matrix-MeDIP-qPCR and methylation -specific PCR (MS-PCR)
[189] (30376874)	HOTAIRM1	HOXA	Promotes tumor growth and invasion by up-regulating HOXA1 and sequestering g9a/EZH2/Dnmts away from the HOXA1 gene in GBM	Upregulated	Modulation of histone and DNA methylation	Oncogene	N/A	N/A	Human (M-38, F-32)	70	qRT-PCR
[190] (31691127)	HOTAIRM1	HOXA2, HOXA3	Maintain the tumorigenicity of GSC through the regulation of HOX gene expression.	Upregulated	HOXA cluster genes	Oncogene	N/A	N/A	Human, mice	N/A	qRT-PCR
[192] (31062400)	HOXC-AS3	HOXB13	Involved in promoting proliferation, migration, and invasion of GBM cells	Upregulated	HOXC-AS3	Oncogene	N/A	N/A	Human	N/A	qRT-PCR
[187] (29644006)	HOTAIR	HOXA9	Transcriptional regulation of genes and is associated with poor prognosis in glioma patients	Upregulated	HOXA9 and chromatin-modifying complexes like PRC2 and LSD1.	Oncogene	5-Aza-2'-deoxycytidine (5-Aza)	N/A	Human	124	qRT-PCR
[213] (36878845)	DLEU1	ATF3	Confer resistance to ferroptosis in GBM cells by binding with the RNA-binding protein ZFP36	Upregulated	HSF1/DLEU1/ZFP36/ATF3/SLC7A11 axis	Oncogene	Erastin	Erastin stimulation significantly reduced cell viability and induced ferroptosis markers such as malondialdehyde (MDA) and labile iron levels while decreasing glutathione (GSH) levels.	Human, mice	50	qRT-PCR, FISH
[193] (39602392)	HAR1A	REST	Acts as a putative tumor suppressor	Downregulated	REST/HAR1A axis	Oncogene	N/A	N/A	Human	N/A	RT-qPCR
[195] (35836243)	PDIA3P1	C/EBPβ	Promote TMZ resistance in GBMby inhibiting C/ebpβ degradation and facilitating proneural-to-mesenchymal transition	Upregulated	PDIA3P1/C/EBPβ/MDM2 axis	repair	TMZ and neflamapimod (NEF)	TMZ treatment upregulates the expression of lncRNA PDIA3P1, which promotes TMZ resistance by stabilizing the C/EBPβ protein and facilitating proneural-to-mesenchymal transition.	Human, mice	N/A	qRT-PCR
[285] (30784292)	TRHDE-AS1	C/EBPβ	Act as a prognostic biomarker for GBM, correlating with genomic landscape and clinical outcomes, and potentially regulating synapse-related	Upregulated	p53 and PI3K/Akt signaling pathways	Tumor suppressor, progression	N/A	N/A	Human	N/A	qRT-PCR, RNA sequencing

			functions and immune cell interactions								
[212] (28714520)	HOXA	C/EBPβ	Explore their potential functions and relationships with mrnas in the context of acquired TMZ resistance.	Upregulated	ECM-receptor interaction and genes such as CD44 and collagen I	Tumor resistance and repair	TMZ	TMZ treatment leads to significant changes in the expression of various lncRNAs, including both upregulation and downregulation, which are associated with the development of TMZ resistance in GBM cells.	Human	N/A	qPCR, microarray analysis.
[194] (35141227)	DANCR	FOXO1, PID1	Promotes chemoresistance in GBM cells by stabilizing itself and inhibiting FOXO1-mediated PID1 expression	Upregulatd	IGF2BP2/DANCR/FOXO1/PID1 axis	Oncogene and chemoresistance	Etoposide	Etoposide resistance in cells is induced by IGF2BP2, which stabilizes DANCR, thereby promoting glioma progression	Human, mice	40	RT-qPCR
[246] (29953649)	RNCR3	KLF16	Acts as a tumor suppressor in GBM by inhibiting cell survival and proliferation and promoting apoptosis through the mir-185-5p/KLF16 axis.	Downregulated	RNCR3/miR-185-5p/KLF16 axis	Tumor suppressor	N/A	N/A	Human	N/A	qRT-PCR, wesern blot
[214] (33460239)	MIR4435-2HG	miR-513a-5p/KLF6	Promotes clear cell renal cell carcinoma progression via the mir-513a-5p/KLF6 axis	Upregulated	MIR4435-2HG in clear cell renal cell carcinoma	Tumor growth	N/A	N/A	Human	40	qRT-PCR
[198] (35359381)	CHRM3-AS2	KLF4	Promotes the malignant progression of glioma by regulating mir-370-5p/KLF4 expression	Upregulated	CHRM3-AS2/miR-370-5p/KLF4 axis	Oncogene	N/A	N/A	Human glioma cell lines and a mouse xenograft	N/A	qRT-PCR
[202] (31478223)	MCM3AP-AS1	KLF5, AGGF1	Involved in regulating GBM angiogenesis and prognosis	Upregulated	global lncRNA-TF network (GLTN)	Oncogene	N/A	N/A	Human	155	RNA seq
[286] (31648104)	MALAT 1	ZHX1	Promotes GBM cell proliferation and progression by acting as a ceRNA against mir-199a	Upregulated	Sponges miR-199a	Oncogene	N/A	N/A	Human	30	qRT-PCR
[197] (33430870)	HOXA-AS2	RBBP4	Promotes GBM carcinogenesis by targeting the mir-885-5p/RBBP4 axis.	Upregulated	HOXA-AS2/miR-885-5p/RBBP4 axis	Oncogene	N/A	N/A	Human, mice	33 (M-13, F-20)	qRT-PCR
[199] (35292358)	HOTAIR	FOSL1	HOTAIR promotes GB|M proliferation and invasion via	Upregulated	TRPM7/HOTAIR/mi	Oncogene	N/A	N/A	Human, mice	152	qRT-PCR, Western

			sponging mir-301a-3p and upregulating FOSL1.		R-301a-3p/FOSL1 axis						blot, RNA Immunoprecipitation
[200] (28168356)	TP73-AS1	RFX1	Acts as a ceRNA and is involved in the regulation of gene expression by binding tomiRNAs	Upregulated	ceRNA network	Oncogene	N/A	N/A	Human cell lines	N/A	qRT-PCR

Table 16 Details of list of articles involved with Epigenetic regulation pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[217] (34094916)	HAS2-AS1	LSD1	Promotes GBM proliferation by sponging mir-137	Upregulated	HAS2-AS1/miR-137/LSD1 axis	Oncogene	TMZ	HAS2-AS1 enhances TMZ resistance in GBM	Human, mice	N/A	qRT-PCR, FISH
[218] (33268783)	LINC00998	CBX3	Acts as a tumor suppressor by inhibiting glioma cell proliferation and blocking the G1/S cell cycle transition	Downregulated	The paper discusses the c-Met/Akt/mTOR signaling pathway	Tumor suppressor	MK2206	Reversed the LINC00998 knockdown-promoted growth of glioma cells and decreased the phosphorylation of key c-Met/Akt/mTOR signaling pathway proteins	Human, mice	33	qRT-PCR
[219] (39453684)	NEAT1	Cx43	Regulates gap junctional intercellular communication by modulating Connexin 43, impacting the response of GBM cells to TMZ chemotherapy.	Upregulated	NEAT1/miR-454-3p/Cx43 signaling pathway	Oncogene	TMZ	Downregulation of NEAT1 resulted in enhanced chemosensitivity to TMZ and extended the survival of mice.	Human cell lines, mice	67	qRT-PCR
[220] (35260196)	OBI1-AS1	CTCF	Acts as an astrocyte marker with a possible role in glioma recurrence and progression	Downregulated	synaptic signal transduction and glutamatergic signaling pathway	Tumor suppressor	N/A	N/A	Human	52	qRT-PCR
[221] (30888082)	AC016405.3	TET2	Acting as a molecular sponge for the oncogenic miRNA mir-19a-5p, thereby preventing it from downregulating TET2, a key gene involved in DNA demethylation and epigenetic regulation	Upregulated	miR-19a-5p sponging.	Tumor suppressor	N/A	N/A	N/A	N/A	N/A

Table 17 Details of list of articles involved with non-coding RNAs

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[287] (27306825)	PCAT-1, MEG3, HOTAIR, ANRIL, and H19.	MEG3	Regulate gene expression in GBM cells, influencing processes such as cell proliferation, apoptosis, and chemoresistance.	Upregulated	p53 pathway	Oncogene	N/A	N/A	N/A	N/A	qRT-PCR
[288] (26918340)	lnc-DLK1-4.	MEG3	Regulating splicing patterns and contributing to glioma genesis.	Upregulated	p53 pathway	Tumor suppressor	N/A	N/A	Human	380	RNA seq
[289] (34934358)	HLA-F-AS1, MEG3	MEG3	HLA-F-AS1 promotes GBM cell migration, invasion, and reduces apoptosis by sponging MEG3.	Upregulated	MEG3	Tumor growth	N/A	N/A	Human	62	RT-qPCR, RNA pull-down assay
[290] (33505440)	VIM-AS1, WWTR1-AS1, and NEAT1	VIM-AS1	lncRNA are involved in regulating or controlling cell invasion and migration in GBM	Upregulated	NF-kB signaling pathway	Oncogene	N/A	N/A	Human	28	RNA-Seq
[291] (31950039)	ANRIL	ANRIL	N/A	Upregulated & downregulated	Antisense RNA inhibiting the transcription of the Oncostatin M receptor	Tumor suppressor and oncogene	N/A	N/A	N/A	N/A	qRT-PCR
[292] (36711961)	GIHCG and LINC01563	GIHCG, LINC01563	Promote GSC proliferation, migration, and maintenance of stemness	Upregulated	GIHCG and LINC01563	Tumor proliferation	N/A	N/A	Human	3	single-molecule RNA fluorescence in situ hybridization (smRNA FISH
[293] (25445282)	POU3F3	linc-POU3F3	Promotes cell viability and proliferation in glioma cells	Upregulated	linc-POU3F3	Tumor progression	N/A	N/A	Human (M-42, F-40)	82	qRT-PCR
[294] (31059035)	IGFBP7-AS1	TP73-AS1, PAXIP1-AS2, and LINC00672	To predict GBM outcomes and regulate glioma cell viability, migration, and invasion.	Upregulated	EMT, p53 signaling, hypoxia	Tumor progression	N/A	N/A	Human	255	RT-qPCR
[222] (37452933)	LINC00599	LINC00599	Tumor-suppressing lncRNA in glioma	Downregulated	EMT	Tumor suppressor	N/A	N/A	Human	60	qRT-PCR

[256] (34540695)	GDNF-AS1, CRNDE, FAM201A, HAR1B, AGAP2-AS1, RNF219-AS1, DGCR10, SNHG18, LINC00906, and HAR1A.	DGCR10 and HAR1B	Serve as prognostic biomarkers for glioma	Upregulated	DGCR10 and HAR1B	Tumor growth	N/A	N/A	Human	666	qPCR, RNA sequencing
[295] (34759954)	RP11-399O19.9 and LINC00087	RP11-399O19.9	RP11-399O19.9 is involved in the regulation of the immune system, especially neutrophil activation, while LINC00087 is involved in intercellular signal	Upregulated	MIR4435-2HG-associated pathways	Oncogene	Clozapine	N/A	Human	N/A	qRT-PCR
[274] (29397407)	TUSC7	miR-10a	Inhibit TMZ resistance in GBM by targeting mir-10a and reducing MDR1 expression.	Downregulated	TUSC7 silences miR-10a, reducing MDR1 activity and enhancing TMZ effects.	Tumor suppressor	TMZ	Upregulates the lncRNA TUSC7, which in turn inhibits TMZ resistance in GBM by targeting miR-10a and reducing MDR1 expression.	N/A	N/A	qRT-PCR
[296] (35609320)	SLC16A1	miR-1269	Regulate the maturation of mir-1269	Upregulated	lncRNA SLC16A1-AS1 binds to premature miR-1269 and blocks its maturation	Tumor suppressor	N/A	N/A	N/A	N/A	N/A
[297] (30992025)	SBF2-AS1	miR-151a-3p	Enhance chemoresistance to TMZ in GBM by being transferred via exosomes and regulating DNA damage repair through the mir-151a-3p/XRCC4 axis.	Upregulated	ceRNA for miR-151a-3p, leading to the disinhibition of XRCC4, which enhances DNA double-strand break (DSB) repair.	Tumor growth	TMZ	The drug TMZ upregulates the lncRNA SBF2-AS1, enhancing chemoresistance in by GBM targeting miR-151a-3p and regulating DNA damage repair through the XRCC4 pathway.	N/A	N/A	N/A

[298] (31789416)	Unigene56159	miR-194-5p	Promotes GBM cell proliferation and invasion by negatively regulating microrna-194-5p	Upregulated	ceRNA by sequestering miR-194-5p, which promotes GBM cell proliferation and invasion	Tumor growth	N/A	N/A	Human (M- 33, F-17)	50	RT-qPCR
[299] (37587895)	LINC00941	miR-526b-5p	Suppresses cell proliferation, colony formation, and migration of human GBM cell lines, indicating its crucial role in promoting GBM progression and survival	Upregulated	Negative regulation of miR-526b-5p and the ERK/Akt signaling pathways	Tumor growth	TMZ	Influencing its expression and function.	Human	63	Cell transfection, RT-qPCR,
[300] (36762036)	KTN1-AS1	miR-505	Facilitate proliferation, migration, and invasion of GBM cells	Upregulated	Targeting miR-505, leading to the upregulation of oncogenes like ZEB2, HMGB1, and RUNX2	Oncogene, Tumor growth	N/A	N/A	N/A	40	qRT-PCR
[273] (32975234)	CASC2	miR-18a	Suppressing GBM cell growth, metastasis, and EMT by targeting mir-18a	Downregulated	CASC2-miR-18a axis as a pathway	Tumor suppressor	N/A	N/A	Human (M-24, F-14), 12 male mice	38	RNA extraction, RT-qPCR
[225] (32626942)	FLVCR1-AS1	miR-30b-3p	Promotes glioma cell proliferation and invasion by negatively regulating mir-30b-3p	Upregulated	FLVCR1-AS1-miR-30b-3p axis as a pathway	Oncongene	N/A	N/A	Human (M-22, F-28)	50	RT-qPCR
[301] (36982952)	LINC01393	miR-128-3p	To promote GBM development and progression by sponging mir-128-3p, leading to the upregulation of NUSAP1 and activation of the NF-κb pathway	Upregulated	N/A	N/A	N/A	N/A	Human, 33 mice	N/A	qRT-PCR
[302] (35287551)	SEMA3B AS1	cyclin D1, miR-195	To act as a tumor suppressor in GBM by regulating the expression of cyclin D1 through mir-195, thereby inhibiting GBM cell proliferation	Downregulated	Interaction between lncRNA SEMA3B-AS1, miR-	Tumor suppressor	N/A	N/A	Human (M-41, F-25)	66	qRT-PCR, Methylation-specific PCR

					195, and cyclin D1						
[226] (29360452)	SNHG7	miR-5095, CTNNB1	Promote GBM progression by inhibiting mir-5095 and activating the Wnt/β-catenin signaling pathway	Upregulated	SNHG7/miR-5095/Wnt/β-catenin signaling axis	Oncongene	N/A	N/A	Human	N/A	qRT-PCR
[227] (34966487)	TALNEC2	miR-21, miR-191	Regulate tumor cell growth, stemness, and radiation response of GSCs	Upregulated	TALNEC2, which is regulated by the E2F1 pathway.	Tumor growth	N/A	N/A	Human, mice	25	RT-qPCR
[303] (33090636)	XIST	miR-152, KLF4	To enhance the stemness of GBM by activating the XIST/mir-152/KLF4 pathway.	Upregulated	SRC-1 pathway through the lncRNA XIST/miR-152/KLF4 axis	Tumor growth	arenobufagin (ARE) and bufalin (BFU)	Reduce the proliferation and stemness of GBM cells by inhibiting the expression of SRC-1, XIST, and KLF4	Human, mice	85	qRT-PCR, RNA sequencing
[304] (36880757)	EGFR-AS1, NEAT1, ATB, HOTAIR, HMMR-AS1, H19, LINC01057, HIF1A-AS2, TALNEC2, AHIF, PCAT1, TP73-AS1, MALAT1, NCK1-AS1, and INCR1.	miR-132	To regulate various aspects of GBM pathophysiology, including proliferation, invasion, radiation and TMZ resistance, and immune modulation	Upregulated	Invasion and proliferation pathway by acting as a molecular sponge	Tumor growth and repair	TMZ	Affects lncRNAs by modulating their expression, which influences GBM pathophysiology, including proliferation, invasion, radiation resistance, and immune modulation.	N/A	N/A	N/A
[242] (38594690)	UNC5B-AS1	miR-21-3p	Suppress cell proliferation in GBM by sponging mir-24-3p. This interaction alleviates the anti-oncogenic effects of UNC5B-AS1 on cell proliferation, suggesting a potential regulatory mechanism in GBM development.	Downregulated	UNC5B-AS1-miR-24-3p network	Tumor suppressor	TMZ	TMZ treatment led to the upregulation of UNC5B-AS1, which in turn suppressed cell proliferation in GBM by sponging miR-24-3p	Human	N/A	qRT-PCR
[157] (29479863)	MALAT1	miR-101	To reverse chemoresistance to TMZ in GBM cells.	Upregulated	MALAT1-miR-101 regulatory pathway	Chemoresistance	TMZ	TMZ treatment led to the upregulation of MALAT1 in GBM cells. This upregulation of MALAT1 contributes to chemoresistance by Promoting cell	Human, mice	N/A	qRT-PCR, in situ hybridization (ISH)

								proliferation and inhibiting apoptosis			
[224] (38725030)	LINC00606	miR-486-3p	Promotes GBM progression by sponging mir-486-3p and interacting with ATP11B.	Upregulated	LINC00606 /miR-486-3p/TCF12/ ATP11B axis	Oncogene	N/A	N/A	Human, mice	120	qRT-PCR, RNA-seq
[305] (35116328)	C10orf25, LINC00343, HOTAIRM1, FGF12-AS2, and H19	C10orf25 /miR-218/DCB LD2	Regulation of gene expression and are associated with the prognosis of GBM	Upregulated	C10orf25/ miR-218/DCBL D2 axis	Oncogene	N/A	N/A	Human	169	RNA seq
[241] (37822583)	SATB2-AS1	miR-671-5p	Inhibits cell proliferation and glycolytic metabolism, while inducing cell apoptosis in glioma cells.	Downregulated	SATB2-AS1/miR-671-5p/CDR1 axis and the SATB2-AS1/miR-671-5p/VSNL1 axis	Tumor suppressor	N/A	N/A	Human (M-35, F-10)	45	RT-qPCR
[229] (33323548)	HOTAIRM1	miR-153-5p	Promotes migration and invasion of GBM	Upregulated	HOTAIRM 1/miR-153-5p/SNAI2 axis	Oncogene	N/A	N/A	Human	15	qRT-PCR
[306] (33507136)	RUNX1-IT1	miR-195	Tumor-suppressive lncRNA in GBM by sponging mir-195 to upregulate cyclin D1, thereby promoting cell proliferation	Upregulated	RUNX1-IT1 promotes GBM a proliferatio n by sponging miR-195	Oncogene	N/A	N/A	Human (M-35, F-25)	60	qRT-PCR
[307] (29296221)	lncHERG	miR-940	Promotes cell proliferation, migration, and invasion in GBM	Upregulated	promotes GBM a progression by sponging miR-940	Tumor growth	N/A	N/A	Human, mice	80	ISH
[308] (33603467)	SLC16A1-AS1	miR-149	Promotes GBM cell proliferation by regulating mir-149 methylation	Upregulated	SLC16A1-AS1 a cell proliferatio n	Tumor growth	N/A	N/A	Human (M-32, F-30)	62	qRT-PCR
[309]	DLEU1	miR-4429	Promotes cell proliferation and inhibits apoptosis in GBM	Upregulated	Inhibits apoptosis by forming a feedback loop with	Tumor growth	N/A	N/A	Human	N/A	qRT-PCR

					SP1 and miR-4429						
[237] (33499874)	LINC00680	miR-568	Enhances hepatocellular carcinoma (HCC) stemness behavior and chemoresistance by sponging mir-568 to upregulate AKT3	Upregulated	Stemness properties by sponging miR-568	Tumor growth	5-fluorouracil (5-Fu)	LINC00680 overexpression significantly decreased chemosensitivity to 5-Fu, while LINC00680 knockdown led to increased chemosensitivity	Human	74	qRT-PCR
[310] (33832517)	OXCT1-AS1	miR-195, CDC25A	Promotes GBM progression by regulating the mir-195/CDC25A axis	Upregulate	To regulate the miR-195/CDC25A axis	Tumor growth	N/A	N/A	Human	26	qRT-PCR
[311] (37444635)	LINC00474 and LINC01091	miR-128-2, NKX2-2-AS1	Involved in gene silencing pathways	Upregulated	DNA replication, chromatin silencing, and gene silencing	Tumor growth	TMZ	Affects the methylation status of the lncRNAs, which in turn influences their expression	Human	50	epigenome-wide DNA-methylation profiling
[312] (33767729)	CRNDE	miR-9-5p	Progression of GBM through sponging mir-9-5p	Upregulated	JAK-STAT signaling, apoptosis, and cytokine-cytokine receptor interactions	Tumor growth	Bacitracin, hecogenin, clemizole, chrysin	Predicted to affect the expression of CRNDE, potentially reducing its role in GBM progression	N/A	34	RT-qPCR, bioinformatics tools
[232] (32813021)	HOXA-AS2	miR-198	Promote TMZ resistance by decreasing miR-198 expression and increasing MGMT levels	Upregulated	miR-198/MGMT signaling pathway	Tumor growth	TMZ	Upregulation of H19 and HOXD-AS2, which decrease miR-198 expression and increase MGMT levels	Human, mice	41	qRT-PCR
[236] (34435542)	LINC01410	miR-370-3p	Suppresses cell viability, promotes apoptosis, and increases sensitivity to TMZ in GBM cells by inactivating the PTEN/AKT pathway via targeting mir-370-3p	Upregulated	miR-370-3p/PTEN/AKT pathway	Tumor growth	TMZ	Increases the expression of LINC01410 in GBM cells	Human (M-18, F-22)	40	qRT-PCR
[313] (36709726)	GBM downregulated RNA (GLIDR).	miR-128-3p	Promotes the aggressiveness and progression of prostate cancer cells by sponging mir-128-3p.	Upregulated	GLIDR ceRNA by sponging miR-128-3p, leading to the regulation of EMT	Tumor growth	N/A	N/A	Human (M-16, F-14)	30	qRT-PCR
[235] (32000032)	LINC00680 and TTN-AS1	miR-320b, EGR3	Promote malignant biological behaviors of GBM cells by interacting with mir-320b	Upregulated	PKP2/EGFR pathway	Tumor growth	N/A	N/A	Human, mice	N/A	qRT-PCR

			and stabilizing EGR3 miRNA.								
[314] (33911899)	MAFG-AS1	miR-34a, DICER, Drosha	Suppresses the maturation of mir-34a to promote GBM cell proliferation	Upregulated	MAFG-AS1 in GBM is its suppression of the maturation of miR-34a	Tumor growth	N/A	N/A	Human (M-35, F-21)	56	RT-qPCR
[315] (32151711)	PSMB8-AS1	DDIT4, miR-22-3p	Acts as a ceRNA of mir-22-3p to regulate DDIT4 expression in GBM	Upregulated	PSMB8-AS1 acts as a ceRNA for miR-22-3p, regulating the expression of DDIT4	Tumor growth	N/A	N/A	Human	N/A	RT-qPCR
[276] (38497174)	FOXD3-AS1	CCND1, miR-3918	Facilitates the CCND1-driven progression of GBM by serving as a ceRNA for mir-3918.	Upregulated	FOXD3-AS1 acts as a ceRNA for miR-3918, regulating the expression of CCND1	Tumor growth	N/A	N/A	Human, mouse	14	RT-qPCR
[316] (33125151)	KTN1-AS1	miR-505-3p	Promotes glioma cell proliferation and invasion by negatively regulating mir-505-3p	Upregulated	KTN1-AS1 functions by negatively regulating miR-505-3p	Tumor growth	N/A	N/A	Human (M-18, F-17), mice	35	RT-qPCR
[317] (32753949)	RNA 1 (PWRN1).	has-miR-21-5p	Suppresses cancer cell proliferation and migration in GBM by inversely regulating hsa-mir-21-5p.	Downregulated	PWRN1 functions by inversely regulating hsa-miR-21-5p	Tumor suppressor	N/A	N/A	Human, mice	51	qRT-PCR
[318] (35418162)	HOTAIR	miR-526b-3p	Involved in promoting TMZ resistance in GBM by regulating the mir-526b-3p/EVA1 axis.	Upregulated	Serum-derived extracellular vesicles	Tumor growth	TMZ	Facilitated by the upregulation of HOTAIR, which in turn affects the miR-526b-3p/EVA1 axis	Human (M-22, F-18), mice	40	RT-qPCR
[319] (35506168)	H19	miR-491-5p	Promotes GBM development by activating autophagy through sponging mir-491-5p.	Upregulated	Progression by sponging miR-491-5p and	Tumor growth	Rapamycin	Rescues the inhibitory effects of H19 knockdown on the proliferation of GBM cells and reverses the inhibition of autophagy	Human (M-12, F-13), mice	25	RT-qPCR

					activating the autophagy signaling pathway.			induced by H19 knockdown.			
[320] (35387643)	HOXA-AS2	miR-2116-3p	Enhances GBM cell malignancy by sponging mir-2116-3p and releasing SERPINA3.	Upregulated	By sponging miR-2116-3p	Tumor growth	N/A	N/A	Human	18	qRT-PCR
[321] (29335913)	HOTAIR	miR-34a	Involved in the regulation of gene expression and is associated with cancer progression	Upregulated	I3K/AKT/ mTOR, p53, and Rb signaling	Tumor growth	TMZ	Affects the expression of HOTAIR, potentially altering its regulatory functions	Human	3	qRT-PCR
[322] (32418155)	DCST1-AS1	miR-29b	Downregulates mir-29b through methylation to promote cancer cell proliferation in GBM	Upregulated	DCST1-AS1, which downregulates miR-29b through methylation	Tumor growth	TMZ	Affects the expression of DCST1-AS1, potentially altering its regulatory functions.	Human (M-38, F-24)	62	qRT-PCR
[323] (34237299)	GLIDR	miR-4677-3p	Promotes glioma progression by regulating the mir-4677-3p/MAGI2 axis	Upregulated	Upregulation of MAGI2 expression	Tumor growth	N/A	N/A	Human glioma cell line	N/A	qRT-PCR
[324] (29991527)	LINC00152	MIR4435-2HG	Promotes cellular invasion in GBM and is associated with poor patient outcomes.	Upregulated	Invasion through a 3′-hairpin structure that regulates EMT	Tumor growth	TMZ	N/A	Human	N/A	qRT-PCR
[325] (31427569)	Linc-00313	miR-342-3p, miR-485-5p	Enhances the stability of UPF1 and regulates the malignant biological behaviors of GBM	Upregulated	UPF1 and Linc-00313	Tumor growth	N/A	N/A	Human	N/A	qRT-PCR
[326] (34328678)	LINC00511	miR-126-5p	Facilitates TMZ resistance in GBM cells by sponging mir-126-5p and activating Wnt/β-catenin signaling	Upregulated	Sponging miR-126-5p and activating Wnt/β-catenin signaling	Tumor growth	TMZ	Silencing LINC00511 impairs TMZ resistance, while overexpression of LINC00511 increases TMZ resistance	Human	N/A	RT-qPCR
[230] (32279420)	HOTAIR	miR-125	Promotes chemoresistance in GBM by regulating the expression of Hexokinase 2 (HK2) through the HOTAIR/mir-125 axis	Upregulated	Regulates Hexokinase 2 (HK2) expression via the miR-125 axis	Tumor growth	TMZ	The absence of HOTAIR in GBM cells suppressed HK2 expression and enhanced the cytotoxicity of TMZ both in vivo and in vitro.	Human, mice	38	qRT-PCR

[327] (29678219)	MNX1-AS1	miR-4443	Promotes GBM progression by inhibiting mir-4443	Upregulated	Proliferation, migration, and invasion in GBM cells	Tumor suppressor	N/A	N/A	Human	44	qRT-PCR
[258] (32784466)	BC200	miR-218-5p	Promotes GBM oncogenicity and TMZ resistance through mir-218-5p expression modulation.	Upregulated	The paper discusses the BC200/miR-218-5p signaling axis	Tumor suppressor	TMZ	Modulates the expression of BC200 RNA, which in turn affects the resistance of GBM cells to the drug.	Human, mice	48	qRT-PCR
[328] (27446363)	HOTAIR	miR-148b-3p	Promotes malignancy by enhancing cell proliferation, cell cycle progression, and invasion.	Upregulated	miR-148b-3p/HOTAIR axis	Tumor suppressor	siRNA HOTAIR (siHOTAIR).	siHOTAIR suppresses the expression of HOTAIR, reducing cell proliferation, cell cycle progression, and invasion.	Human glioma cell	180	qRT-PCR
[329] (34478013)	LINC00152	miR-107	Promotes tumor proliferation and invasion in gliomas	Upregulated	LINC00152/miR-107/RAB10 axis.	Oncogene	TMZ	N/A	Glioma cell lines and mouse models	73	qRT-PCR
[264] (33747903)	HOTAIR, SOX21-AS1, and STEAP3-AS1	miRNAs	Involved in constructing a prognostic model for GBM by regulating gene expression and interacting with miRNAs and mRNAs	Upregulated & downregulated	HOTAIR, SOX21-AS1, and STEAP3-AS1, are identified as prognostic markers	HOTAIR and STEAP3-AS1: Tumor growth, SOX21-AS1: Tumor suppressor	TMZ	Used in standard chemoradiotherapy, and the study suggests that patients treated with TMZ showed better overall survival, indicating its effectiveness in conjunction with the lncRNA signature	Human	151	qRT-PCR
[330] (39538257)	miR3681HG.	miR3681HG	Associated with a reduced overall survival in GBM patients.	Downregulated	TREM-1 signaling pathway	Tumor growth	TMZ	N/A	Human	N/A	RNA seq
[240] (38864705)	AL161785.1, LINC02611, and PCED1B-AS1	mRNA	Involved in the pathogenesis of GBM by regulating miRNA availability and controlling mRNA stability	Upregulated	lncRNA-associated ceRNA network pathway	Tumor growth	N/A	N/A	Human	169	RNA seq, qRT-PCR
[234] (31545240)	EGFR-AS1	miR-133b	Migration, invasion, and apoptosis in glioma cells by targeting mir-133b/RACK1	Upregulated	miR-133b/RACK1 signaling pathway	Tumor growth	N/A	N/A	Human, mice	14	qRT-PCR
[228] (32420340)	MEG3	miR-6088, and	Inhibits the proliferation and migration of glioma cells by	Downregulated	miR-6088/SMARCB1 axis	Tumor suppressor	N/A	N/A	N/A	N/A	N/A

		SMARCB1	regulating the mir-6088/SMARCB1 axis								
[331] (39145837)	H19	miR-29a-3p	N/A	Upregulated	FoxO signaling pathway and focal adhesion pathway	Tumor growth	N/A	N/A	N/A	N/A	N/A
[332] (31985002)	MCM3AP-AS1	miR-93	Inhibits cell proliferation in cervical squamous cell carcinoma by down-regulating mirna-93	Downregulated	Pathway of regulating miR-93 methylation and expression	Tumor suppressor	N/A	N/A	Human (F-64)	N/A	qRT-PCR
[333] (32943928)	SNHG9	miR-21	Downregulates mir-21 through methylation to suppress cancer cell proliferation	Downregulated	Regulating miR-21 methylation and expression	Tumor suppressor	N/A	N/A	Human (M-48, F-16)	64	RT-qPCR
[334] (30691465)	MIR17HG	miR-346, miR-425-5p	Stabilizes the RNA binding protein FXR1, promoting the malignant biological behavior of glioma cells	Upregulated	Pathway of stabilizing the lncRNA MIR17HG	Tumor growth	N/A	N/A	Human, mice	N/A	qRT-PCR
[335] (34596120)	LINC00261 and HOXA10-AS	miRNAs	Act as prognostic biomarkers for patients with GBM	Upregulated	LINC00261 and HOXA10-AS are part of a ceRNA network	Tumor growth, Tumor suppressor, Repair	N/A	N/A	Human	156	qRT-PCR
[254] (33363617)	SNHG9	CRY2, miR-214-5p	Acts as a tumor suppressor gene in ovarian cancer by regulating the mir-214-5p/CRY2 axis.	Downregulated	miR-214-5p/CRY2 axis	Tumor suppressor	N/A	N/A	Human	25	qRT-PCR
[336] (30657584)	GAPLINC	miR-331-3p	Promotes the growth and metastasis of GBM by sponging mir-331-3p.	Upregulated	Sponging miR-331-3p	Oncogene	N/A	N/A	Human	N/A	RT-qPCR
[239] (30096248)	H19	miR-326	Involved in the pathogenesis of GBM	Upregulated	Overexpression, negatively impacting overall survival	Oncogene	N/A	N/A	Human	M-37, F-13	qRT-PCR
[231] (32721218)	HOTAIR	miR-519a-3p	Regulates TMZ resistance in GBM through the mir-519a-3p/RRM1 axis	Upregulated	miR-519a-3p/RRM1 axis through exosome-mediated transfer	Oncogene	TMZ	Modulates the resistance through the miR-519a-3p/RRM1 axis	Human (51), mouse	51	qRT-PCR

[223] (32427712)	SNHG4	miR-138	Regulates the mir-138/c-Met axis to promote the proliferation of GBM.	Upregulated	miR-138/c-Met axis	Oncogene	N/A	N/A	Human	62 (M-35, F-25)	qRT-PCR
[337] (33991848)	RP3-439F8.1	NR5A2, miR-139-5p	Promotes GBM cell proliferation and progression by sponging mir-139-5p to upregulate NR5A2.	Upregulated	β-catenin/TCF4 signaling pathway.	Oncogene	N/A	N/A	Human	N/A	qRT-PCR
[338] (29202181)	MALAT1	siRNA	Plays a role in tumor cell infiltration and therapeutic resistance of GBM	Upregulated	Therapeutic resistance in GBM, enhances sensitivity to chemotherapy.	Tumor growth	TMZ	Combined with nanocomplex-mediated silencing of MALAT1, improves the sensitivity of GBM cells to the drug.	Human, mice	N/A	qRT-PCR

Table 18 Details of list of articles involved with RNA binding / Translation / Post-transcriptional regulation pathway

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[243] (27738870)	BACE1-AS, linc-RoR, and SOX2-OT.	PHLDA1 and ELAV1	To regulate signaling pathways involved in pediatric astrocytoma.	Upregulated	MAPK, Wnt, FAK, and PI3K-Akt	Cellular proliferation	N/A	N/A	Human pediatric astrocytoma samples	26	GeneChip Human Transcriptome Array 2.0 (HTA 2.0).
[244] (31719831)	ELAVL2	MTAP, KLHL9, ELAVL2	Regulating gene expression and has been linked to the overall survival in gliomas	N/A	cell cycle regulation, p53 signaling, and TGF-beta signaling	Tumor growth, suppression, repair	N/A	N/A	Human	N/A	Pearson correlation coefficient (PCC)
[266]	HAS2-AS1	PRPS1	Promotes tumor progression in GBM by functioning as a competing endogenous RNA	Upregulated	miR-608/PRPS1 axis	Oncogene	N/A	N/A	Human, animal	N/A	qRT-PCR, FISH
[339] (30029885)	LINC01446	TPT1	Promotes GBM progression by modulating the mir-489-3p/TPT1 axis.	Upregulated	LINC01446/miR-489-3p/TPT1 cascade	Oncogene	N/A	N/A	Human	31	qRT-PCR
[247] (31102349)	FOXD1-AS1	eIF5A	Acts as an oncogene in glioma, promoting cell proliferation and inhibiting apoptosis	Upregulated	miR339/342-eIF5a axis	Oncogene	N/A	N/A	Human (M-52, F-23), mice	75	qRT-PCR

Table 19 Details of list of articles involved with Neurotrophic / Growth Factors

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[248] (37566001)	BDNF-AS	BDNF	Tumor suppressor in GBM	Upregulated	BDNF-AS pathway	Tumor suppressor	Propofol	Increases BDNF-AS expression, inhibiting GSC growth	Human	N/A	RT-qPCR, microfluid chip technology
[250] (27270310)	RP11-838N2.4	EphA8	Enhances the cytotoxic effects of TMZ by inhibiting the functions of mir-10a in GBM cell lines	Downregulated	RP11-838N2.4/miR-10a/EphA8 axis	Tumor suppressor	TMZ	Increases the expression of lncRNA RP11-838N2.4, which in turn enhances the drug's cytotoxic effects on GBM cells	Human cell lines, mice	38	qRT-PCR
[11] (32188434)	HOXB-AS3, LGALS8-AS1, LINC00032, LINC00311, LINC00494, LINC00544, LINC00589, LINC00626, MEIS1-AS3, and VAV3-AS1	ASIC5	Involved in the prognosis of GBM patients. They play roles in various biological processes, including transcription regulation and gene expression	Upregulated	Calcium signaling, neuroactive ligand-receptor interaction, and Wnt signaling	Oncogene	N/A	N/A	Human	151	RNA seq
[219] (39453684)	NEAT1	Cx43	Regulates gap junctional intercellular communication by modulating Connexin 43, impacting the response of GBM cells to TMZ chemotherapy.	Upregulated	NEAT1/miR-454-3p/Cx43 signaling pathway	Oncogene	TMZ	Downregulation of NEAT1 resulted in enhanced chemosensitivity to TMZ and extended the survival of mice.	Human cell lines, mice	67	qRT-PCR
[12] (35852867)	RP11-552D4.1	neuronal	Facilitates neuronal proliferation	Upregulated	RP11-552D4.1/m6A-related lncRNA network	Oncogene	Metformin	The high-risk group had a higher half inhibitory concentration (IC50) of metformin	Human	169	qRT-PCR
[249] (32459347)	MEG3	DLK1-DIO3	Acts as a tumor suppressor by regulating cell adhesion, EMT, and cell proliferation	Downregulated	DLK1-DIO3 imprinted region-associated regulatory network	Tumor suppressor	Valproic acid (VPA)	Increase in MEG3 levels, suggesting that epigenetic modifications contribute to MEG3 silencing	Human, mice	N/A	qRT-PCR

Table 20 Details of list of articles with Novel Uncharacterized lncRNAs

Publication (PMID)	LncRNA Name	Gene Target	LncRNA Function	Regulation	Signaling Pathway	Gene Function	Drug	Drug Effects on LncRNA	Model System	Sample Demographics	LncRNA Detection Technique
[340] (32962742)	LPP-AS2	N/A	N/A	N/A	miR-7-5p/EGFR/PI3K/AKT/c-MYC	Oncogene	N/A	N/A	N/A	N/A	RT-qPCR
[341] (37452786)	TP73-AS1	N/A	Functions as a regulator of TMZ sensitivity in GBM	Downregulated	Regulator of TMZ sensitivity	Tumor suppressor	TMZ	Downregulation of TP73-AS1 expression in TMZ-sensitive parental U87MG cells decreased their sensitivity to TMZ	Human	N/A	qRT-PCR
[277] (28926136)	CRNDE, GAS5, H19, HOTAIR, MALAT1, and TUG1.	N/A	Promotes tumor invasion and progression, acts as a tumor suppressor gene by promoting cell apoptosis.	HOTAIR- up/ GAS5-do	Tumor growth and resistance mechanisms	Tumor suppressor and oncogene	N/A	N/A	Human	106	qRT-PCR
[5] (38086292)	H19, MALAT1, HOTAIR	N/A	Modulation of biological processes such as migration, proliferation, and stemness maintenance, impacting the chemosensitivity of GBM cells.	Upregulated / downregulated	STAT signaling, β-catenin, and interleukin functions	Tumor suppressor and oncogene	TMZ	Dysregulation of specific lncRNAs, which modulate DNA repair, apoptosis, and cell cycle regulation pathways.	Human, animal	N/A	next generation
[342] (23726844)	KIAA0495, PART1, MGC21881, MIAT, GAS5, and PAR5	N/A	Tumor suppressor, prostate carcinogenesis, cell differentiation, cell apoptosis	Upregulated / downregulated	MGMT promoter methylation and epigenetic regulation	Tumor suppressor	TMZ	N/A	Human	382	lncRNA mining approach, TCGA, GEO
[343] (38458555)	DRAIC	N/A	Act as a tumor suppressor in some cancers, such as prostate adenocarcinoma and GBM, by inhibiting cell invasion and migration	Downregulated	NF-κB signaling pathway	Tumor suppressor	N/A	N/A	Human	N/A	qRT-PCR
[344] (38086498)	H19, MALAT1, HOTAIR, XIST, UCA1	N/A	Immunomodulation, cancer metastasis, cancer development, and drug resistance in GBM	Upregulated	Wnt/β-catenin and PI3K/AKT signaling	Oncogene, tumor progression and drug resistance	TMZ	Affects the expression of lncRNAs by inhibiting their pro-tumorigenic activities	Human	N/A	qRT-PCR
[260] (29715460)	CASP5	N/A	Promotes the malignant phenotypes of human GBM by enhancing cell proliferation, migration, and invasion.	Upregulated	cell proliferation, migration, and invasion	Oncogene	N/A	N/A	Human	N/A	qRT-PCR
[345] (30181543)	N/A	N/A	N/A	N/A	Reweighted Random	Oncogene	N/A	N/A	N/A	N/A	

					Survival Forest (RRSF) model						
[346] (36747529)	DLEU1, AC005005.3, ZEB1-AS1, and UNC5B-AS1.	N/A	Significantly correlated with the prognosis of GBM and are involved in immune cell infiltration	Upregulated & downregulated	Immune cell infiltration and tumor microenvironment modulation	Oncogene	TMZ	Upregulates the expression of CD274, which is associated with the immune response in GBM	Human	169	qRT-PCR
[347] (25462570)	hcmv-miR-UL112-3p	N/A	Suggested to play a role in the establishment and maintenance of viral latency	N/A	hcmv-miR-UL112-3p	Repair	N/A	N/A	Human	87	microarray analysis
[348] (30034397)	CASC2	N/A	Interacts with mir-338-3p and inhibits its expression, which in turn regulates the expression of coagulation factor X (FX) and influences macrophage polarization	N/A	CASC2c-FX pathway	Oncogene	Rapamycin	Did not inhibit the chemotaxis of FX on PMA-primed THP-1 cells, suggesting that FX recruits' macrophages in an mTOR-independent manner	Human, mice	N/A	qRT-PCR
[349] (35341001)	DLGAP1-AS1	N/A	Promoting tumor progression by regulating ATG4A and serving as a potential biomarker for poor prognosis	Upregulated	Autophagy signaling pathway	Oncogene	N/A	N/A	Human	N/A	qRT-PCR
[350] (32488114)	NEAT1 and FTX	N/A	Contribute to GBM progression and radio-resistance.	Upregulated	Transcription factors like FOXM1 and E2Fs	Oncogene	N/A	N/A	Human	N/A	RNA sequencing and bioinformatics analysis
[351] (23046790)	DKK1-AS1 and CTSC-AS1	N/A	Implicated in GBM-related pathways, influencing cell proliferation and tumor progression	Upregulated	PTEN regulation	Tumor suppressor	N/A	N/A	Human	N/A	Tag-seq (high-throughput transcript tag sequencing) and qRT-PCR
[352] (27923049)	TUNAR, CRNDE	N/A	Positive regulator of neuronal development and differentiation.	Upregulated	Tumor progression pathways	Tumor suppressor	N/A	N/A	Human	15	qRT-PCR
[107] (31589963)	MALAT	N/A	Involved in the progression and chemo-resistance of GBM)	Upregulated	p53-HIF, β-catenin, and mTOR signaling	Oncogene and tumor suppressor	TMZ	Affects the expression levels of lncRNAs, particularly HOTAIR and MALAT1, which are associated with chemo-resistance in GBM.	Human	35	qRT-PCR
[353] (33969526)	N/A	N/A	N/A	N/A	Chromatin remodeling and	Tumor growth	N/A	N/A	N/A	N/A	N/A

					oncogenic signaling						
[354] (35668225)	LINC00565 and LINC00641	N/A	Prognostic biomarkers for GBM patients	Upregulated	MAPK, ECM receptor interaction, and focal adhesion pathways	Tumor suppressor, oncogene	TMZ	N/A	Human (M-24, F-11)	35	qRT-PCR
[355] (33489915)	CYTOR (ENSG00000222041)	N/A	Pathogenesis of glioma by influencing cell proliferation and invasion	Upregulated & downregulated	DNA methylation pathways	Tumor suppressor and oncogene	N/A	N/A	Human	537	qRT-PCR, RNA sequencing
[356] (39302097)	N/A	N/A	N/A	N/A	p53 inactivation	Oncogene	N/A	N/A	N/A	N/A	N/A
[357] (25378224)	HOTAIR	N/A	In chromatin remodeling and gene expression regulation.	Upregulated & downregulated	DNA replication and focal adhesion signaling	Tumor suppressor, oncogene and repair mechanism	TMZ	In chromatin remodeling and gene expression regulation.	Human	10	Agilent Microarray, qRT-PCR
[358] (31191605)	N/A	N/A	Regulating gene expression and being involved in the progression of complex diseases	N/A	two-side sparse self-representation (TSSR) model	Tumor suppressor	N/A	N/A	Human	N/A	N/A
[359] (30529802)	N/A	N/A	Involved in the regulation network of DHA, affecting genes associated with receptor binding, oxidoreductase activity, and transmembrane transporter activity	Downregulated	PPAR signaling, AMPK signaling, and EGFR resistance pathways	Tumor suppressor	Docosahexaenoic acid (DHA)	Modulates the expression of lncRNAs, leading to changes in gene expression related to cancer cell viability, migration, invasion, and apoptosis	Human	N/A	qRT-PCR
[252] (28527107)	AC005013.5, UBE2R2-AS1, ENTPD1-AS1, RP11-89C21.2, AC073115.6, and XLOC_004803[	N/A	Involved in immune-related biological processes and pathways, which are significant in the context of GBM tumorigenesis	Upregulated & downregulated	Immune-related pathways	Tumor suppressor and oncogene	N/A	N/A	Human (M-263, F-156)	419	Affymetrix Human Exon 1.0 ST Array
[360] (28978068)	AK098425, AL833059, AK056155, and CR613436	N/A	Cancer-related biological processes and pathways, and their deregulation may lead to GBM	Upregulated & downregulated	Immune response, lysosome, Toll-like receptor signaling	Oncogene	N/A	N/A	Human	276	microarray probes repurposing
[361] (32099410)	HCG25, NDUFA6-DT, DPP10-AS1, TPT1-AS1, and AGAP2-AS1	N/A	Prognosis and pathogenesis of GBM	Upregulated & downregulated	PI3K-Akt signaling, cellular senescence	Oncogene	N/A	N/A	Human	149	qRT-PCR

[362] (34653676)	USP30-AS1	N/A	Contributes to mitochondrial quality control in GBM cells by regulating mitochondrial homeostasis and mitophagy.	Upregulated	Mitochondrial homeostasis disruption	Oncogene	N/A	N/A	Human	N/A	qRT-PCR
[363] (39429673)	CRNDE, LINC00957, and AC072061.1[_	N/A	Potential diagnostic and prognostic biomarkers in GBM	Upregulated & downregulated	MAPK signaling and Wnt signaling	Tumor suppressor and oncogene	TMZ	Affects the survival rate and prognosis	Human (M-366, F-230)	499	RNA seq, qRT-PCR
[263] (37833349)	RARA-AS1	N/A	Promotes proliferation and migration in GBM	Upregulated	Immune checkpoints and mismatch repair genes	Oncogene	KIN001-055, GSK-650394, Shikonin, and QS11	These drugs have lower IC50 values in the RARA-AS1 high-expression group, indicating that a relatively lower drug concentration can achieve better therapeutic effects in this group	Human	N/A	qRT-PCR
[364] (33665208)	AC046143.1, AC021054.1, AC080112.1, MIR222HG, and PRKCQ-AS1	N/A	Prognostic target for GBM, with the high-risk group showing significantly distinct immune states	Upregulated & downregulated	Immune system processes and immune response pathways	Tumor progression and immune regulation	N/A	N/A	Human	151	RNA sequencing and Pearson correlation analysis
[365] (31692451)	LINC00152	N/A	Prognostic biomarker in GBM, affecting survival	Upregulated	Metabolic, mTOR, and camp signaling	Oncogene	TMZ	Enhances effect on GBM cells	Human	N/A	RNA-Seq, methylation, CNV
[366] (29955818)	Various lncRNAs (e.g., ceRNAs)	N/A	Study focuses on constructing miRNA sponge regulatory networks for multiple cancers, including GBM	Upregulated	PI3K-Akt signaling and immune response	Oncogene	N/A	N/A	Human	451	microarray analysis
[367] (3285105)	CPB2-AS1, AC092171.2, LINC00665, LINC00460, PRRT3-AS1, and DNAH10OS	N/A	Immune regulation and are potential prognostic factors for GBM	Upregulated & downregulated	Extracellular matrix organization and PPAR signaling	Tumor suppressor and oncogene	nti-PD-1 drug pembrolizumab	Excellent antitumor effects in melanoma but is less effective in GBM	Human	66	qRT-PCR
[368] (37308741)	N/A	N/A	N/A	N/a	HOXD-AS2-STAT3 feedback loop	Oncogene	N/A	N/A	N/A	N/A	N/A
[369] (35212938)	N/A	N/A	N/A	N/a	PI3K/AKT/MAPK and Wnt/β-catenin being activated	Oncogene	N/A	N/A	N/A	N/A	N/A

[370] (30463803)	CRNDE	N/A	Identified as a potential biomarker for cancer diagnosis and prognosis.	Upregulated	PI3K-AKT and Wnt signaling	Oncogene	N/A	N/A	N/A	11574	qRT-PCR
[371] (34686327)	HOXA10-AS	N/A	Enhance GBM progression by scaffolding EZH2 and activating the WNT/β-catenin pathway.	N/A	PI3K/AKT/mtor and Wnt signaling	Oncogene	N/A	N/A	Human, mice	N/A	RT-qPCR
[372] (30742682)		N/A	To regulate GBM cell proliferation, invasion, and migration under hypoxic conditions.	N/A	Carcinogenesis, epigenetic modifications, and therapeutic resistance	Tumor suppressor, oncogene and repair mechanism	N/A	N/A	Human	N/A	qRT-PCR
[373] (37540752)	DARS1-AS1	N/A	Promote GBM tumorigenesis and radio resistance by regulating posttranscriptional circuits and enhancing DNA repair mechanisms.	N/A	DARS1-AS1/YBX1 axis	Tumor growth and repair	TMZ	Sensitivity of GBM cells to TMZ by impairing DNA repair mechanisms and increasing radiosensitivity.	Human	N/A	qRT-PCR, RNA sequencing
[267] (33438023)	MVIH	N/A	Impairs GBM cell proliferation and invasion through an mir-302a-dependent mechanism	Downregulated	lncRNA-MVIH/miR-302a	Chemoresistance, tumor progression	TMZ	Decreasing GBM cell proliferation and invasion, enhancing the effectiveness of chemotherapeutic agents, resistance mechanisms	Human	34	qRT-PCR
[374] (38162904)	AC011405.1, HOXC13-AS, LINC01127, and LINC01574	N/A	Potential targets for enhancing the delivery and efficacy of lncRNA-based therapeutics in GBM treatment	Upregulated	Network of graphene therapy	Tumor growth, repair and therapeutic resistance	16 compounds in graphene therapy	Potentially enhance the delivery and efficacy of lncRNA-based therapeutics in GBM	Human (M-103, F-56)	159	Tumour immune escape and immunotherapy analysis
[375] (31316603)	HOTAIR, H19, WT1-AS, LINC00475, and others	N/A	ceRNA, influencing GBM progression	Upregulated / downregulated	Transcriptional regulation	Tumor suppressor and oncogene	N/A	N/A	Human	N/A	edgeR and GEO2R
[376] (30367041)	LINC-PINT	N/A	Encode a peptide that suppresses GBM cell proliferation by interacting with the polymerase associated factor complex (PAF1c) and inhibiting the transcriptional elongation of multiple oncogenes.	N/A	circular RNA network involving LINC-PINT	Tumor suppressor	N/A	N/A	N/A	N/A	qRT-PCR
[377] (32039732)	SNHG12	N/A	To promote TMZ resistance in GBM cells by acting as a molecular sponge for mir-129-5p, leading to the upregulation of MAPK1 and E2F7	Upregulated	lncRNA SNHG12-mediated network, DNA methylation	Tumor growth and chemoresistance	TMZ	Promotes the upregulation of lncRNA SNHG12 in GBM cells, leading to TMZ resistance.	Human, mice	60	qRT-PCR, fluorescence in situ hybridization (FISH)

[378] (36354672)	MIR34AHG and MIR3142HG	N/A	Neutrosphere formation, potentially influencing GBM progression	Upregulated	EGFR/FGFR signaling	Tumor suppressor, tumor growth	N/A	N/A	Human	N/A	RNA sequencing
[257] (34800915)	RBPMS-AS1	N/A	Enhance radiosensitivity	Downregulated	microRNA-301a-3p/ CAMTA1 axis	Tumor suppressor	N/A	N/A	N/A	N/A	qRT-PCR