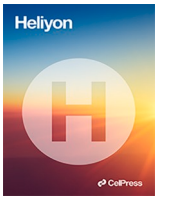
Heliyon 10 (2024) e37527

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Review article

LINC01094: A key long non-coding RNA in the regulation of cancer progression and therapeutic targets

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ARTICLE INFO

Keywords:
lncRNA
LINC01094
Malignant cancers
Biological
Clinical therapies

ABSTRACT

LINC01094 is a long non-coding RNA that plays a crucial role in cancer progression by modulating key signaling pathways, such as PI3K/AKT, Wnt/β-catenin and TGF-β Signaling Pathway Feedback Loop. In this review we summarize the recent research on the functional mechanisms of LINC01094 in various cancers, including its impact on tumor growth, metastasis, and resistance to therapy. We also discuss the therapeutic potential of targeting LINC01094 and highlight the current strategies and challenges in this area. Perspectives on future development of LINC01094-based therapies are also provided.

1. Introduction

Cancer is the second leading cause of global morbidity and the primary driver of diminished survival rates worldwide. In recent years, there has been a rapid increase in the incidence and mortality rates of cancer [1,2]. Despite the broad array of conventional therapies—including surgical interventions, radiotherapy, immunotherapy, and chemotherapy—the prognosis for most patients remains poor owing to individual variabilities, tumor heterogeneity, and the inherent limitations of therapeutic modalities. Overall survival (OS) rates remain low, due to persistent challenges and unresolved issues [3–6]. Molecular-targeted therapy has emerged as a novel approach that circumvents these limitations, promising new approaches to cancer management [7–9].

Long non-coding RNAs (lncRNAs) are crucial regulators of gene expression and play important roles in cellular processes and disease states [10]. LncRNAs are RNA molecules longer than 200 nucleotides that do not encode proteins, but instead modulate gene expression through various mechanisms, including chromatin remodeling, transcriptional regulation, and post-transcriptional modifications [11]. LncRNAs are involved in critical biological processes including cell proliferation, differentiation, and apoptosis [12] and have been associated with a wide range of diseases beyond cancer; for example, digestive system diseases [13], cardiovascular diseases [14], neurodegenerative disorders [15], and metabolic conditions [16]. Consequently, lncRNAs have emerged as novel therapeutic targets and potential biomarkers for patient diagnosis and prognosis.

The gene *long non-coding RNA 1094* (*LINC01094*), situated on the q21.21 region of human chromosome 4 (4q21.21), is highly conserved and widely expressed in various tissues. As such, the gene has immense potential as a tool in cancer diagnosis, prognostic evaluation, and therapeutic interventions. Recent studies have revealed the aberrant expression of LINC01094 in 11 types of cancers,

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https://doi.org/10.1016/j.heliyon.2024.e37527
Received 27 April 2024; Received in revised form 25 July 2024; Accepted 4 September 2024
Available online 7 September 2024

and it has been notably implicated as a major regulatory factor in lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), gastric cancer (GC), colorectal cancer (CRC), glioma, pancreatic cancer (PC), laryngeal squamous cell carcinoma, ovarian cancer (OC), hepatocellular carcinoma (HCC), clear cell renal cell carcinoma (ccRCC), and breast cancer (BC). Additionally, LINC01094 is differentially expressed in chronic rhinosinusitis with nasal polyps (CRSwNP) [17], calcific aortic valve disease (CAVD) [18], postmenopausal osteoporosis (PMOP) [19], schizophrenia (SCZ) [20], multiple sclerosis (MS) [21], osteoarthritis (OA) [22] and normal pregnancy [23].

LINC01094 has emerged as a focal point in cancer research owing to its regulatory role in several malignancies. It promotes cancer progression by modulating key signaling pathways, such as PI3K/AK,TGF-β, and Wnt/β-catenin signaling pathway, through interactions with microRNAs. These interactions affect various cellular processes including cancer cell proliferation, migration, invasion, and epithelial-mesenchymal transition (EMT). For example, LINC01094 sequesters miR-577 in pancreatic cancer, leading to the upregulation of LIN28B and activation of the PI3K/AKT pathway [24]. Additionally, LINC01094 influences the Wnt/β-catenin pathway, further contributing to tumor progression [25]. Recent studies have highlighted its role in the modulation of drug resistance. By affecting crucial pathways involved in apoptosis and the cell cycle, LINC01094 contributes to resistance against chemotherapy and targeted therapies [26]. Its multifaceted involvement in cancer biology underscores its therapeutic potential. Current strategies for targeting LINC01094 include the use of antisense oligonucleotides (ASOs), small interfering RNAs (siRNAs), CRISPR/Cas9-mediated gene editing, and small molecule inhibitors [27]. These approaches aim to disrupt the functioning of LINC01094, thereby impeding cancer progression and enhancing the efficacy of conventional treatments. Understanding the detailed mechanisms by which LINC01094 functions is essential for optimizing targeted strategies and improving cancer treatment outcomes.

In this review we give a comprehensive overview of the latest research on the expression patterns, clinical significance, molecular mechanisms, and biological functions of LINC01094. Furthermore, we discuss the potential clinical applications of LINC01094 as a therapeutic target and diagnostic marker and explore its efficacy in treatment outcomes across various tumors.

2. Expression and clinical characteristics of LINC01094 in various cancer types

Long non-coding RNA (lncRNAs) are a class of non-protein-coding transcripts that have attracted increasing attention. As shown in Table 1, the expression level of LINC01094 is significantly dysregulated in various diseases, such as pancreatic cancer, gastric cancer, colorectal cancer, and hepatocellular carcinoma, and is associated with multiple clinical characteristics.

2.1. Pancreatic cancer

The prognosis of pancreatic cancer (PC) is generally poor; the high mortality rate of PC makes it the leading cause of cancer-related deaths globally, and the global disease burden of this cancer has more than doubled over the past 25 years [38,39]. The current treatments for PC cancer include surgery, chemotherapy, radiotherapy, targeted therapy, and combination therapy. However, despite efforts to improve prognosis, the 5-year survival rate of remains low [40]. The lack of effective diagnostic methods, dense stromal barriers that protect tumors from effective drug penetration, and the emergence of chemotherapy resistance have contributed to the limited improvement in PC treatment outcomes [41,42]. Research findings indicate that fluorescence in situ hybridization (FISH) staining of PC tissue microarrays revealed significantly higher levels of LINC01094 compared to levels in adjacent normal tissues [43]. Additionally, Luo et al. found that the expression level of LINC01094 in PC tissues was much higher than that in normal non-tumor pancreatic tissues and was correlated with poor prognosis. Furthermore, *LINC01094* silencing inhibited cell proliferation compared to control cells, whereas LINC01094 overexpression had the opposite effect. In addition, downregulation of LINC01094 reduced the

Table 1
The Clinicopathological characteristics of LINC01094 in various malignancies.

Cancer type	Number of cases	Expression	Clinicopathological characteristics	Prognosis	Refs.
Pancreatic cancer (PC)	91	high	poor overall survival,Tumor size, Lymphatic metastasis, Distant metastasis, TNM stage	poor	[24]
Gastric cancer (GC)	106	high	unfavorable prognosis, T and N stages, Neuroinvasion	poor	[28]
Colorectal cancer (CRC)	122	high	the absence of vascular invasion, positive lymph node metastasis, advanced TNM stage	poor	[29]
Hepatocellular carcinoma (HCC)	36	high	the incidences of lym-phatic, distant metastasis	poor	[30]
Ovarian cancer (OC)	90	high	/	poor	[25]
Breast cancer (BC)	/	high	overall survival time	poor	[31]
Glioma	86	high	grades	poor	[32]
Glioblastoma (GBM)	51	high	the mean tumor diameter, Karnofsky Performance Scale (KPS) score	poor	[33]
Clear cell renal cell carcinoma (ccRCC)	56	high	TNM stage, Fuhrman grade, vascular invasion, and lymph node metastasis	poor	[34]
Lung squamous cell carcinoma (LUSC)	/	high	age, tumor-stage, node-stage, metastasis-stage and stages, the gender and tobacco	poor	[35]
Lung adenocarcinoma (LUAD)	/	high	worse prognosis probability	poor	[36]
Laryngeal squamous cell carcinoma (LSCC)	111	high	/	poor	[37]

migration and invasion capabilities of PC cells, whereas its overexpression significantly increased the migration and invasion capabilities of CFPAC-1 cells [24]. Therefore, increased levels of LINC01094 can significantly promote the proliferation, invasion, and distant migration capabilities of PC cells. These findings suggest that LINC01094 could serve as a novel diagnostic biomarker and therapeutic target for pancreatic cancer.

2.2. Gastric cancer

Gastric cancer (GC) ranks fifth in global incidence and fourth in terms of mortality rates [44–46]. Owing to the lack of early diagnostic markers, patients are often diagnosed with tumors that have metastasized to proximal or even distant areas within the body, resulting in a median survival period of less than one year [47]. Early detection and effective monitoring of tumor progression are crucial to reduce the burden and mortality rate of gastric cancer [48]. Gong et al. found that the expression level of LINC01094 in tumor tissues was significantly higher than that in normal tissues, with patients in the high expression group exhibiting higher T and N stages, correlating with poor prognosis. Experimental data showed that LINC01094 knockdown weakened proliferation and migration capabilities, whereas LINC01094 overexpression enhanced these capabilities [28]. High LINC01094 expression indicates poor prognosis in gastric cancer and is associated with the epithelial-mesenchymal transition pathway and macrophage infiltration [49]. Moreover, it appears from the results of a copper apoptosis-related model that LINC01094 can effectively predict the prognosis of patients with GC, enabling risk stratification, assessing potential immunotherapy, and evaluation of treatment sensitivity [26,50] Additionally, Yuan et al. [51,52] demonstrated that LINC01094, one of the lncRNAs associated with platelet activation and angiogenesis, affects the prognosis and immunotherapy of patients with GC. Furthermore, in autophagy-related lncRNA (ARlncs) and necroptosis-related lncRNA (NRL) models, LINC01094 was found to be a useful tool in the prognosis of GC based on molecular characteristics, with the potential of improving treatment strategies and facilitating precision therapies [53,54]. These findings provide new directions for the diagnosis and treatment of GC.

2.3. Colorectal cancer

Colorectal cancer (CRC) ranks third in incidence among common cancers and second in mortality, with over 1.85 million cases and 850,000 deaths annually [55–57]. Deaths related to CRC are preventable if the disease is diagnosed early. However, despite various early detection methods, poor prognosis and late detection remain serious concerns [58]. There is increasing evidence that the level of expression of LINC01094—which is elevated in CRC patient tissues and CRC cells—is an independent prognostic factor. High levels of expression of LINC01094 have been associated with non-vascular invasion and are significantly correlated with positive lymph node metastasis and advanced TNM stage. The results of in vitro studies have demonstrated that high LINC01094 expression promotes tumor cell proliferation, migration, and invasion, whereas its downregulation has the opposite effect [29]. Although LINC01094 shows promise as an indicator in at the cellular and tissue level, its clinical applications are limited; thus animal studies and tests with human blood are required.further investigation. For instance, studies involving LINC01094 in CRC have been limited to tissue testing and, lacking validation usingthrough animal experiments and human blood tests. Notwithstanding these limitations, it is clear that LINC01094 may serve as a promising diagnostic indicator, therapeutic target, and prognostic marker of CRC.

2.4. Ovarian cancer

Ovarian cancer is the most lethal gynecological cancer, with a 5-year survival rate of approximately 47 %, resulting in over 15,000 deaths annually [59,60]. Dysregulation of lncRNAs is common in ovarian cancer and largely contributes to malignant phenotypic changes [61]. Reports indicate that LINC01094 is expressed at a significantly higher level in ovarian cancer tissues than in adjacent normal tissues. Additionally, it has been reported that LINC01094 is expressed significantly higher in patients with higher FIGO stages and lymph node metastasis than in those with lower stages and no lymph node metastasis, suggesting an association between LINC01094 and ovarian cancer progression. Furthermore, compared to negative control cells, LINC01094 was found to promote the proliferation, migration, invasion, and EMT of ovarian cancer cells, blocking cell apoptosis at the G2/M phase. Conversely, inhibiting LINC01094 expression weakens these effects [25,62]. These results indicated that LINC01094 promotes the growth and proliferation of ovarian cancer cells. In constructing a ceRNA regulatory network model related to apoptosis in ovarian cancer cells, high-risk patients who had elevated levels of LINC01094 exhibited higher infiltration of macrophages and tumor-associated fibroblasts [63]. Considering these results together, LINC01094 may serve as a potential therapeutic target against ovarian cancer.

2.5. Breast cancer

Despite global research efforts, breast cancer remains the leading cause of cancer-related death among women worldwide [55,64]. Breast cancer exhibits heterogeneity in terms of morphological characteristics, biological behaviors, and responses to treatment [65]. Recently, it has been reported that the expression of LINC01094 is significantly higher in breast cancer tissues than in adjacent normal tissues, and high LINC01094 expression is associated with shorter overall survival in patients. Additionally, experimental results show that overexpression of LINC01094 significantly promotes the proliferation of breast cancer cells, inhibits cell apoptosis, accelerates cell cycle progression, while knockdown of LINC01094 significantly reduces the proliferation of breast cancer cells, blocks the G0/G1 cell cycle, and induces cell apoptosis. Animal experiments have also demonstrated that LINC01094 overexpression promotes lung metastasis of breast cancer in vivo, with a much more severe degree of metastasis compared to the control group [31]. Therefore,

LINC01094 may be involved in tumorigenesis, and opens new perspectives for innovative and developmental approaches to breast cancer treatment.

2.6. Clear cell renal cell carcinoma

Clear cell renal cell carcinoma (ccRCC) is the most common subtype of kidney cancer, characterized by high malignancy and resistance to chemotherapy and radiotherapy, making it a major cause of kidney cancer-related deaths [66,67]. Surgical resection is the optimal treatment for ccRCC has always been surgical resection. However, even with complete resection, up to 40 % of ccRCC tumors eventually progress to metastatic disease [68]. Xu et al. [34] found that LINC01094 is highly expressed in the cytoplasm of ccRCC tissues and cells. Furthermore, expression of LINC01094 is associated with TNM staging, Fuhrman grading, vascular invasion, and lymph node metastasis. Similarly, Jiang et al. [69] discovered that downregulation of LINC01094 inhibits cell proliferation, migration, and epithelial-mesenchymal transition (EMT) process, thereby hindering the progression of ccRCC. Additionally, the knockdown of LINC01094 promotes apoptosis in ccRCC cells exposed to radiation [70]. Studies have also shown that a TME-related lncRNA model constructed around LINC01094 reliably predicts the prognosis and treatment of ccRCC patients [71]. In conclusion, LINC01094 plays a crucial role in ccRCC tumorigenesis and may provide a direction for the diagnosis and prognosis of clear cell renal cell carcinoma. However, its clinical application is limited, and further clinical and basic research is required.

2.7. Glioblastoma

Among diseases of the central nervous system, glioblastoma is the second leading cause of death and exhibits characteristics that make its treatment challenging, such as cellular infiltration, heterogeneity, and the presence of stem cell-like cells, leading to tumor recurrence [72–74]. Studies have found that the expression level of *LINC01094* is elevated in glioblastoma tissues compared to that in adjacent normal tissues [75]. LINC01094 is upregulated in glioblastoma and correlates with glioblastoma grading. LINC01094 overexpression significantly promotes the proliferation of LN229 cells, and, conversely, knockdown of LINC01094 suppresses the proliferation of U251 cells [32]. Similarly, Li et al. [76] demonstrated that LINC01094 is upregulated in glioblastoma tissues compared to that in non-tumor tissues, and silencing LINC01094 inhibits the growth and invasion of glioblastoma cells. Current research indicates that LINC01094 significantly promotes the proliferation and invasion of glioblastoma cells. Statistical analysis showed that high LINC01094 expression was associated with average tumor diameter and Karnofsky Performance Score (KPS) [24]. Overall, these results suggest that LINC01094 expression is elevated in GBM and is associated with tumor progression. These findings further elucidate the biological function of LINC01094 in glioblastoma and provide a promising therapeutic target for glioblastoma patients.

2.8. Other tumors

Mao et al. [30] discovered that knocking down LINC01094 significantly reduced the migration and invasion rates of SK-HEP-1 and

Table 2
The biological functions and mechanisms of LINC01094 in malignancies.

Cancer type	Property	Function	Related pathways	Refs.
Pancreatic cancer (PC)	Oncogene	Promote the cell proliferation and metastasis	LINC01094/miR-577/LIN28B/PI3K/AKT	[24]
Gastric cancer (GC)	Oncogene	Promotes Cells Proliferation、 Metastasis and EMT	LINC01094-AZGP1/PTEN/AKT	[28]
Colorectal cancer (CRC)	oncogene	Promote the cell proliferation, migration, and invasion	LINC01094/miR-1266-5p/SLPI	[29]
Hepatocellular carcinoma (HCC)	oncogene	Promote the cell migration and invasion	LINC01094/miR-26b-3p/MDM4	[30]
	oncogene	Promote the cell migration, invasion, and EMT	LINC01094/miR-122-5p/TGFBR2-SAMD2-SMAD3 positive feedback loop	[82]
Ovarian cancer (OC)	oncogene	Promote the cell proliferation, migration, and invasion	LINC01094/miR-532-3p/Wnt/β-catenin	[25]
	oncogene	Promote the cell proliferation, migration, invasion and EMT	LINC01094/miR-577/Wnt/β-catenin	[62]
Breast cancer (BC)	oncogene	cell proliferation, cell cycle progression, and apoptosis	LINC01094/miR-340-5p/E2F3	[31]
Glioma	oncogene	Promote Proliferation, Migration and Invasion	LINC01094/miR-330-3p/MSI1	[32]
	oncogene	Promote the cell migration and invasion	LINC01094/miR-224-5p/CHSY1	[75]
Glioblastoma (GBM)	oncogene	Proliferation, apoptosis, migration, in vitro invasion and in vivo tumor growth	LINC01094/miR-577/BDNF	[33]
	oncogene	Promote Proliferation and Invasion	LINC01094/miR-126-5p/DCTN4	[76]
Clear cell renal cell carcinoma (ccRCC)	oncogene	promote the proliferation, migration, and invasion, but inhibited cell apoptosis	LINC01094/miR-184/SLC2A3	[34]
	oncogene	promote cell proliferation, migration, and EMT process	FOXM1/LINC01094/miR-224-5p/CHSY1	[69]
	oncogene	strengthened resistance of cells responding to irradiation	LINC01094/miR-577/CHEK2/FOXM1	[70]
Lung adenocarcinoma (LUAD)	oncogene	promote cell EMT and mobility	LINC01094-SPI1/CCL7	[36]

Hep3B cells, indicating that LINC01094 can promote HCC metastasis. Additionally, the LINC01094-associated molecule CCL7 can affect M2 TAM infiltration, with CCL7 knockdown inhibiting the EMT and migration of LUAD cells, as well as suppressing macrophage chemotaxis and M2 polarization. This suggests that LINC01094 promotes LUAD development and leads to a poor prognosis [36]. Sun et al. [35] indicated that LINC01094 may serve as a new metastasis-related biomarker to predict the prognosis of lung squamous cell carcinoma. Qian et al. [37] established an immune-related LINC01094-based prognostic model of LSCC, demonstrating that this approach can assist clinicians in devising personalized treatment of LSCC cases. Considering the results of these various studies, one can conclude that LINC01094 is a promising prognostic aid and therapeutic target in HCC, LUAD, LUSC, and LSCC.

3. Mechanism of action of LINC01094 in tumors

3.1. Regulation of tumor progression by LINC01094-Related gene networks

Recent studies of lncRNAs have shown that they can act as competitive endogenous RNA (ceRNAs) and participate in various biological processes in tumors [77,78]. LncRNAs regulate post-transcriptional gene expression by acting as miRNA sponges, thereby altering biological functions [79,80]. Similarly, lncRNAs can interact with one or more RNA-binding proteins (RBPs) [81]. Research findings indicate that LINC01094 plays a crucial role in the regulation of cell proliferation, migration, invasion, cell cycle, angiogenesis, and radioresistance. In Table 2 and Fig. 1, we summarize the molecular mechanisms by which LINC01094 regulates disease progression. Recent studies have suggested that LINC01094 functions as an oncogenic factor via various regulatory mechanisms in multiple cancers.

LIN28B is an RNA-binding protein that targets multiple miRNAs and regulates their maturation and activity. In pancreatic cancer, LIN28B inhibits the biogenesis of let-7 microRNA and plays a role in epithelial-mesenchymal transition [83,84]. LINC01094 promotes LIN28B expression by sequestering miR-577, thereby enhancing cancer cell proliferation and invasion, while inhibiting apoptosis, thus promoting pancreatic cancer initiation and progression [24].

AZGP1 has been identified as a critical therapeutic target in cancer [85]. In gastric cancer, AZGP1 acts as a protein partner of LINC01094, and LINC01094 antagonizes the function of AZGP1, activates the PTEN/AKT pathway, and suppresses the malignant phenotype of GC [28].

SLPI is a multifunctional protein involved in immune response regulation and protease activity inhibition. Its overexpression is associated with anti-inflammatory effects, regulation of cell proliferation, angiogenesis, and TME modulation of the tumor microenvironment [86]. In colorectal cancer, LINC01094 sequesters miR-1266-5p, leading to increased SLPI expression [29].

MDM4 is upregulated in human cancers, promoting cell overgrowth and inhibiting apoptosis by blocking the p53 pathway [87]. In

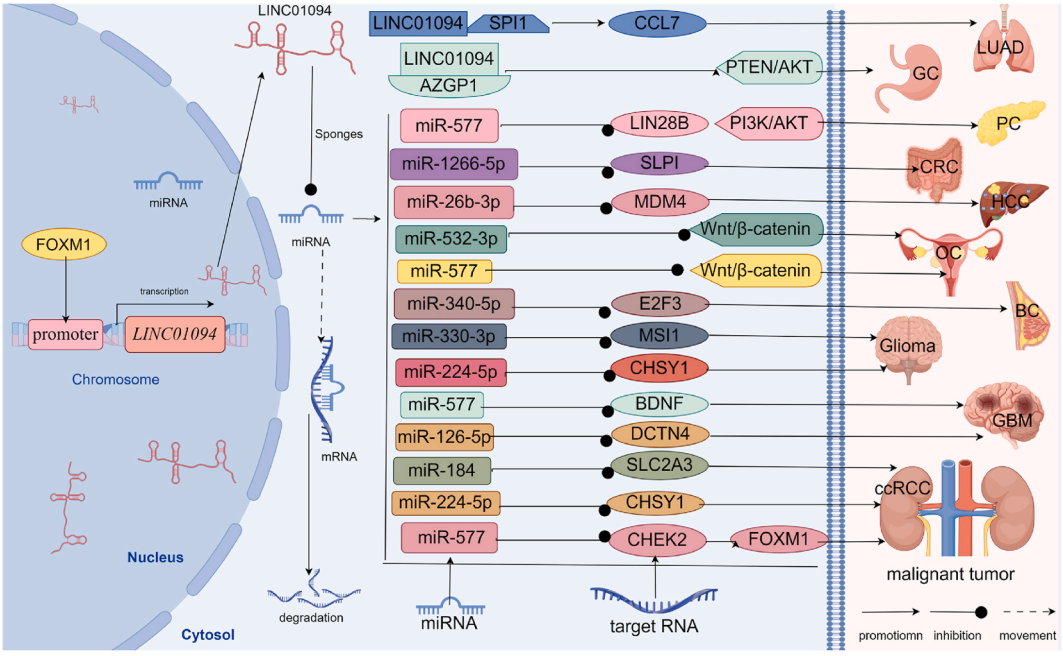

Fig. 1. LINC01094-related gene network and potential downstream regulatory mechanisms (image drawn with Figdraw 2.0). A variety of microRNAs (miRNAs), genes, and their roles in different types of cancer are illustrated. Long stranded non-coding RNAs (lncRNAs) affect gene expression by binding to miRNAs and acting as "sponges". The regulatory pathways between *LINC01094* , miRNAs, and their target genes are highlighted, demonstrating the promotion and inhibition of cellular processes during cancer development. BC, breast cancer; GC, gastric cancer; PC, pancreatic cancer; CRC, colorectal cancer; LUAD, lung adenocarcinoma; HCC, Hepatocellular carcinoma; GBM, glioblastoma; ccRCC, clear cell renal cell carcinoma; OC, ovarian cancer.

hepatocellular carcinoma (HCC), LINC01094 promotes HCC growth and metastasis through the LINC01094/miR-26b-3p/MDM4 axis [30].

In ovarian cancer, LINC01094 activates the Wnt/β-catenin pathway by acting as a sponge for miR-532-3p and miR-577, thereby promoting cancer cell proliferation, migration, invasion, and EMT, thus facilitating disease progression [25,62].

The E2F transcription factor 3 (E2F3) plays an oncogenic role in tumorigenesis and is significantly associated with poor prognosis in various cancers. A complex network exists between E2F3 and miRNAs to regulate tumor cell proliferation, apoptosis, metastasis, and drug resistance [88]. In breast cancer, LINC01094 upregulates E2F3 gene expression by acting as a sponge for miR-340-5p, thereby enhancing cancer cell proliferation, regulating cell cycle progression, and inhibiting apoptosis [31].

The RNA-binding protein Musashi-1 (MSI1) promotes stemness during development and cancer by controlling target mRNA turnover and translation. MSI1 is involved in the regulation of cancer hallmarks, such as the cell cycle and Notch signaling transduction [89]. In gliomas, LINC01094 can sponge miR-330-3p, which in turn inhibits MSI1 expression, promotes glioma cell proliferation, migration, and invasion, and regulates the malignant biological behavior of glioma cells. Additionally, research has found that LINC01094 can also sponge miR-224-5p to increase CHSY1 expression, thereby promoting tumor initiation and progression [32,75].

Brain-derived neurotrophic factor (BDNF) belongs to the neurotrophic factor family and plays an oncogenic role in various human tumors by promoting cancer cell growth, survival, proliferation, apoptosis, and migration [90]. Dynactin is a protein complex composed of multiple subunits that has not been extensively studied in cancer research [91]. In glioblastoma, LINC01094 is upregulated in GBM cells and acts as a sponge for miR-577, thereby increasing BDNF expression. LINC01094 also sponges miR-126-5p to increase DCTN4 expression, leading to a poor prognosis in patients with high LINC01094 expression [33,76].

SLC2A3 encodes the major neuronal glucose transporter 3 (GLUT3), which is associated with various tumors [92]. Checkpoint kinase 2 (CHEK2) is a serine/threonine kinase involved in controlling DNA repair, cell cycle arrest, and apoptotic pathways in response to initial damage [93]. FOXM1 is a transcription factor of LINC01094. In clear cell renal cell carcinoma (ccRCC), LINC01094 promotes ccRCC cell proliferation, migration, invasion, and EMT via the LINC01094/miR-184/SLC2A3 axis and the FOXM1/LINC01094/miR-224-5p/CHSY1 axis, inhibits apoptosis, and promotes ccRCC progression [34,69]. Research has also found that LINC01094 promotes ccRCC radioresistance through the miR-577/CHEK2/FOXM1 axis, affecting the difficulty of ccRCC treatment [70].

CCL7 belongs to the chemokine ligand family and plays an important role in immune cell recruitment and stromal cell biology in

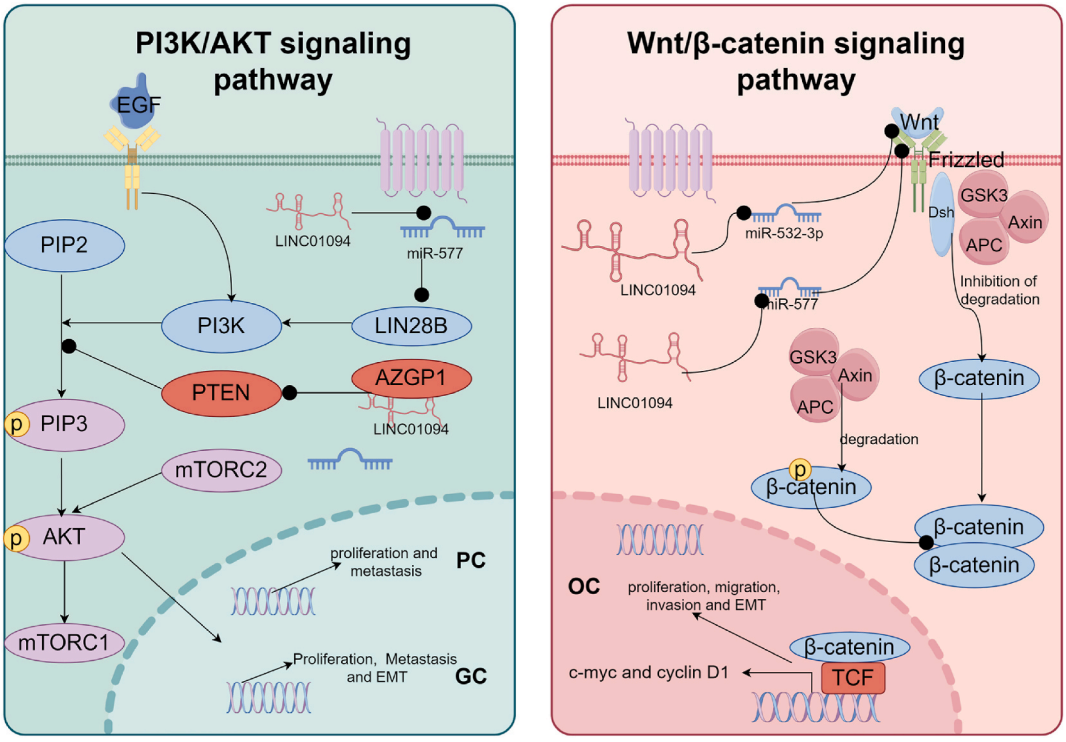

Fig. 2. Role of LINC01094 in the PI3K/AKT (Left) and Wnt/β-catenin (Right) signaling pathways (illustration drawn with Figdraw 2.0). LINC01094 plays an important role in both pathways.The PI3K/AKT signaling pathway starts from Epidermal Growth Factor (EGF), and through a series of molecular interactions, it ultimately activates AKT to promote protein synthesis, cell proliferation and metastasis. LINC01094 regulates the PTEN/AKT signaling pathway and promotes cell proliferation and metastasis by adsorbing miR-577. In the Wnt/β-catenin signaling pathway, LINC01094 affects β-catenin accumulation and intranuclear translocation by regulating miR-577, activating the transcription of genes associated with cell proliferation, migration, invasion and epithelial-mesenchymal transition (EMT). Both pathways play important roles in cell growth, differentiation and survival, and their aberrant regulation is often associated with cancer. PC, Pancreatic cancer; GC, Gastric cancer; OC, Ovarian cancer.

the tumor microenvironment [94,95]. In lung adenocarcinoma (LUAD), LINC01094 binds to SPI1 to promote its nuclear translocation, activating CCL7 transcription and leading to M2 macrophage aggregation and dissemination in tumor cells [36].

In summary, LINC01094 contributes to cancer cell growth and development, radiotherapy resistance, and poor prognosis by sponging miRNAs.

3.2. Signaling pathways associated with LINC01094

LINC01094 is involved in the regulation of the AKT signaling pathway [24,28], the Wnt/β-catenin signaling pathway [25,62] (as shown in Fig. 2) and the TGF-β Signaling Pathway positive feedback loop (as shown in Fig. 3).

3.2.1. PI3K/AKT signaling pathway

Abnormal activation of the PI3K/AKT pathway plays a crucial role in cancer development and is associated with cell proliferation, autophagy, apoptosis, angiogenesis, epithelial-mesenchymal transition (EMT), and chemotherapy resistance [96]. PTEN is a tumor suppressor gene that negatively regulates the PI3K/AKT pathway, thereby inhibiting cell proliferation and promoting apoptosis and is one of the most commonly mutated genes in cancer [97].

Studies have shown that AZGP1 is a protein-binding partner of LINC01094, which antagonizes the function in AZGP1, thereby downregulating PTEN expression and activating the PI3K/AKT pathway to promote tumor development. Overexpression of AZGP1 does not significantly change the RNA level of PTEN, but increased PTEN protein levels, indicating that AZGP1 may regulate PTEN post-transcriptionally or post-translationally rather than transcriptionally. Additionally, the effects of increased cell migration, PTEN downregulation, and pAKT upregulation caused by LINC01094 overexpression were reversed by AZGP1 overexpression and the AKT phosphorylation inhibitor perifosine, indicating that LINC01094 is an upstream regulator of the PTEN/AKT pathway [28].

LINC01094, as a ceRNA for miR-577, affects LIN28B expression in pancreatic cancer. PCNA and MMP-9 are the downstream target genes of the PI3K/Akt signaling pathway [98]. Compared to the control group, in cells with LINC01094 knockdown, the expression of LIN28B, PCNA, and MMP9, as well as the phosphorylation level of PI3K/Akt, were significantly reduced, whereas the total protein levels of Akt and PI3K did not change significantly. Conversely, in cells with LINC01094 overexpression, the opposite effect was observed, and the total protein levels of Akt and PI3K did not change significantly. This indicates that, in pancreatic cancer, LINC01094 weakens the inhibitory effect of miR-577 on LIN28B through sponge activity, thereby activating the PI3K/Akt pathway and worsening

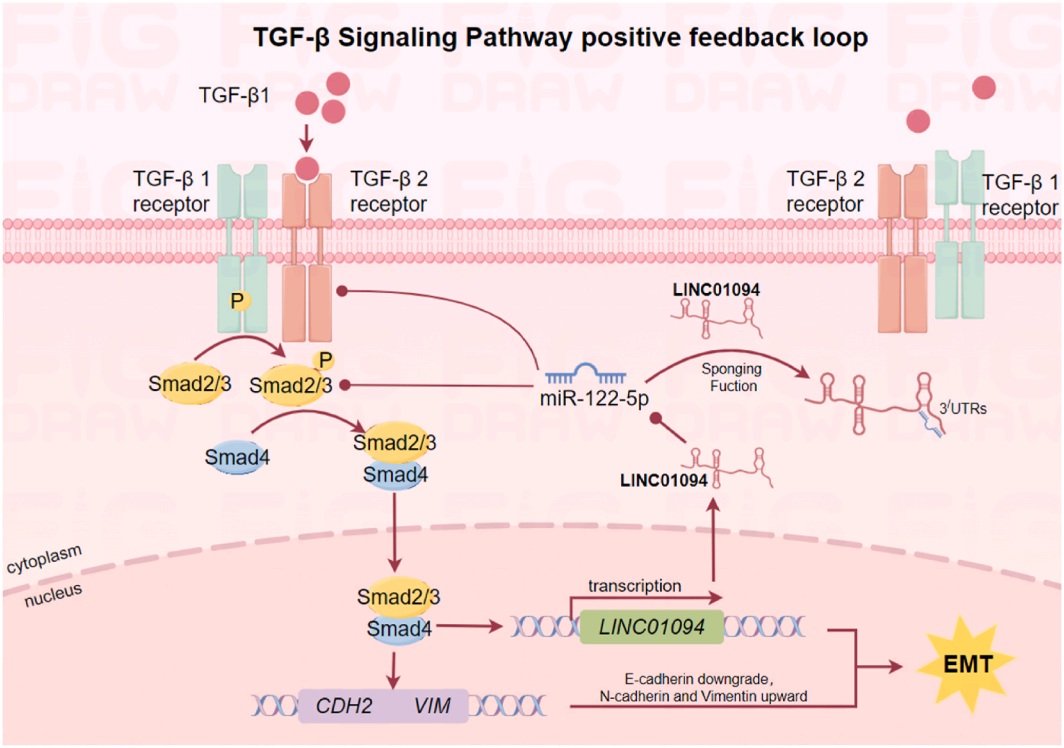

Fig. 3. Role of LINC01094 in the TGF-β Signaling Pathway positive feedback loop. (by Figdraw 2.0). TGF-β1 and TGF-β2 bind to their receptors, initiating a series of molecular interactions, including phosphorylation of Smad2/3. Phosphorylated Smad2/3 binds to Smad4, forming a complex that enters the nucleus, affects gene transcription. LINC01094 promotes epithelial-mesenchymal transition (EMT) through the adsorption of miR-122-5p, which regulates the expression of TGFBR2, Smad2, and Smad3. In addition, TGF-β1 increased the expression of LINC01094, forming a positive feedback loop that further enhanced the regulatory mechanism.

the prognosis of patients with pancreatic cancer.

3.2.2. Wnt/β-catenin signaling pathway

The Wnt/β-catenin signaling cascade represents a highly conserved pathway, with aberrations in its activity prominently driving cancer stem cell renewal, cellular proliferation, and differentiation, thus exerting pivotal roles in tumorigenesis and therapeutic responsiveness [99,100]. Wnt, an extracellularly secreted glycoprotein, comprises 19 human proteins [101]. In the absence of Wnt stimulation, β-catenin undergoes phosphorylation by the Axin-APC-GSK-3β complex, leading to its ubiquitination and subsequent degradation [102,103].

In the case of ovarian cancer, LINC01094 governs the Wnt/β-catenin signaling axis via miR-532-3p modulation. Downstream effectors of β-catenin, such as c-myc and cyclin D1, play crucial roles in regulating tumor cell proliferation, cycle progression, and invasion [104,105]. In ovarian cancer, inhibition of miR-532-3p can reverse si-LINC01094-induced β-catenin expression, c-myc, and cyclin D1. Both in vivo and in vitro experiments have demonstrated comparable effects on xenograft tumor growth rate and cellular behavior following transfection with miR-532-3p inhibitors or LINC01094 knockdown [25]. Similarly, Moufarrij et al. [62] uncovered in OC cells that LINC01094, acting as a sponge for miR-577, activates the Wnt/β-catenin pathway, thereby promoting cell proliferation, migration, invasion, and EMT. Thus, the Wnt/β-catenin signaling axis can be intricately regulated by the upstream molecule LINC01094, impacting tumor initiation and progression.

3.2.3. TGF-β signaling pathway positive feedback loop

The TGF-β signaling pathway plays a crucial role in numerous biological processes, including cell growth, differentiation, apoptosis, migration, and the development and progression of cancer [106]. In cancer cells, the TGF-β signaling pathway is initiated by the binding of TGF-β ligands to TGFBR2, which activates and phosphorylates TGFBR1. This leads to the phosphorylation of SMAD2/3, which then forms a complex with SMAD4 and translocates to the nucleus to regulate the transcription of target genes, affecting various biological processes such as cell proliferation, differentiation, migration, and apoptosis [107].

Recent studies have shown that overexpression of LINC01094 can promote EMT in HCC cells through the TGF-β/SMAD signaling pathway [82]. LINC01094 acts as a competing endogenous RNA (ceRNA) that regulates the expression of TGFBR2, SMAD2, and SMAD3 by sponging miR-122-5p, thereby promoting HCC metastasis. Experimental results demonstrated that LINC01094 knockdown in SNU-387 and HuH-7 cells increased the expression of epithelial markers such as E-cadherin and ZO-1, while decreasing the expression of the mesenchymal marker vimentin, significantly reducing cell migration and invasion. Conversely, LINC01094 overexpression in Hep3B cells yielded the opposite result. Interestingly, LINC01094 is significantly positively correlated with the TGFB1 gene, and TGF-β1 enhances the transcriptional expression of LINC01094, forming a positive feedback loop. Evidently, LINC01094 plays a vital role in promoting EMT, which leads to tumor metastasis in hepatocellular carcinoma via a TGF-β signaling pathway positive feedback loop. Targeting LINC01094 to disrupt this feedback loop is crucial to improve patient prognosis.

4. Conclusion and future perspectives

Long non-coding RNAs (lncRNAs) play pivotal roles in gene regulation and have been implicated in various genetic diseases and cancers [108]. LncRNAs serve as functional units, highlighting the critical importance of their subcellular localization for their functionality [109]. LINC01094 dysregulation is associated with a spectrum of diseases and significantly correlates with clinical features of gastric cancer, colorectal cancer, glioma, pancreatic cancer, ovarian cancer, hepatocellular carcinoma, clear cell renal cell carcinoma, and breast cancer. Patients with high LINC01094 expression in multiple cancers often have shorter survival times. LINC01094 significantly promotes tumor progression, invasion, and growth by modulating cellular biological functions. Additionally, upregulation of LINC01094 has been linked to reduced radiosensitivity in clear-cell renal cell carcinoma. Mechanistically, LINC01094 acts as a competitive endogenous RNA in gene regulation, sequestering miRNAs and modulating downstream target genes. Key pathways, including the Wnt/β-catenin, PI3K/AKT, and TGF-β signaling pathways, have been identified as targets of LINC01094.

Although numerous studies have elucidated the biological effects and molecular mechanisms of LINC01094 in various cancers, the range of cancer types studied is limited. However, the comprehensive role of LINC01094 in cancer remains to be explored. For example, in studies related to clear cell renal cell carcinoma, LINC01094 was transcriptionally activated by FOXM1 and acted as a sponge for miR-224-5p, thereby promoting CHSY1 and facilitating tumor progression. Intriguingly, LINC01094 enhances radioresistance in ccRCC through the miR-577/CHEK2/FOXM1 axis, suggesting a potential positive feedback loop for regulating tumor initiation and progression.

In terms of its therapeutic implications, the molecular structure and function of LINC01094 remain unknown. Without a detailed understanding of its structure and function, the development of therapeutic strategies based on LINC01094 remains challenging. Moreover, LINC01094 acts as a miR-577 sponge and is crucial in pancreatic cancer, ovarian cancer, clear-cell renal cell carcinoma, and glioblastoma. Taken together, LINC01094 and miR-577 may serve as novel targets for precise cancer therapy. Furthermore, unlike protein-coding genes, lncRNAs exhibit poor conservation across species and experimental results from animal models are insufficient to meet clinical research needs [110]. Currently, most studies rely on in vitro models or xenografts in mice, which may not accurately reflect the clinical scenarios. Further research is needed to ascertain whether LINC01094 exerts corresponding anti-disease effects on humans.

Targeting LINC01094 using specific inhibitors is a promising approach for cancer diagnosis and prognosis. Various strategies, including RNA interference, antisense oligonucleotides, and small-molecule inhibitors have been explored to modulate LINC01094 expression. These approaches aim to disrupt the function of LINC01094 in tumor progression and enhance the effectiveness of existing

therapies. However, challenges such as specificity, delivery, and potential off-target effects must be addressed.

The exploration of LINC01094 as a therapeutic target remains in the early stages of development. Future studies should focus on the development of effective delivery systems for LINC01094-targeted therapies and investigate their efficacy in clinical trials. Additionally, understanding the precise molecular mechanisms by which LINC01094 influences tumor biology could lead to novel therapeutic strategies. Clinical studies are needed to validate the therapeutic potential of LINC01094 and explore its role in overcoming drug resistance.

This review summarizes the aberrant expression, biological function, and prognostic value of LINC01094 in cancer cells. Additionally, it describes the mechanistic and molecular basis of related gene networks centered around LINC01094，which plays a pivotal role in cancer progression by modulating key signaling pathways such as PI3K/AKT and Wnt/β-catenin. Aberrant expression is linked to poor prognosis and resistance to therapy in various cancers. Targeting LINC01094 offers a promising avenue for novel therapeutic strategies; however, challenges remain in terms of specificity and delivery. Future studies should focus on elucidating the detailed mechanisms of LINC01094 action and validating its therapeutic potential in clinical settings.

Data availability statement

All data are included in the article.

CRediT authorship contribution statement

Qiang Yi: Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Gangfeng Zhu:** Writing – review & editing, Validation, Supervision, Investigation, Data curation. **Weijian Zhu:** Writing – review & editing, Visualization, Supervision, Investigation, Conceptualization. **Jiaqi Wang:** Writing – review & editing, Visualization, Supervision, Methodology, Formal analysis. **Xinting Ouyang:** Writing – review & editing, Visualization, Supervision, Resources, Project administration. **Kuan Yang:** Validation, Investigation. **Yu Fan:** Validation, Formal analysis. **Jinghua Zhong:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Appendix

Abbreviation	Full Name or Explanation	Abbreviation	Full Name or Explanation
LINC01094	Long Intergenic Non-Protein Coding RNA 1094	**LIN28B**	Lin-28 Homolog B
ceRNA	Competing Endogenous RNA	**EMT**	Epithelial-Mesenchymal Transition
PI3K	Phosphatidylinositol-4,5-Bisphosphate 3-Kinase	**FISH**	Fluorescence In Situ Hybridization
AKT	Serine/Threonine Kinase	**CFPAC-1**	Cystic Fibrosis Pancreatic Adenocarcinoma-1
Wnt	Wingless-related Integration Site	**STAD**	Stomach Adenocarcinoma
lncRNA	Long Non-Coding RNA	**ARlncs**	Androgen-Responsive Long Non-Coding RNAs
OS	Overall Survival	**NRL**	Necroptosis-Related LncRNA
LUAD	Lung Adenocarcinoma	**TME**	Tumor Microenvironment
LSCC	Laryngeal Squamous Cell Carcinoma	**CCL7**	C-C Motif Chemokine Ligand 7
LUSC	Lung Squamous Cell Carcinoma	**RBP**	RNA Binding Protein
GC	Gastric Cancer	**AZGP1**	Alpha-2-Glycoprotein 1, Zinc-Binding
GBM	Glioblastoma	**SLPI**	Secretory Leukocyte Protease Inhibitor
CRC	Colorectal Cancer	**MDM4**	MDM4 P53 Binding Protein Homolog
PC	Pancreatic Cancer	**E2F3**	E2F Transcription Factor 3
OC	Ovarian Cancer	**MSI1**	Musashi RNA Binding Protein 1
HCC	Hepatocellular Carcinoma	**BDNF**	Brain-Derived Neurotrophic Factor
ccRCC	Clear Cell Renal Cell Carcinoma	**SLC2A3**	Solute Carrier Family 2 Member 3
BC	Breast Cancer	**PTEN**	Phosphatase and Tensin Homolog
CRSwNP	Chronic Rhinosinusitis with Nasal Polyps	**PCNA**	Proliferating Cell Nuclear Antigen
CAVD	Calcific Aortic Valve Disease	**MMP9**	Matrix Metallopeptidase 9
PMOP	Postmenopausal Osteoporosis	**Axin-APC-GSK-3β**	Axin-Adenomatous Polyposis Coli-Glycogen Synthase Kinase 3 Beta
SCZ	Schizophrenia	**CHEK2**	Checkpoint Kinase 2
MS	Multiple Sclerosis	**OA**	Osteoarthritis

References

[1] J. Rao Bommi, S. Kummari, K. Lakavath, R.A. Sukumaran, L.R. Panicker, J.L. Marty, K. Yugender Goud, Recent trends in biosensing and diagnostic methods for novel cancer biomarkers, Biosensors 13 (3) (2023), https://doi.org/10.3390/bios13030398.

[2] A. Ferencz, D. Szatmári, D. Lőrinczy, Thermodynamic sensitivity of blood plasma components in patients afflicted with skin, breast and pancreatic forms of cancer, Cancers 14 (24) (2022), https://doi.org/10.3390/cancers14246147.

[3] E. Jung, J. Alfonso, H. Monyer, W. Wick, F. Winkler, Neuronal signatures in cancer, Int. J. Cancer 147 (12) (2020) 3281–3291, https://doi.org/10.1002/ijc.33138.

[4] J. Shi, Z. Sun, Z. Gao, D. Huang, H. Hong, J. Gu, Radioimmunotherapy in colorectal cancer treatment: present and future, Front. Immunol. 14 (2023) 1105180, https://doi.org/10.3389/fimmu.2023.1105180.

[5] M. Turri-Zanoni, G. Gravante, P. Castelnuovo, Molecular biomarkers in sinonasal cancers: new frontiers in diagnosis and treatment, Curr. Oncol. Rep. 24 (1) (2022) 55–67, https://doi.org/10.1007/s11912-021-01154-3.

[6] Y. Zhang, Y. Wang, J. Chen, Y. Xia, Y. Huang, A programmed cell death-related model based on machine learning for predicting prognosis and immunotherapy responses in patients with lung adenocarcinoma, Front. Immunol. 14 (2023) 1183230, https://doi.org/10.3389/fimmu.2023.1183230.

[7] F. Moosavi, E. Giovannetti, G.J. Peters, O. Firuzi, Combination of HGF/MET-targeting agents and other therapeutic strategies in cancer, Crit. Rev. Oncol. Hematol. 160 (2021) 103234, https://doi.org/10.1016/j.critrevonc.2021.103234.

[8] G. Jose, Y.J. Lu, J.T. Hung, A.L. Yu, J.P. Chen, Co-delivery of CPT-11 and panobinostat with anti-GD2 antibody conjugated immunoliposomes for targeted combination chemotherapy, Cancers 12 (11) (2020), https://doi.org/10.3390/cancers12113211.

[9] S. Xie, M. Wang, C. Zeng, Y. Ou, L. Zhao, D. Wang, L. Chen, F. Kong, D. Yi, Research progress of targeted therapy combined with immunotherapy for hepatocellular carcinoma, Front. Oncol. 13 (2023) 1197698, https://doi.org/10.3389/fonc.2023.1197698.

[10] F. Kopp, J.T. Mendell, Functional classification and experimental dissection of long noncoding RNAs, Cell 172 (3) (2018) 393–407, https://doi.org/10.1016/j.cell.2018.01.011.

[11] A.A. Yarmishyn, I.V. Kurochkin, Long noncoding RNAs: a potential novel class of cancer biomarkers, Front. Genet. 6 (2015) 145, https://doi.org/10.3389/fgene.2015.00145.

[12] W.X. Peng, P. Koirala, Y.Y. Mo, LncRNA-mediated regulation of cell signaling in cancer, Oncogene 36 (41) (2017) 5661–5667, https://doi.org/10.1038/onc.2017.184.

[13] S.C. Akıncılar, L. Wu, Q.F. Ng, J.Y.H. Chua, B. Unal, T. Noda, W.H.J. Chor, M. Ikawa, V. Tergaonkar, NAIL: an evolutionarily conserved lncRNA essential for licensing coordinated activation of p38 and NFκB in colitis, Gut 70 (10) (2021) 1857–1871, https://doi.org/10.1136/gutjnl-2020-322980.

[14] Q. Zhang, C. Song, M. Zhang, Y. Liu, L. Wang, Y. Xie, H. Qi, L. Ba, P. Shi, Y. Cao, H. Sun, Super-enhancer-driven lncRNA Snhg7 aggravates cardiac hypertrophy via Tbx5/GLS2/ferroptosis axis, Eur. J. Pharmacol. 953 (2023) 175822, https://doi.org/10.1016/j.ejphar.2023.175822.

[15] L.L. Bu, Y.Y. Xie, D.Y. Lin, Y. Chen, X.N. Jing, Y.R. Liang, S.D. Peng, K.X. Huang, E.X. Tao, LncRNA-T199678 mitigates α-synuclein-induced dopaminergic neuron injury via miR-101-3p, Front. Aging Neurosci. 12 (2020) 599246, https://doi.org/10.3389/fnagi.2020.599246.

[16] Y. Hu, Y. Zhang, S. Wang, R. Wang, Q. Yuan, W. Wu, Y. Gui, J. Zhao, X. Li, Y. He, C. Yuan, LncRNA Gm15232 promotes lipogenesis in aging mice through the miR-192-3p/GCR pathway, J Gerontol A Biol Sci Med Sci 79 (4) (2024), https://doi.org/10.1093/gerona/glae066.

[17] Z. Liu, Y. Fu, W. Huang, C. Li, X. Wei, J. Zhan, J. Zheng, LINC01094 promotes human nasal epithelial cell epithelial-to-mesenchymal transition and pyroptosis via upregulating HMGB1, Rhinology 62 (1) (2024) 88–100, https://doi.org/10.4193/Rhin23.184.

[18] K. Huang, L. Wu, Y. Gao, Q. Li, H. Wu, X. Liu, L. Han, Transcriptome sequencing data reveal LncRNA-miRNA-mRNA regulatory network in calcified aortic valve disease, Front Cardiovasc Med 9 (2022) 886995, https://doi.org/10.3389/fcvm.2022.886995.

[19] Q. Fei, X. Bai, J. Lin, H. Meng, Y. Yang, A. Guo, Identification of aberrantly expressed long non-coding RNAs in postmenopausal osteoporosis, Int. J. Mol. Med. 41 (6) (2018) 3537–3550, https://doi.org/10.3892/ijmm.2018.3575.

[20] H. Sabaie, M.M. Moghaddam, M.M. Moghaddam, N.K. Ahangar, M.R. Asadi, B.M. Hussen, M. Taheri, M. Rezazadeh, Bioinformatics analysis of long non-coding RNA-associated competing endogenous RNA network in schizophrenia, Sci. Rep. 11 (1) (2021) 24413, https://doi.org/10.1038/s41598-021-03993-3.

[21] H. Sabaie, S. Khorami Rouz, G. Kouchakali, S. Heydarzadeh, M.R. Asadi, M. Sharifi-Bonab, B.M. Hussen, M. Taheri, S.A. Ayatollahi, M. Rezazadeh, Identification of potential regulatory long non-coding RNA-associated competing endogenous RNA axes in periplaque regions in multiple sclerosis, Front. Genet. 13 (2022) 1011350, https://doi.org/10.3389/fgene.2022.1011350.

[22] F. Huang, Z. Su, J. Yang, X. Zhao, Y. Xu, Knocking-down long non-coding RNA LINC01094 prohibits chondrocyte apoptosis via regulating microRNA-577/metal-regulatory transcription factor 1 axis, J. Orthop. Surg. 32 (2) (2024) 10225536241254588, https://doi.org/10.1177/10225536241254588.

[23] E.L. Kleinbrink, N. Gomez-Lopez, D. Ju, B. Done, A.S. Goustin, A.L. Tarca, R. Romero, L. Lipovich, Gestational age dependence of the maternal circulating long non-coding RNA transcriptome during normal pregnancy highlights antisense and pseudogene transcripts, Front. Genet. 12 (2021) 760849, https://doi.org/10.3389/fgene.2021.760849.

[24] C. Luo, K. Lin, C. Hu, X. Zhu, J. Zhu, Z. Zhu, LINC01094 promotes pancreatic cancer progression by sponging miR-577 to regulate LIN28B expression and the PI3K/AKT pathway, Mol. Ther. Nucleic Acids 26 (2021) 523–535, https://doi.org/10.1016/j.omtn.2021.08.024.

[25] H. Chen, Y. Liu, P. Liu, Q. Dai, P. Wang, LINC01094 promotes the invasion of ovarian cancer cells and regulates the Wnt/β-catenin signaling pathway by targeting miR-532-3p, Exp. Ther. Med. 22 (5) (2021) 1228, https://doi.org/10.3892/etm.2021.10662.

[26] H. Tu, Q. Zhang, L. Xue, J. Bao, Cuproptosis-related lncRNA gene signature establishes a prognostic model of gastric adenocarcinoma and evaluate the effect of antineoplastic drugs, Genes 13 (12) (2022), https://doi.org/10.3390/genes13122214.

[27] Y. Chen, Z. Li, X. Chen, S. Zhang, Long non-coding RNAs: from disease code to drug role, Acta Pharm. Sin. B 11 (2) (2021) 340–354, https://doi.org/10.1016/j.apsb.2020.10.001.

[28] Z. Gong, Y. Zhang, Y. Yang, Y. Yang, J. Zhang, Y. Wang, L. Zhao, N. Yu, Z. Wu, W. Guo, LncRNA LINC01094 promotes cells proliferation and metastasis through the PTEN/AKT pathway by targeting AZGP1 in gastric cancer, Cancers 15 (4) (2023), https://doi.org/10.3390/cancers15041261.

[29] G. Zhang, Y. Gao, Z. Yu, H. Su, Upregulated long intergenic non-protein coding RNA 1094 (LINC01094) is linked to poor prognosis and alteration of cell function in colorectal cancer, Bioengineered 13 (4) (2022) 8526–8537, https://doi.org/10.1080/21655979.2022.2051839.

[30] Y. Mao, Z. Hu, Y. Zeng, Y. Zhou, Z. Shi, LINC01094 accelerates the metastasis of hepatocellular carcinoma via the miR-26b-3p/MDM4 axis, Cell Mol Biol (Noisy-le-grand) 69 (6) (2023) 181–185, https://doi.org/10.14715/cmb/2023.69.6.27.

[31] X. Wu, C. Kong, Y. Wu, Long intergenic non-protein coding RNA 1094 (LINC01094) promotes the progression of breast cancer (BC) by regulating the microRNA-340-5p (miR-340-5p)/E2F transcription factor 3 (E2F3) axis, Bioengineered 12 (1) (2021) 9046–9057, https://doi.org/10.1080/21655979.2021.1993715.

[32] B. Zhu, W. Liu, H. Liu, Q. Xu, W. Xu, LINC01094 down-regulates miR-330-3p and enhances the expression of MSI1 to promote the progression of glioma, Cancer Manag. Res. 12 (2020) 6511–6521, https://doi.org/10.2147/cmar.S254630.

[33] X. Dong, X. Fu, M. Yu, Z. Li, Long intergenic non-protein coding RNA 1094 promotes initiation and progression of glioblastoma by promoting microRNA-577-regulated stabilization of brain-derived neurotrophic factor, Cancer Manag. Res. 12 (2020) 5619–5631, https://doi.org/10.2147/cmar.S256147.

[34] H. Xu, X. Wang, J. Wu, H. Ji, Z. Chen, H. Guo, J. Hou, Long non-coding RNA LINC01094 promotes the development of clear cell renal cell carcinoma by upregulating SLC2A3 via MicroRNA-184, Front. Genet. 11 (2020) 562967, https://doi.org/10.3389/fgene.2020.562967.

[35] Q. Sun, Y. Gao, Y. Zhang, H. Cao, J. Liu, S.Y. Neo, K. Chen, Y. Bi, J. Wu, Prognostic profiling of the EMT-associated and immunity-related LncRNAs in lung squamous cell carcinomas, Cells 11 (18) (2022), https://doi.org/10.3390/cells11182881.

[36] Z. Wu, X. Bai, Z. Lu, S. Liu, H. Jiang, LINC01094/SPI1/CCL7 Axis promotes macrophage accumulation in lung adenocarcinoma and tumor cell dissemination, J Immunol Res 2022 (2022) 6450721, https://doi.org/10.1155/2022/6450721.

[37] L. Qian, T. Ni, B. Fei, H. Sun, H. Ni, An immune-related lncRNA pairs signature to identify the prognosis and predict the immune landscape of laryngeal squamous cell carcinoma, BMC Cancer 22 (1) (2022) 545, https://doi.org/10.1186/s12885-022-09524-1.

[38] A.P. Klein, Pancreatic cancer epidemiology: understanding the role of lifestyle and inherited risk factors, Nat. Rev. Gastroenterol. Hepatol. 18 (7) (2021) 493–502, https://doi.org/10.1038/s41575-021-00457-x.

[39] J. Cai, H. Chen, M. Lu, Y. Zhang, B. Lu, L. You, T. Zhang, M. Dai, Y. Zhao, Advances in the epidemiology of pancreatic cancer: trends, risk factors, screening, and prognosis, Cancer Lett. 520 (2021) 1–11, https://doi.org/10.1016/j.canlet.2021.06.027.

[40] H. Duan, L. Li, S. He, Advances and prospects in the treatment of pancreatic cancer, Int J Nanomedicine 18 (2023) 3973–3988, https://doi.org/10.2147/ijn.S413496.

[41] B. Farran, G.P. Nagaraju, Exosomes as therapeutic solutions for pancreatic cancer, Drug Discov. Today 25 (12) (2020) 2245–2256, https://doi.org/10.1016/j.drudis.2020.09.037.

[42] A.S. Chadha, A. Khoo, M.L. Aliru, H.K. Arora, J.R. Gunther, S. Krishnan, Recent advances and prospects for multimodality therapy in pancreatic cancer, Semin. Radiat. Oncol. 26 (4) (2016) 320–337, https://doi.org/10.1016/j.semradonc.2016.05.002.

[43] B. Huang, J. Liu, J. Lu, W. Gao, L. Zhou, F. Tian, Y. Wang, M. Luo, D. Liu, C. Xie, Z. Xun, C. Liu, Y. Wang, H. Ma, J. Guo, Aerial view of the association between m6A-related LncRNAs and clinicopathological characteristics of pancreatic cancer, Front. Oncol. 11 (2021) 812785, https://doi.org/10.3389/fonc.2021.812785.

[44] J.Y. Xia, A.A. Aadam, Advances in screening and detection of gastric cancer, J. Surg. Oncol. 125 (7) (2022) 1104–1109, https://doi.org/10.1002/jso.26844.

[45] V. Balendra, C. Amoroso, B. Galassi, J. Esposto, C. Bareggi, J. Luu, L. Scaramella, M. Ghidini, High-salt diet exacerbates H. pylori infection and increases gastric cancer risks, J Pers Med 13 (9) (2023), https://doi.org/10.3390/jpm13091325.

[46] R. Ivyna de Araújo Rêgo, G.F. Guedes Silvestre, D. Ferreira de Melo, S.L. Albino, M.M. Pimentel, S.B. Silva Costa Cruz, S.D. Silva Wurzba, W.F. Rodrigues, B. P. Goulart de Lima Damasceno, L.R. Cançado Castellano, Flavonoids-rich plant extracts against Helicobacter pylori infection as prevention to gastric cancer, Front. Pharmacol. 13 (2022) 951125, https://doi.org/10.3389/fphar.2022.951125.

[47] T.H. Patel, M. Cecchini, Targeted therapies in advanced gastric cancer, Curr. Treat. Options Oncol. 21 (9) (2020) 70, https://doi.org/10.1007/s11864-020-00774-4.

[48] T. Matsuoka, M. Yashiro, Novel biomarkers for early detection of gastric cancer, World J. Gastroenterol. 29 (17) (2023) 2515–2533, https://doi.org/10.3748/wjg.v29.i17.2515.

[49] Y. Ye, O. Ge, C. Zang, L. Yu, J. Eucker, Y. Chen, LINC01094 predicts poor prognosis in patients with gastric cancer and is correlated with EMT and macrophage infiltration, Technol. Cancer Res. Treat. 21 (2022) 15330338221080977, https://doi.org/10.1177/15330338221080977.

[50] B. Zhao, W. Wu, L. Liang, X. Cai, Y. Chen, W. Tang, Prediction model of clinical prognosis and immunotherapy efficacy of gastric cancer based on level of expression of cuproptosis-related genes, Heliyon 9 (8) (2023) e19035, https://doi.org/10.1016/j.heliyon.2023.e19035.

[51] M. Yuan, Y. Jia, Y. Xing, Y. Wang, Y. Liu, X. Liu, D. Liu, Screening and validation of platelet activation-related lncRNAs as potential biomarkers for prognosis and immunotherapy in gastric cancer patients, Front. Genet. 13 (2022) 965033, https://doi.org/10.3389/fgene.2022.965033.

[52] P. Xu, S. Liu, S. Song, X. Yao, X. Li, J. Zhang, Y. Liu, Y. Zheng, G. Gao, J. Xu, Identification and validation of a novel angiogenesis-related gene signature for predicting prognosis in gastric adenocarcinoma, Front. Oncol. 12 (2022) 965102, https://doi.org/10.3389/fonc.2022.965102.

[53] W. Wang, Q. Pei, L. Wang, T. Mu, H. Feng, Construction of a prognostic signature of 10 autophagy-related lncRNAs in gastric cancer, Int. J. Gen. Med. 15 (2022) 3699–3710, https://doi.org/10.2147/ijgm.S348943.

[54] L. Luo, L. Li, L. Liu, Z. Feng, Q. Zeng, X. Shu, Y. Cao, Z. Li, A necroptosis-related lncRNA-based signature to predict prognosis and probe molecular characteristics of stomach adenocarcinoma, Front. Genet. 13 (2022) 833928, https://doi.org/10.3389/fgene.2022.833928.

[55] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA Cancer J Clin 71 (3) (2021) 209–249, https://doi.org/10.3322/caac.21660.

[56] L.H. Biller, D. Schrag, Diagnosis and treatment of metastatic colorectal cancer: a review, JAMA 325 (7) (2021) 669–685, https://doi.org/10.1001/jama.2021.0106.

[57] R. Ahmad, J.K. Singh, A. Wunnava, O. Al-Obeed, M. Abdulla, S.K. Srivastava, Emerging trends in colorectal cancer: dysregulated signaling pathways, Int. J. Mol. Med. 47 (3) (2021), https://doi.org/10.3892/ijmm.2021.4847 (Review).

[58] Y. Zhang, Y. Wang, B. Zhang, P. Li, Y. Zhao, Methods and biomarkers for early detection, prediction, and diagnosis of colorectal cancer, Biomed. Pharmacother. 163 (2023) 114786, https://doi.org/10.1016/j.biopha.2023.114786.

[59] R. Zhang, M.K.Y. Siu, H.Y.S. Ngan, K.K.L. Chan, Molecular biomarkers for the early detection of ovarian cancer, Int. J. Mol. Sci. 23 (19) (2022), https://doi.org/10.3390/ijms231912041.

[60] S. Moufarrij, M. Dandapani, E. Arthofer, S. Gomez, A. Srivastava, M. Lopez-Acevedo, A. Villagra, K.B. Chiappinelli, Epigenetic therapy for ovarian cancer: promise and progress, Clin Epigenetics 11 (1) (2019) 7, https://doi.org/10.1186/s13148-018-0602-0.

[61] J.Y. Wang, A.Q. Lu, L.J. Chen, LncRNAs in ovarian cancer, Clin. Chim. Acta 490 (2019) 17–27, https://doi.org/10.1016/j.cca.2018.12.013.

[62] J. Xu, P. Zhang, H. Sun, Y. Liu, LINC01094/miR-577 axis regulates the progression of ovarian cancer, J. Ovarian Res. 13 (1) (2020) 122, https://doi.org/10.1186/s13048-020-00721-9.

[63] H. Xu, M. Lu, Y. Liu, F. Ren, L. Zhu, Identification of a pyroptosis-related long non-coding RNA Signature for prognosis and its related ceRNA regulatory network of ovarian cancer, J. Cancer 14 (16) (2023) 3151–3168, https://doi.org/10.7150/jca.88485.

[64] R.H.G. Wright, M. Beato, Role of the NUDT enzymes in breast cancer, Int. J. Mol. Sci. 22 (5) (2021), https://doi.org/10.3390/ijms22052267.

[65] L.P. Guido, C. Gomez-Fernandez, Advances in the molecular taxonomy of breast cancer, Arch. Med. Res. 51 (8) (2020) 777–783, https://doi.org/10.1016/j.arcmed.2020.08.001.

[66] J. Liu, J. Xu, T. Zhang, K. Xu, P. Bao, Z. Zhang, K. Xue, R. He, L. Ma, Y. Wang, Decoding the immune microenvironment of clear cell renal cell carcinoma by single-cell profiling to aid immunotherapy, Front. Immunol. 13 (2022) 791158, https://doi.org/10.3389/fimmu.2022.791158.

[67] Q. Wang, H. Tang, X. Luo, J. Chen, X. Zhang, X. Li, Y. Li, Y. Chen, Y. Xu, S. Han, Immune-associated gene signatures serve as a promising biomarker of immunotherapeutic prognosis for renal clear cell carcinoma, Front. Immunol. 13 (2022) 890150, https://doi.org/10.3389/fimmu.2022.890150.

[68] C. Hao, R. Li, Z. Lu, K. He, J. Shen, T. Wang, T. Qiu, Predicting prognosis, immunotherapy and distinguishing cold and hot tumors in clear cell renal cell carcinoma based on anoikis-related lncRNAs, Front. Immunol. 14 (2023) 1145450, https://doi.org/10.3389/fimmu.2023.1145450.

[69] Y. Jiang, H. Zhang, W. Li, Y. Yan, X. Yao, W. Gu, FOXM1-Activated LINC01094 promotes clear cell renal cell carcinoma development via MicroRNA 224-5p/CHSY1, Mol. Cell Biol. 40 (3) (2020), https://doi.org/10.1128/mcb.00357-19.

[70] Y. Jiang, W. Li, Y. Yan, X. Yao, W. Gu, H. Zhang, LINC01094 triggers radio-resistance in clear cell renal cell carcinoma via miR-577/CHEK2/FOXM1 axis, Cancer Cell Int. 20 (2020) 274, https://doi.org/10.1186/s12935-020-01306-8.

[71] L. Zhou, H. Fang, F. Guo, M. Yin, H. Long, G. Weng, Computational construction of TME-related lncRNAs signature for predicting prognosis and immunotherapy response in clear cell renal cell carcinoma, J. Clin. Lab. Anal. 36 (8) (2022) e24582, https://doi.org/10.1002/jcla.24582.

[72] P. Śledzińska, M.G. Bebyn, J. Furtak, J. Kowalewski, M.A. Lewandowska, Prognostic and predictive biomarkers in gliomas, Int. J. Mol. Sci. 22 (19) (2021), https://doi.org/10.3390/ijms221910373.

[73] S. Maksoud, The DNA double-strand break repair in glioma: molecular players and therapeutic strategies, Mol. Neurobiol. 59 (9) (2022) 5326–5365, https://doi.org/10.1007/s12035-022-02915-2.

[74] K. Bilmin, T. Kujawska, P. Grieb, Sonodynamic therapy for gliomas. Perspectives and prospects of selective sonosensitization of glioma cells, Cells 8 (11) (2019), https://doi.org/10.3390/cells8111428.

[75] L. Liu, Q. Xu, Y. Xiong, H. Deng, J. Zhou, LncRNA LINC01094 contributes to glioma progression by modulating miR-224-5p/CHSY1 axis, Hum. Cell 35 (1) (2022) 214–225, https://doi.org/10.1007/s13577-021-00637-6.

[76] X.X. Li, Q. Yu, Linc01094 accelerates the growth and metastatic-related traits of glioblastoma by sponging miR-126-5p, OncoTargets Ther. 13 (2020) 9917–9928, https://doi.org/10.2147/ott.S263091.

[77] S. Yang, X. Wang, X. Zhou, L. Hou, J. Wu, W. Zhang, H. Li, C. Gao, C. Sun, ncRNA-mediated ceRNA regulatory network: transcriptomic insights into breast cancer progression and treatment strategies, Biomed. Pharmacother. 162 (2023) 114698, https://doi.org/10.1016/j.biopha.2023.114698.

[78] Z. Tang, X. Li, Y. Zheng, J. Liu, C. Liu, X. Li, The role of competing endogenous RNA network in the development of hepatocellular carcinoma: potential therapeutic targets, Front. Cell Dev. Biol. 12 (2024) 1341999, https://doi.org/10.3389/fcell.2024.1341999.
[79] S. Zhang, Y. Li, S. Xin, L. Yang, M. Jiang, Y. Xin, Y. Wang, J. Yang, J. Lu, Insight into LncRNA- and CircRNA-mediated CeRNAs: regulatory network and implications in nasopharyngeal carcinoma-A narrative literature review, Cancers 14 (19) (2022), https://doi.org/10.3390/cancers14194564.
[80] N. Natarelli, A. Boby, S. Aflatooni, J.T. Tran, M.J. Diaz, K. Taneja, M. Forouzandeh, Regulatory miRNAs and lncRNAs in skin cancer: a narrative review, Life 13 (8) (2023), https://doi.org/10.3390/life13081696.
[81] F. Ferrè, A. Colantoni, M. Helmer-Citterich, Revealing protein-lncRNA interaction, Brief Bioinform 17 (1) (2016) 106–116, https://doi.org/10.1093/bib/bbv031.
[82] X. Yang, C. Xu, C. Liu, X. Wu, X. Chen, J. Hou, L. Wang, TGF-β1-Induced LINC01094 promotes epithelial-mesenchymal transition in hepatocellular carcinoma through the miR-122-5p/TGFBR2-SAMD2-SMAD3 Axis, Funct. Integr. Genomics 24 (4) (2024) 123, https://doi.org/10.1007/s10142-024-01403-1.
[83] T. Gewalt, K.W. Noh, L. Meder, The role of LIN28B in tumor progression and metastasis in solid tumor entities, Oncol. Res. 31 (2) (2023) 101–115, https://doi.org/10.32604/or.2023.028105.
[84] T. Knowles, T. Huang, J. Qi, S. An, N. Burket, S. Cooper, J. Nazarian, A.M. Saratsis, LIN28B and let-7 in diffuse midline glioma: a review, Cancers 15 (12) (2023), https://doi.org/10.3390/cancers15123241.
[85] L. Deng, W. Bao, B. Zhang, S. Zhang, Z. Chen, X. Zhu, B. He, L. Wu, X. Chen, T. Deng, B. Chen, Z. Yu, Y. Wang, G. Chen, AZGP1 activation by lenvatinib suppresses intrahepatic cholangiocarcinoma epithelial-mesenchymal transition through the TGF-β1/Smad3 pathway, Cell Death Dis. 14 (9) (2023) 590, https://doi.org/10.1038/s41419-023-06092-5.
[86] X. Zhang, S.S. Liu, J. Ma, W. Qu, Secretory leukocyte protease inhibitor (SLPI) in cancer pathophysiology: mechanisms of action and clinical implications, Pathol. Res. Pract. 248 (2023) 154633, https://doi.org/10.1016/j.prp.2023.154633.
[87] J. Wu, G. Lu, X. Wang, MDM4 alternative splicing and implication in MDM4 targeted cancer therapies, Am. J. Cancer Res. 11 (12) (2021) 5864–5880.
[88] Y. Gao, B. Feng, L. Lu, S. Han, X. Chu, L. Chen, R. Wang, MiRNAs and E2F3: a complex network of reciprocal regulations in human cancers, Oncotarget 8 (36) (2017) 60624–60639, https://doi.org/10.18632/oncotarget.17364.
[89] N. Bley, A. Hmedat, S. Müller, R. Rolnik, A. Rausch, M. Lederer, S. Hüttelmaier, Musashi-1-A stemness RBP for cancer therapy? Biology 10 (5) (2021) https://doi.org/10.3390/biology10050407.
[90] M. Malekan, S.S. Nezamabadi, E. Samami, M. Mohebalizadeh, A. Saghazadeh, N. Rezaei, BDNF and its signaling in cancer, J. Cancer Res. Clin. Oncol. 149 (6) (2023) 2621–2636, https://doi.org/10.1007/s00432-022-04365-8.
[91] S. Wang, Q. Wang, X. Zhang, X. Liao, G. Wang, L. Yu, W. Zhang, Q. Zhou, S. Hu, W. Yuan, Distinct prognostic value of dynactin subunit 4 (DCTN4) and diagnostic value of DCTN1, DCTN2, and DCTN4 in colon adenocarcinoma, Cancer Manag. Res. 10 (2018) 5807–5824, https://doi.org/10.2147/cmar.S183062.
[92] G.C. Ziegler, P. Almos, R.V. McNeill, C. Jansch, K.P. Lesch, Cellular effects and clinical implications of SLC2A3 copy number variation, J. Cell. Physiol. 235 (12) (2020) 9021–9036, https://doi.org/10.1002/jcp.29753.
[93] P. Apostolou, I. Papasotiriou, Current perspectives on CHEK2 mutations in breast cancer, Breast Cancer 9 (2017) 331–335, https://doi.org/10.2147/bctt.S111394.
[94] M. Zhang, W. Yang, P. Wang, Y. Deng, Y.T. Dong, F.F. Liu, R. Huang, P. Zhang, Y.Q. Duan, X.D. Liu, D. Lin, Q. Chu, B. Zhong, CCL7 recruits cDC1 to promote antitumor immunity and facilitate checkpoint immunotherapy to non-small cell lung cancer, Nat. Commun. 11 (1) (2020) 6119, https://doi.org/10.1038/s41467-020-19973-6.
[95] Y.S. Lee, Y.B. Cho, CCL7 signaling in the tumor microenvironment, Adv. Exp. Med. Biol. 1231 (2020) 33–43, https://doi.org/10.1007/978-3-030-36667-4_4.
[96] Y. Peng, Y. Wang, C. Zhou, W. Mei, C. Zeng, PI3K/Akt/mTOR pathway and its role in cancer therapeutics: are we making headway? Front. Oncol. 12 (2022) 819128 https://doi.org/10.3389/fonc.2022.819128.
[97] Y. Fang, W. Ji, C. Yan, Research progress of PI3K/PTEN/AKT signaling pathway associated with renal cell carcinoma, Dis. Markers 2022 (2022) 1195875, https://doi.org/10.1155/2022/1195875.
[98] H. Liao, L. Zhang, S. Lu, W. Li, W. Dong, KIFC3 promotes proliferation, migration, and invasion in colorectal cancer via PI3K/AKT/mTOR signaling pathway, Front. Genet. 13 (2022) 848926, https://doi.org/10.3389/fgene.2022.848926.
[99] Y. Zhou, J. Xu, H. Luo, X. Meng, M. Chen, D. Zhu, Wnt signaling pathway in cancer immunotherapy, Cancer Lett. 525 (2022) 84–96, https://doi.org/10.1016/j.canlet.2021.10.034.
[100] Y. Zhang, X. Wang, Targeting the Wnt/β-catenin signaling pathway in cancer, J. Hematol. Oncol. 13 (1) (2020) 165, https://doi.org/10.1186/s13045-020-00990-3.
[101] R. Hayat, M. Manzoor, A. Hussain, Wnt signaling pathway: a comprehensive review, Cell Biol. Int. 46 (6) (2022) 863–877, https://doi.org/10.1002/cbin.11797.
[102] N. Carayol, C.Y. Wang, IKKalpha stabilizes cytosolic beta-catenin by inhibiting both canonical and non-canonical degradation pathways, Cell. Signal. 18 (11) (2006) 1941–1946, https://doi.org/10.1016/j.cellsig.2006.02.014.
[103] X. Sun, X. Peng, Y. Cao, Y. Zhou, Y. Sun, ADNP promotes neural differentiation by modulating Wnt/β-catenin signaling, Nat. Commun. 11 (1) (2020) 2984, https://doi.org/10.1038/s41467-020-16799-0.
[104] A. Vallée, Y. Lecarpentier, Crosstalk between peroxisome proliferator-activated receptor gamma and the canonical WNT/β-Catenin pathway in chronic inflammation and oxidative stress during carcinogenesis, Front. Immunol. 9 (2018) 745, https://doi.org/10.3389/fimmu.2018.00745.
[105] M. Tafrihi, R. Nakhaei Sistani, E-Cadherin/β-Catenin complex: a target for anticancer and antimetastasis plants/plant-derived compounds, Nutr. Cancer 69 (5) (2017) 702–722, https://doi.org/10.1080/01635581.2017.1320415.
[106] M. Zhao, L. Mishra, C.X. Deng, The role of TGF-β/SMAD4 signaling in cancer, Int. J. Biol. Sci. 14 (2) (2018) 111–123, https://doi.org/10.7150/ijbs.23230.
[107] S. Colak, P. Ten Dijke, Targeting TGF-β signaling in cancer, Trends Cancer 3 (1) (2017) 56–71, https://doi.org/10.1016/j.trecan.2016.11.008.
[108] Y. Ramakrishnaiah, L. Kuhlmann, S. Tyagi, Towards a comprehensive pipeline to identify and functionally annotate long noncoding RNA (lncRNA), Comput. Biol. Med. 127 (2020) 104028, https://doi.org/10.1016/j.compbiomed.2020.104028.
[109] M.C. Bridges, A.C. Daulagala, A. Kourtidis, LNCcation: lncRNA localization and function, J. Cell Biol. 220 (2) (2021), https://doi.org/10.1083/jcb.202009045.
[110] M.K. Gibert Jr., A. Sarkar, B. Chagari, C. Roig-Laboy, S. Saha, S. Bednarek, B. Kefas, F. Hanif, K. Hudson, C. Dube, Y. Zhang, R. Abounader, Transcribed ultraconserved regions in cancer, Cells 11 (10) (2022), https://doi.org/10.3390/cells11101684.