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Review Article

OTUD6B-AS1: a multifaceted regulator of cancer with critical clinical implications

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Abstract: OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1), a novel long non-coding RNA (lncRNA), has recently emerged as a critical regulator in various tumors. Current research underscores its dual functionality, acting either as an oncogene or a tumor suppressor depending on the tumor context. In this work, we compile and discuss findings from a range of studies investigating the expression patterns of OTUD6B-AS1 in different cancers and its consequent effects on tumor behavior, both in vitro and in vivo. We delve into the mechanisms through which OTUD6B-AS1 influences cancer initiation and progression, focusing on its role in regulating essential cellular processes such as cell growth, migration, invasion, angiogenesis, ferroptosis, and treatment resistance. Operating through complex interactions with microRNAs (miRNAs), proteins, and pivotal signaling pathways - most notably Wnt/β-catenin - OTUD6B-AS1 exhibits variable roles across cancer types and cellular environments. Additionally, we assess the clinical relevance of OTUD6B-AS1 expression levels, evaluating its potential as a biomarker for cancer prognosis and diagnosis, as well as a target for therapeutic intervention. By consolidating existing knowledge, this work aims to highlight the clinical implications of OTUD6B-AS1 and encourage further research in oncology, ultimately contributing to the advancement of targeted cancer therapies.

Keywords: Long non-coding RNA, OTU Deubiquitinase 6B-Antisense Transcript 1, human tumors, biological role, regulatory mechanisms, cancer biomarker

Introduction

Advancements in cancer research have led to the identification and validation of numerous biomarkers that play critical roles in tumorigenesis [1-4]. Among these biomarkers, long non-coding RNAs (lncRNAs) - RNA molecules longer than 200 nucleotides that lack the ability to code for proteins - have emerged as key players in the mechanisms underlying cancer development [5-8]. Due to their involvement in various regulatory processes, lncRNAs represent a promising new class of cancer biomarkers [9-11].

This growing interest particularly highlights lncRNAs such as OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1), which has been associated not only with systemic sclerosis [12, 13], but also with various human tumors [14-18]. Extensive research has revealed abnormal expression patterns of OTUD6B-AS1 in tumor tissues, correlating with several clinicopathological features, including clinical stage and prognostic survival time [19-24]. Moreover, abnormal expression patterns of OTUD6B-AS1 have also been observed in cancer cell lines [14, 18-24], OTUD6B-AS1 plays a crucial and variable role in a multitude of cellular processes, including proliferation, apoptosis, autophagy, invasion, metastasis, ferroptosis, and resistance. These functions occur through mechanisms such as competing endogenous RNA (ceRNA) activity and interactions with proteins [14, 15, 17-22, 25]. These findings underscore the potential of OTUD6B-AS1 as a valuable biomarker for tumors and suggest promising avenues for therapeutic targeting.

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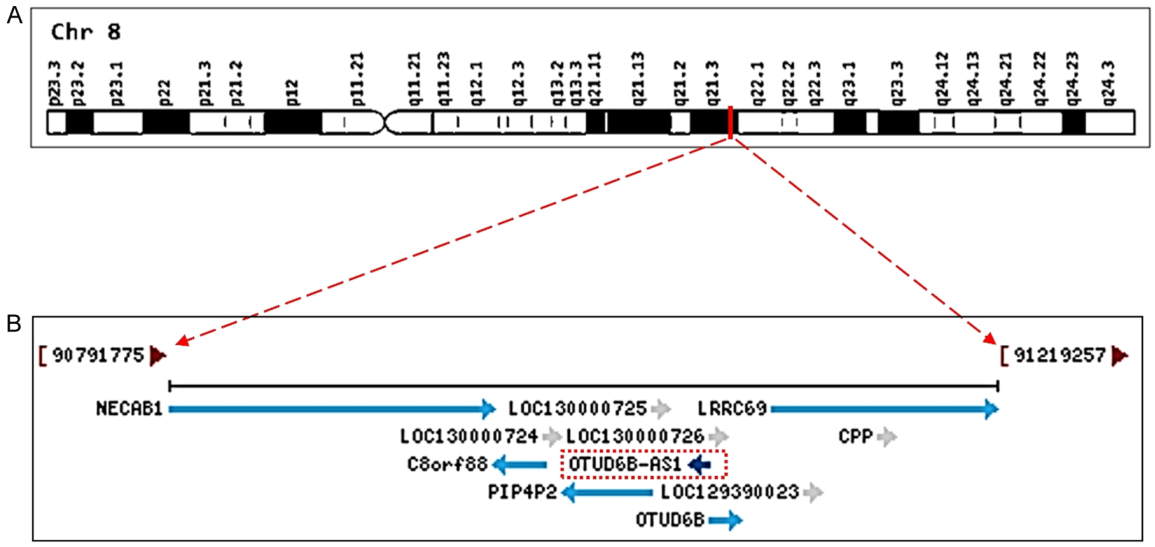

Figure 1. Overview of Homo sapiens (human) OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) gene. A. Genomic location of the OTUD6B-AS1 gene, as extracted from the GeneCards database (https://www.genecards.org/cgi-bin/carddisp.pl?gene=OTUD6B-AS1). B. Genomic context of OTUD6B-AS1, based on information derived from the National Center for Biotechnology Information (NCBI) database (https://www.ncbi.nlm.nih.gov/gene/100506365).

In this study, we aim to provide an overview of the expression patterns, clinical implications, biological functions (both in vitro and in vivo), and molecular mechanisms of OTUD6B-AS1 across various cancer types. We will also discuss its prognostic value in pan-cancer, potential as a non-invasive biomarker, and its associated ceRNA networks in cancer cells. By enhancing our understanding of OTUD6B-AS1's role as a significant lncRNA in tumor development, we could facilitate its future clinical applications in cancer management.

Characteristics of OTUD6B-AS1

The OTUD6B-AS1 gene, classified as an RNA gene within the lncRNA category, is located on chromosome 8q21.3, as illustrated in **Figure 1A**. This gene consists of three exons and spans a sequence of 10,284 nucleotides (nt). It is positioned adjacent to the OTUD6B, PIP4P2, and C8orf88 genes, as depicted in **Figure 1B**. OTUD6B-AS1 is transcribed from the antisense strand relative to the OTUD6B gene, which is situated on chromosome 8 in a head-to-head orientation with OTUD6B-AS1.

Studies have demonstrated that OTUD6B-AS1 lncRNA is primarily localized in the cytoplasm of cancer cells, including RKO-R, HCT116-R [19], and T24 cells [25]. It is predicted to be associated with ribosomes, the nucleoplasm, membranes, the nucleus, and exosomes, as shown in **Figure 2**. Additionally, the minimum free energy (MFE) secondary structure of OTUD6B-AS1 was predicted using the RNAfold web server, as depicted in **Figure 3**. With a minimum free energy of -1071.84 kcal/mol, this optimal secondary structure provides insights into the RNA's stability and its potential functional roles.

Expression level of OTUD6B-AS1 in human tumours

Recent investigations have unveiled dysregulated expression of OTUD6B-AS1 across various human malignancies. It was observed that OTUD6B-AS1 is up-regulated in breast cancer [16, 17], hepatocellular carcinoma (HCC) [18], cervical cancer [22], and osteosarcoma [24], while it is down-regulated in thyroid carcinoma [14], colorectal cancer (CRC) [19, 20], and clear cell renal cell carcinoma (ccRCC) [21] (**Table 1**).

To comprehensively assess OTUD6B-AS1 expression across diverse cancers, an analysis was performed utilizing TNMplot (https://tnmplot.com/analysis/) [26] (**Figure 4**). This analysis revealed significant upregulation of OTUD6B-AS1 in tumor samples from acute myeloid leukemia (AML), breast cancer, esophageal cancer, liver cancer, lung cancer, pancre-

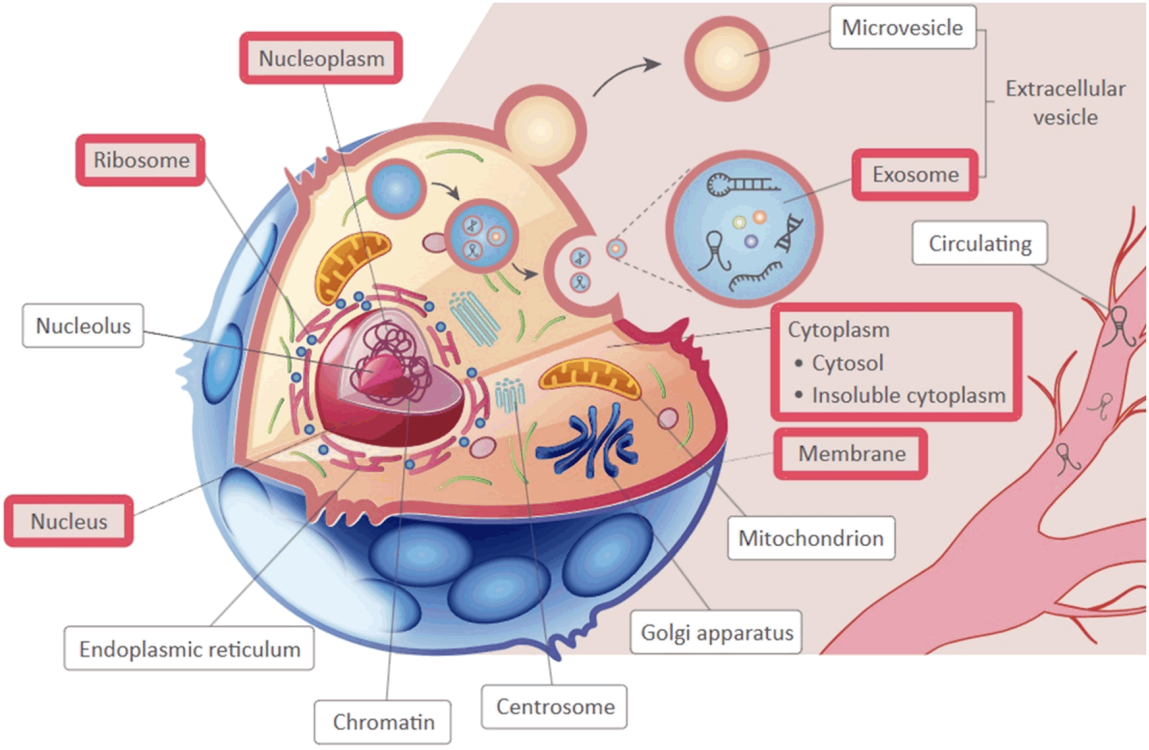

Figure 2. The predicted sub-cellular localization of OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1), with identified locations highlighted within a red frame, sourced from LnCeCell (http://bio-bigdata.hrbmu.edu.cn/LnCeCell/), which data from Publication, lncATLAS, CSCD, and exoRBase.

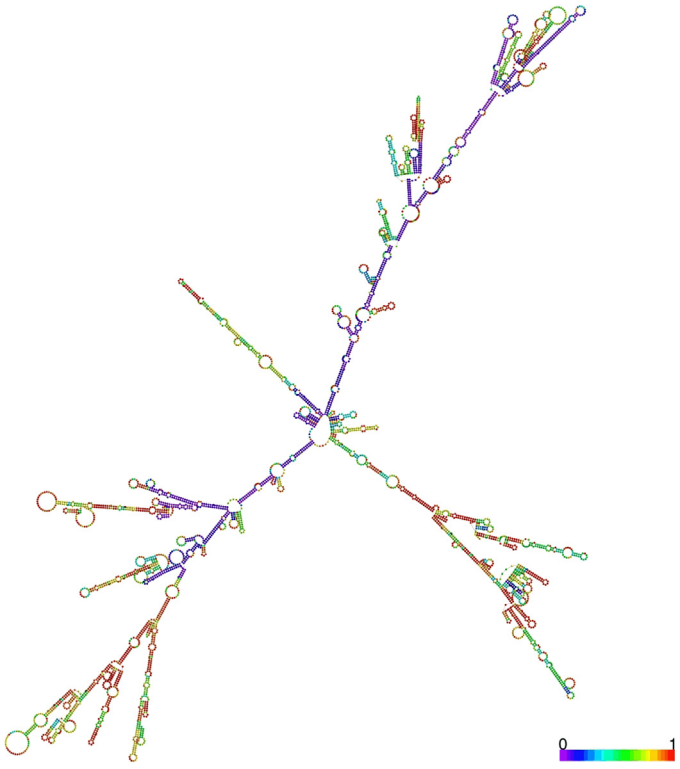

Figure 3. Minimum free energy secondary structure of lncRNA OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1), with coloring indicative of base-pairing probability.

atic cancer, kidney chromophobe, skin cancer, and stomach cancer. Conversely, significant downregulation of OTUD6B-AS1 was noted in renal clear cell carcinoma, renal papillary cell carcinoma, testicular cancer, and uterine endometrial carcinoma.

Clinical value of OTUD6B-AS1 in human tumours

Findings from various studies underscore the potential of OTUD6B-AS1 as a biomarker for cancer phenotypes, its association with patient survival outcomes, and its diagnostic utility [14-24], as summarised in **Table 1**. Multiple studies report a direct correlation between high OTUD6B-AS1 expression and adverse outcomes in breast cancer [15-17]. Elevated OTUD6B-AS1 levels are associated with features of aggressive disease, including lymph node metastasis, larger tumor size, deeper invasion, and advanced tumor stage, with patients exhibiting high OTUD6B-AS1

Table 1. The expression, prognostic implications, and diagnostic significance of OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) across various types of cancer

Cancer type	Expression	Diagnostic	Significant clinical variables	End-point	Unfavorable	Ref.
Thyroid carcinoma	Down-regulated	-	Tumor size, lymphatic metastasis, clinical stage	-	-	[14]
Breast cancer	-	-	Axillary lymph node metastasis, tumor size, tumor stage	Overall survival	High expression	[15]
	Up-regulated	-	Clinical stage; lymph node metastasis; invasion depth	Overall survival	High expression	[16]
	Up-regulated	-	-	Overall survival	High expression	[17]
Hepatocellular carcinoma	Up-regulated	-	-	Overall survival	High expression	[18]
Colorectal cancer	Down-regulated	-	-	-	-	[19]
	Down-regulated	-	-	-	-	[20]
Clear cell renal cell carcinoma	Down-regulated	AUC: 0.792, Sensitivity: 0.773, Specificity: 0.814	Clinical stage, tumor depth, lymph node metastasis, distant metastasis, survival staus	Overall survival	Low expression	[21]
Cervical cancer	Up-regulated	-	Tumor grade, clinical stage	Overall survival	High expression	[22]
Ovarian cancer	-	-	-	Overall survival	High expression	[23]
Osteosarcoma	Up-regulated	-	-	-	-	[24]

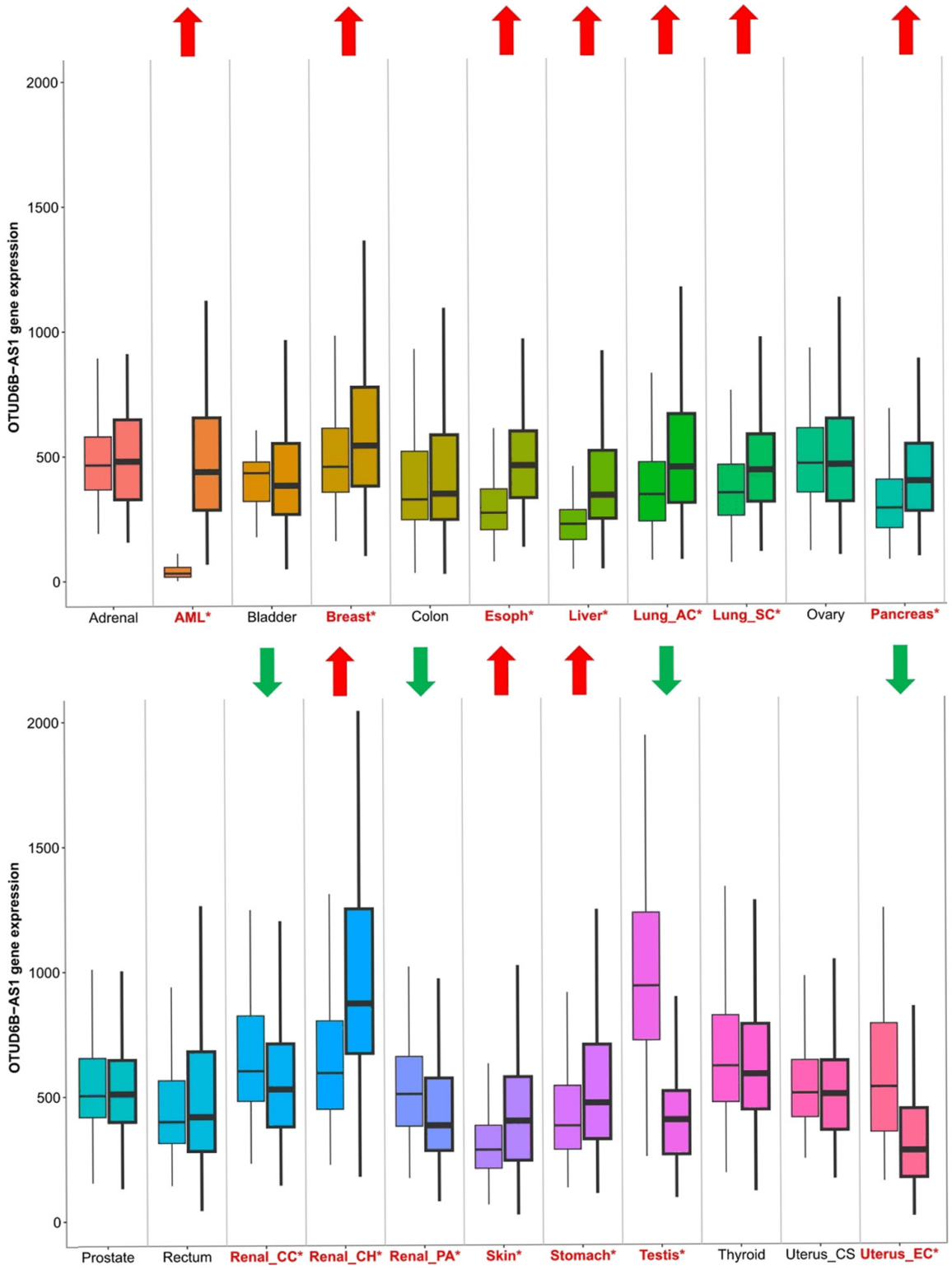

Figure 4. Comparison of OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) expression levels between tumor samples and normal tissues. In the upper section, cancer types where OTUD6B-AS1 is significantly upregulated are denoted in red with upward arrows, while those where it is significantly downregulated are highlighted in green with downward arrows. Significant differences between cancer and normal tissues are indicated by red asterisks. The data originates from TNMplot (https://tnmplot.com/analysis/), which incorporates samples from various databases including Gene Expression Omnibus (GEO), Genotype-Tissue Expression (GTEx), The Cancer Genome Atlas (TCGA), and The Therapeutically Applicable Research to Generate Effective Treatments (TARGET).

expression experiencing shorter overall survival (OS).

Additionally, several lncRNA-based prognostic models incorporating OTUD6B-AS1 - such as cuproptosis-related lncRNAs and an aging-related lncRNA signature - have been developed and demonstrate notable prognostic value in breast cancer cases [16, 27-32]. Collectively, these findings suggest that OTUD6B-AS1 may serve as a promising prognostic marker for breast cancer patients.

In HCC [18], OTUD6B-AS1 shows significantly increased expression levels in tumor tissues, correlating with decreased patient survival. Consistent upregulation across HCC tissue samples indicates its potential as a prognostic marker for this cancer type. In cervical and ovarian cancers [22, 23], OTUD6B-AS1 is significantly overexpressed in cancerous tissues compared to normal counterparts. In cervical cancer [22], OTUD6B-AS1 expression levels are also associated with tumor grade and stage, with upregulation linked to shorter survival times in both cancer types [22, 23].

Conversely, OTUD6B-AS1 expression is downregulated in thyroid carcinoma tissues [14]. This reduction is associated with larger tumor sizes, the presence of lymphatic metastasis, and advanced clinical stage, suggesting a complex role for OTUD6B-AS1 in thyroid carcinoma, potentially acting in a manner that influences tumor suppression or progression mechanisms. Additionally, OTUD6B-AS1 is notably downregulated in ccRCC [21], where lower expression levels are associated with poor OS. Its expression inversely correlates with disease severity, including tumor metastasis, tumor depth, and tumor stages.

Furthermore, the lncRNA OTUD6B-AS1 demonstrates clear diagnostic discrimination (AUC = 0.792), with a sensitivity of 77.3% and specificity of 81.4% for differentiating cancer tissues from normal tissues [21]. Thus, OTUD6B-AS1 may serve as a valuable prognostic and diagnostic biomarker in ccRCC.

Role of OTUD6B-AS1 in tumorigenesis and development

Research has demonstrated abnormal expression levels of OTUD6B-AS1 in cancer cell lines [14, 18-24] and has investigated its role in various human tumors using both cell lines and xenograft models [14, 15, 17-22, 25] (**Table 2**). OTUD6B-AS1 has been linked to the pathogenesis and development of several cancers, including thyroid carcinoma [14], breast cancer [15, 17], HCC [18], CRC [19, 20], bladder cancer [25], ccRCC [21], and cervical cancer [22]. Its role varies depending on the tumor context.

In breast cancer [15, 17], HCC [18], and cervical cancer [22], OTUD6B-AS1 acts oncogenically by modulating cellular processes that promote tumor survival and drug resistance. Conversely, in thyroid carcinoma [14], CRC [19, 20], bladder cancer [25], and ccRCC [21], OTUD6B-AS1 exhibits tumor-suppressive properties, where its overexpression can inhibit cancer cell growth, migration, and invasion, as well as reduce resistance to chemotherapy and radiotherapy.

This dualistic nature underscores the complex involvement of OTUD6B-AS1 in cancer biology, functioning either as an oncogene or tumor suppressor depending on the specific cellular environment and regulatory networks involved.

Biological functions of OTUD6B-AS1 in tumors

Various research consistently demonstrates that modulating the expression of OTUD6B-AS1 in cancer cells significantly impacts cell growth, migration, invasion, and treatment resistance, both in vitro and in vivo [14, 15, 17-22, 25] (**Figure 5**). This underscores the pivotal role of OTUD6B-AS1 in regulating cellular processes crucial to cancer progression. The findings highlight the dual oncogenic and tumor-suppressive functions of OTUD6B-AS1 in cancer development. OTUD6B-AS1 plays a critical role in various cancers by regulating cellular behavior, the cell cycle, growth, stress responses, survival mechanisms, and the tumor microenvironment. Understanding the specific functions of OTUD6B-AS1 in different cancers can aid in the development of targeted therapies.

In terms of cellular behavior, OTUD6B-AS1 promotes cell proliferation in breast cancer [15] and HCC [18], driving rapid tumor growth, while it inhibits cell proliferation in CRC [20] and ccRCC [21]. Additionally, OTUD6B-AS1 enhances migration and invasion in breast cancer [15] and HCC [18], and promote EMT in breast can-

Table 2. The expression of OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) in cancer cells and its diverse functions and molecular mechanisms in various human tumors

Cancer type	Cell lines	Cell expression	Cellular functions	Animal models	Phenotypes	Related molecule/ pathway	Role	Ref.
Thyroid carcinoma	SW579, TPC-1, and Nthy-ori	Down-regulated in cancer cell lines	Cell viability, migration, invasion	-	-	OTUD6B-AS1/miR-183-5p and miR-21	Tumor-suppressive	[14]
Breast cancer	BT474, and HUVEC	-	Cell proliferation, migration, invasion, EMT, angiogenesis	-	-	EMT- and angiogenesis-related signaling	Oncogenic	[15]
	MDA-MB-231 and HCC1937	-	Cell autophagy, DNA damage, paclitaxel resistance	-	-	OTUD6B-AS1/miR-26a-5p/MTDH	Oncogenic	[17]
Hepatocellular carcinoma	HepG2, Hep3B, SNU-475, Huh-7, HL-7702 and 293T	Up-regulated in cancer cell lines	Cell proliferation, invasion	Xenograft tumour model: BALB/c nude mice (4-6 weeks old)	Tumor volume, tumor weight	OTUD6B-AS1/miR-664b-3p/GSKIP, Wnt/β-catenin signalling	Oncogenic	[18]
Colorectal cancer	HCT116, RKO, SW620, LoVo and HIEC-6	Down-regulated in cancer cell lines	Ferroptosis, radioresistance	-	-	HuR/TRIM16	Tumor-suppressive	[19]
	Caco2, HCT116, LoVo, SW480, SNU-C1 and HIEC	Down-regulated in cancer cell lines	Cell proliferation, migration, invasion	-	-	OTUD6B-AS1/miR-3171	Tumor-suppressive	[20]
Bladder cancer	T24 cells	-	Cell viability, apoptosis, AS_2O_3 resistance	Xenograft tumour model: BALB/c nude mice (4 weeks old; 50% female and 50% male)	Tumor volume, tumor weight	OTUD6B-AS1/miR-6734-5p/IDH2	Tumor-suppressive	[25]
Clear cell renal cell carcinoma	786-O, Caki-1, 769-P, OS-RC-2, ACHN and HK-2	Down-regulated in cancer cell lines	Cell proliferation migration, invasion, apoptosis, cell cycle progression, EMT	Xenograft tumour model: Female nude mice that were (4 weeks old)	Tumor volume, tumor weight	Wnt/β-catenin signaling	Tumor-suppressive	[21]
Cervical cancer	HeLa, CaSki, SiHa and Ect1/E6E; CDDP-resistant HeLa and SiHa cells	Up-regulated in cervical cancer cell lines than normal cells; elevated in CDDP-resistant cervical cancer cells	Cisplatin resistance	Subcutaneous tumour model	Tumor growth and tumor weight	OTUD6B-AS1/miR-206/ CCND2	Oncogenic	[22]
Ovarian cancer	TOV-21G, A2780,SKOV3 and IOSE80	Down-regulated in cancer cell lines	-	-	-	-	-	[23]
Osteosarcoma	SaOS-2, G-292, SJSA-1, HOS, 143B, U2-OS, MNNG/ HOS and MG-63; hFOB	Up-regulated in SaOS-2, HOS, Down-regulated in SJSA-1, 143B, U2-OS, MNNG/HOS	-	-	-	-	-	[24]

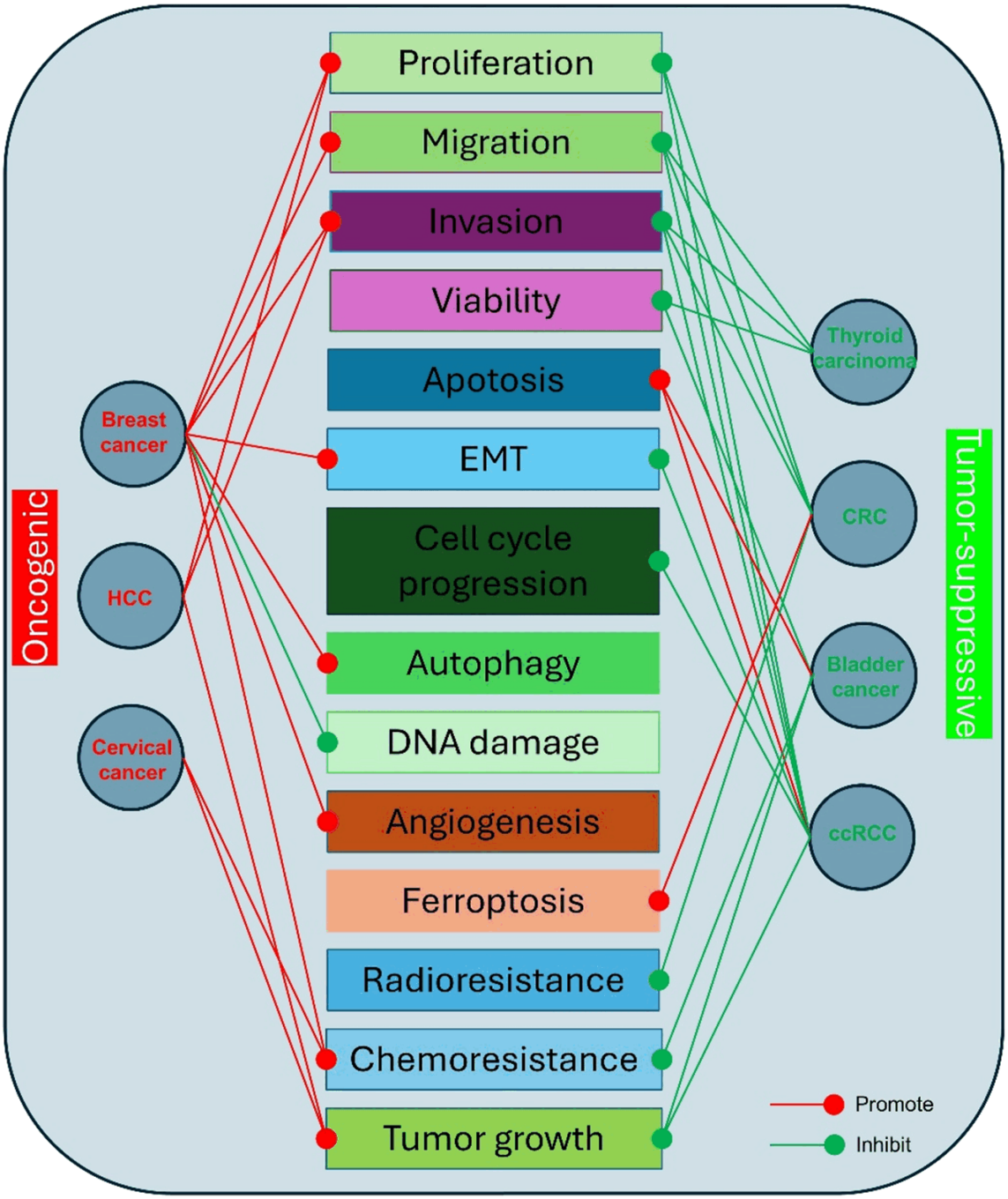

Figure 5. The role of lncRNA OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) in various cancers, acting either as an oncogene or a tumor suppressor.

cer [15], thereby increasing metastatic potential. In contrast, it inhibits these processes in thyroid carcinoma [14], CRC [20], and ccRCC [21]. Furthermore, OTUD6B-AS1 reduces cell viability in thyroid carcinoma [14] and bladder cancer [25], making cancer cells less resistant to treatments, while promotes apoptosis in bladder cancer [25] and ccRCC [21]. In regulating the cell cycle and growth, OTUD6B-AS1 inhibits proliferation in ccRCC [21] by modulating cell cycle progression. In vivo studies indicate that OTUD6B-AS1 contributes to tumor growth in HCC [18] and cervical cancer [22], while it inhibits tumor growth in bladder cancer

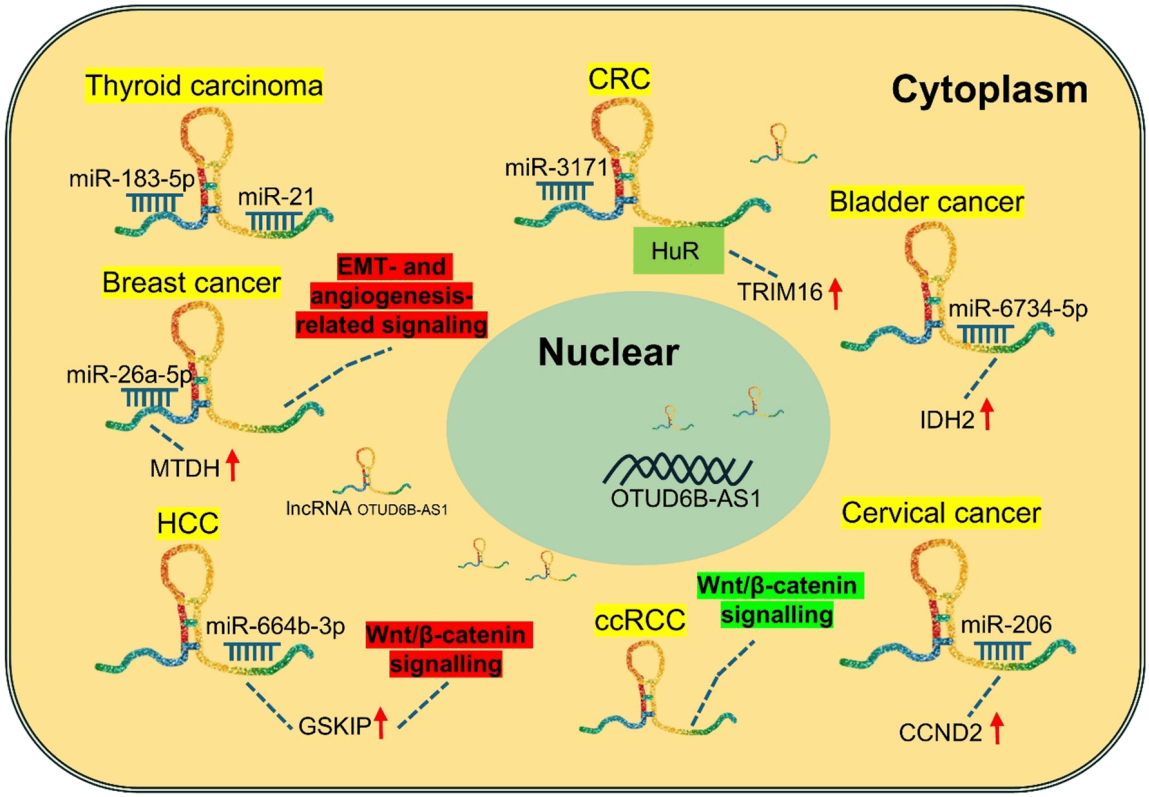

Figure 6. Molecular regulatory mechanisms of lncRNA OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) in various cancers.

[25] and ccRCC [21]. Regarding stress and survival mechanisms, OTUD6B-AS1 promotes autophagy and inhibits DNA damage repair in breast cancer [17], aiding cell survival under stress. It increases chemoresistance in breast and cervical cancers [17, 22], while reducing chemoresistance in bladder cancer [25] and radioresistance in CRC [19]. Additionally, OTUD6B-AS1 influences ferroptosis in CRC, affecting cancer cell survival. In terms of microenvironment regulation, OTUD6B-AS1 promotes angiogenesis in breast cancer [15], supplying tumors with the necessary oxygen and nutrients to support growth and expansion.

Molecular regulatory mechanisms of OTUD6B-AS1

LncRNAs can act as molecular sponges for microRNAs (miRNAs) through a competitive endogenous RNA (ceRNA) mechanism, which influences the availability of miRNAs and, consequently, modulates the expression of their target mRNAs [33-36]. One significant lncRNA, OTUD6B-AS1, possesses multiple potential miRNA-binding sites, allowing it to regulate various mRNAs by competing for miRNA molecules [14, 17, 18, 20, 22, 25]. This competitive interaction alters downstream gene expression and significantly impacts cancer cell behavior and tumor progression. In human cancer cells [14, 17, 18, 20, 22, 25], OTUD6B-AS1 competitively binds to several miRNAs, including miR-26a-5p, miR-664b-3p, miR-6734-5p, and miR-206. This binding facilitates the upregulation of key genes such as MTDH, GSKIP, IDH2, and CCND2 (**Figure 6**), leading to increased production of proteins that regulate malignant traits, including cell proliferation, invasion, migration, and tumor resistance, thereby influencing cancer initiation and progression.

Furthermore, it has been reported that the cytoplasmic localization of lncRNAs enables them to interact with RNA-binding proteins, thereby enhancing the mRNA stability of downstream targets [37-39]. In CRC, aside from its function as a ceRNA by binding to miR-3171 [20], a study by Zhang et al. [19] discovered that OTUD6B-AS1 can also bind to the RNA-

binding protein HuR. This interaction increases the mRNA stability of TRIM16 (**Figure 6**), which in turn enhances GPX4-mediated ferroptosis and reduces radioresistance in CRC.

OTUD6B-AS1 also plays a significant role in regulating cancer progression through various signaling pathways [15, 18, 21] (**Figure 6**). In breast cancer, Wang et al. [15] found that OTUD6B-AS1 enhanced the tube formation capacity of HUVEC cells. It downregulated E-cadherin while upregulating markers such as MMP1, SMAD5, Snail, Twist1, thereby promoting breast cancer progression and participating in EMT- and angiogenesis-related signaling. In HCC, Kong et al. [18] reported that OTUD6B-AS1 acts as a ceRNA for miR-664b-3p, resulting in the upregulation of GSKIP and subsequent activation of the Wnt/β-catenin signaling pathway. This activation promotes cell proliferation and invasion in HCC cells. Conversely, in ccRCC [21], OTUD6B-AS1 exhibited a tumor-suppressive role; its overexpression decreased the activity of the Wnt/β-catenin pathway, thereby inhibiting the progression of ccRCC.

Future perspectives

LncRNAs are increasingly recognized as pivotal regulators of cellular processes, orchestrating a wide range of biological functions from chromatin remodeling to gene expression regulation [40-42]. Among these lncRNAs, OTUD6B-AS1 has attracted significant attention for its multifaceted roles in human cancers [14-18]. Recent advances in cancer biology have illuminated the complexity of lncRNA functions, demonstrating that molecules like OTUD6B-AS1 can serve as both oncogenes and tumor suppressors, depending on the cellular context and environmental influences [14-18].

OTUD6B-AS1's capacity to modulate various pathways and molecular interactions uniquely positions it within oncogenic networks, thereby influencing critical processes such as cancer cell proliferation, apoptosis, migration, and invasion. The dual roles of OTUD6B-AS1, which may either promote or inhibit tumor progression, highlight the intricate balance of cellular signaling pathways in cancer development. This dualistic nature not only complicates our understanding of lncRNA biological functions but also paves the way for novel approaches to targeted cancer therapies.

Several studies have linked the expression of long non-coding RNA (lncRNA) OTUD6B-AS1 to OS across various cancers, including breast cancer [15-17], HCC [18], ccRCC [21], cervical cancer [22], and ovarian cancer [23]. To further investigate the role of OTUD6B-AS1 in a broader spectrum of cancers, we examined the relationship between its expression and patient prognoses in 33 different tumor types. This analysis focused on OS and disease-free survival (DFS), utilizing the GEPIA2 online tool (http://gepia2.cancer-pku.cn/#index) [43] (see **Figure 7A**). Kaplan-Meier curves reveal a significant prognostic relevance of OTUD6B-AS1 in breast cancer (BRCA), cervical cancer (CESC), kidney renal clear cell carcinoma (KIRC), lower grade glioma (LGG), melanoma (SKCM), and thyroid carcinoma (THCA) (see **Figure 7B**). Notably, low expression levels of OTUD6B-AS1 are associated with poor survival outcomes, particularly in KIRC, LGG, and SKCM, with implications for both OS and DFS, as well as shorter DFS in THCA (**Figure 7B**). Conversely, lower expression of OTUD6B-AS1 is linked to better OS in BRCA and improved DFS in CESC (**Figure 7B**).

Regarding its diagnostic value in cancer, only one study has clearly demonstrated that OTUD6B-AS1 can effectively differentiate cancer tissues from normal tissues, achieving an Area Under the Curve (AUC) of 0.792 [21]. However, the diagnostic potential of tissue lncRNA OTUD6B-AS1 in other solid tumors remains unclear. Additionally, obtaining lncRNA from tumor tissues is invasive and often not easily accessible. Given that numerous lncRNAs in the blood, including exosomal lncRNAs, have been recognized as promising diagnostic tools for tumors [44-46], we are now focusing on the potential of OTUD6B-AS1 as a minimally invasive diagnostic tool. Utilizing exoRBase [47], a repository of long RNAs derived from extracellular vesicles obtained through RNA-seq data analyses, we assessed the expression of OTUD6B-AS1 across various human body fluids, including urine, cerebrospinal fluid, bile, and blood samples from different cancer types (**Figure 8A**). Furthermore, we observed significant differential expression of OTUD6B-AS1 in the blood of individuals with various cancers - such as BRCA, esophageal squamous cell carcinoma (ESCC), glioblastoma multiforme (GBM), gastric cancer (GC), KIRC, melano-

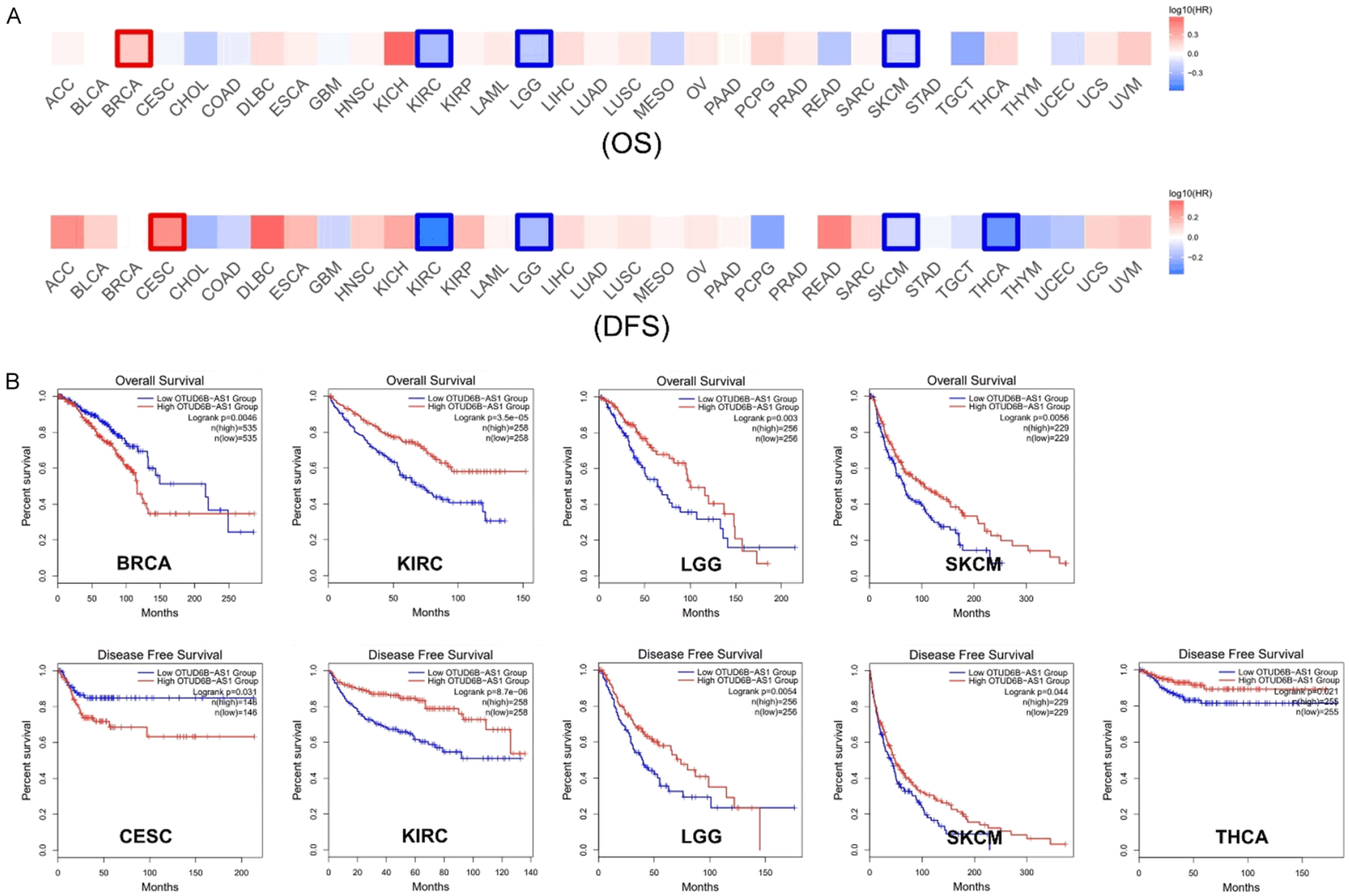

Figure 7. The prognostic value of OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) across various cancers. A. Survival map showing the association between OTUD6B-AS1 expression levels and overall survival (OS) and disease-free survival (DFS) across 33 different cancer types. B. Kaplan-Meier curves demonstrating its significant prognostic relevance in breast cancer (BRCA), cervical cancer (CESC), kidney renal clear cell carcinoma (KIRC), brain lower grade glioma (LGG), melanoma (SKCM), and thyroid carcinoma (THCA) in terms of OS and DFS. The data is sourced from Gene Expression Profiling Interactive Analysis 2 (GEPIA2) (http://gepia2.cancer-pku.cn/#index).

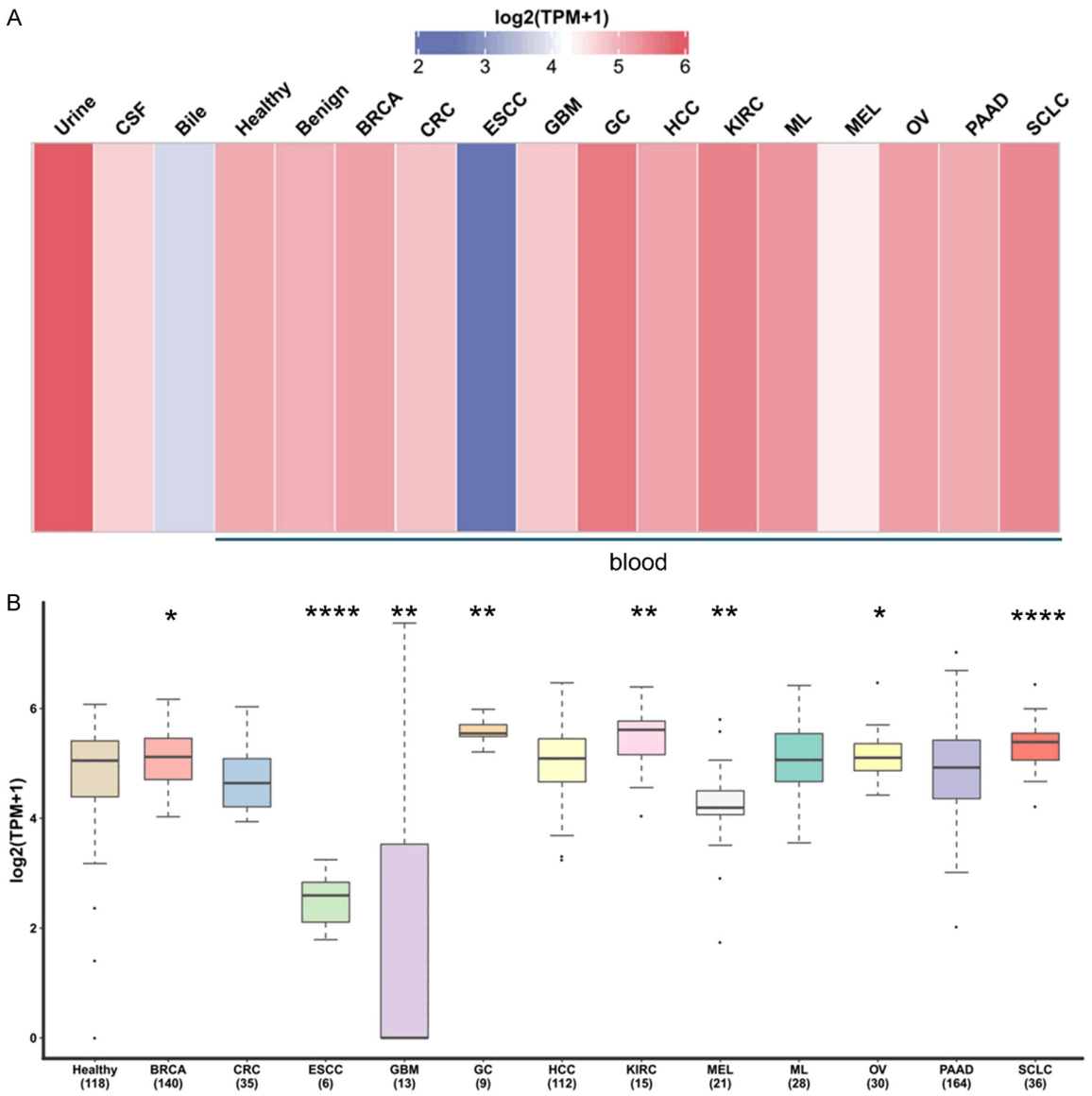

Figure 8. Comparison of OTU Deubiquitinase 6B-Antisense Transcript 1 (OTUD6B-AS1) levels within extracellular vesicles. A. The heatmap illustrates the expression of OTUD6B-AS1 across various human body fluids and in blood samples from different types of cancer. B. Significant differential expression of OTUD6B-AS1 in blood extracellular vesicles is observed between several types of cancer vs. healthy individuals, including breast cancer (BRCA), esophageal squamous cell carcinoma (ESCC), glioblastoma multiforme (GBM), gastric cancer (GC), kidney renal cell carcinoma (KIRC), melanoma (MEL), ovarian cancer (OV), and small cell lung cancer (SCLC). The significance levels are denoted by asterisks above the comparison boxes: * for $P < 0.05$, ** for $P < 0.01$, and **** for $P < 0.0001$. The data is sourced from exoRBase (http://www.exorbase.org/).

ma (MEL), ovarian cancer (OV), and small cell lung cancer (SCLC) - when compared to healthy donors (**Figure 8B**). These findings underscore the potential of OTUD6B-AS1 as a promising diagnostic marker across a range of tumors. Moving forward, further studies are needed to evaluate the sensitivity and specificity of exosomal OTUD6B-AS1 in blood samples, thereby opening an exciting avenue for research into novel circulating oncological biomarkers.

Recent studies have elucidated that OTUD6B-AS1 functions primarily as a ceRNA, sequestering miRNAs such as miR-26a-5p, miR-664b-3p, miR-6734-5p, miR-206, miR-21, miR-3171, and miR-183-5p. This sequestration modulates the

expression of target genes that are either oncogenic or tumor-suppressive, thereby influencing the malignancy of cancer cells and their resistance to radio-chemotherapy. The role of lncRNA-associated ceRNA networks in determining cancer cell fate and tumor progression is increasingly recognized [34, 48-52].

Utilizing the LnCeCell database [53], we have delineated ceRNA networks associated with OTUD6B-AS1 at the single cancer cell level. Our analysis highlights that the OTUD6B-AS1-associated ceRNA network is linked to key cancer hallmarks, such as self-sufficiency in growth signals and insensitivity to anti-growth signals (**Figure 9A**). Furthermore, we identified the top 10 functional roles enriched among OTUD6B-AS1-associated ceRNAs (**Figure 9B**). Our results indicate that these ceRNAs, connected to OTUD6B-AS1, are involved in critical oncogenic processes, including transcription initiation at the RNA polymerase II promoter and the localization of cellular components. These functions are essential for regulating gene expression and are closely tied to the misregulation of genes that can lead to oncogenesis.

Additionally, these ceRNAs impact vital cellular operations like signal transduction, cell division, and programmed cell death. Cancer cells may exploit these pathways to enhance their survival and proliferation. Moreover, these ceRNAs are associated with several key cancer-related pathways, including the ATF2 pathway and the caspase pathway (**Figure 9C**). These pathways play a crucial role in various cancers [54-61], regulating cellular survival, proliferation, and apoptosis.

Current research primarily focuses on ceRNA network that OTUD6B-AS1 involved in the tumor progression [14, 17, 18, 20, 22, 25]. When lncRNA acts as a ceRNA, it can bind to specific miRNAs, thereby reducing the binding of miRNAs to their target mRNAs, which results in the upregulation of mRNA levels. OTUD6B-AS1 has been found to competitively bind several miRNAs, including miR-26a-5p, miR-664b-3p, miR-6734-5p, and miR-206, leading to the upregulation of genes such as MTDH, GSKIP, IDH2, and CCND2 (see **Figure 6**). Additionally, ceRNA interactions may also influence the stability and localization of lncRNAs [62, 63]. Competing RNAs can affect the half-life of lncRNAs or their intracellular transport, thereby impacting their functional availability [64-67]. Furthermore, it has been reported that OTUD6B-AS1 interacts with the RNA-binding protein HuR, which enhances the mRNA stability of TRIM16 and mediates radioresistance in CRC [19]. This finding underscores the intricate nature of RNA interactions and their essential role in regulating gene expression.

Moreover, the expression of OTUD6B-AS1 may be regulated by additional mechanisms, including epigenetic modifications and transcription factors. Although research on these regulatory mechanisms remains limited, insights can be derived from studies of other lncRNAs. For instance, the expression of MALAT1 can be influenced by histone modifications [68, 69]. And several transcription factors, such as c-MYC [70], and p53 [71], can also regulate MALAT1 transcription. Similarly, HOTAIR is regulated by transcription factors such as Snail and EZH2 during the epithelial-mesenchymal transition (EMT) [72, 73] and is also significantly influenced by chromatin modifications mediated by the Polycomb Repressive Complex 2 (PRC2) [74, 75]. Thus, future investigations into OTUD6B-AS1 should focus on elucidating its epigenetic regulation and mapping its interactions with transcription factors, which will enhance our understanding of its potential roles in oncogenesis and tumor progression.

Conclusion

In summary, OTUD6B-AS1 is a critical tumor-related lncRNA that influences key cellular processes, including growth, migration, and treatment resistance. Its diverse interactions with microRNAs and signaling pathways highlight its complex role in various cancers. Clinically, OTUD6B-AS1 shows promise as a biomarker for cancer prognosis and diagnosis. Given its potential to advance targeted cancer therapies, OTUD6B-AS1 emerges as a valuable candidate for both cancer biomarkers and therapeutic targets.

Disclosure of conflict of interest

None.

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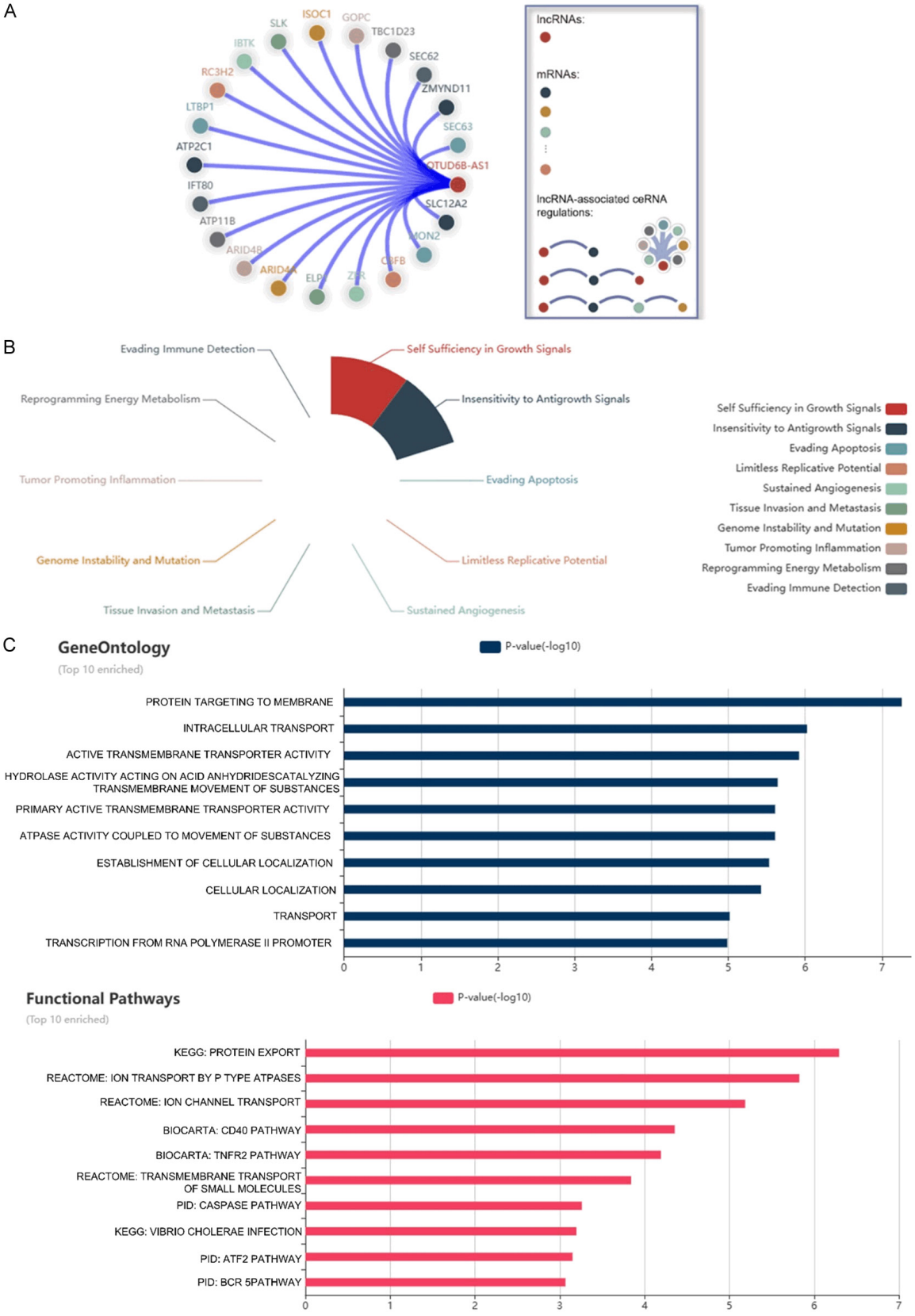

Figure 9. Competing endogenous RNA (CeRNA) networks associated with OTU Deubiquitinase 6B-Antisense Transcript 1.

References

[1] Passaro A, Al Bakir M, Hamilton EG, Diehn M, André F, Roy-Chowdhuri S, Mountzios G, Wistuba II, Swanton C and Peters S. Cancer biomarkers: emerging trends and clinical implications for personalized treatment. Cell 2024; 187: 1617-1635.

[2] Sarhadi VK and Armengol G. Molecular biomarkers in cancer. Biomolecules 2022; 12: 1021.

[3] Nair M, Sandhu SS and Sharma AK. Cancer molecular markers: a guide to cancer detection and management. Semin Cancer Biol 2018; 52: 39-55.

[4] Das S, Dey MK, Devireddy R and Gartia MR. Biomarkers in cancer detection, diagnosis, and prognosis. Sensors (Basel) 2023; 24: 37.

[5] Mattick JS, Amaral PP, Carninci P, Carpenter S, Chang HY, Chen LL, Chen R, Dean C, Dinger ME, Fitzgerald KA, Gingeras TR, Guttman M, Hirose T, Huarte M, Johnson R, Kanduri C, Kapranov P, Lawrence JB, Lee JT, Mendell JT, Mercer TR, Moore KJ, Nakagawa S, Rinn JL, Spector DL, Ulitsky I, Wan Y, Wilusz JE and Wu M. Long non-coding RNAs: definitions, functions, challenges and recommendations. Nat Rev Mol Cell Biol 2023; 24: 430-447.

[6] Fatica A and Bozzoni I. Long non-coding RNAs: new players in cell differentiation and development. Nat Rev Genet 2014; 15: 7-21.

[7] Marchese FP, Raimondi I and Huarte M. The multidimensional mechanisms of long noncoding RNA function. Genome Biol 2017; 18: 206.

[8] Kadian LK, Verma D, Lohani N, Yadav R, Ranga S, Gulshan G, Pal S, Kumari K and Chauhan SS. Long non-coding RNAs in cancer: multifaceted roles and potential targets for immunotherapy. Mol Cell Biochem 2024; 479: 3229-3254.

[9] Coan M, Haefliger S, Ounzain S and Johnson R. Targeting and engineering long non-coding RNAs for cancer therapy. Nat Rev Genet 2024; 25: 578-595.

[10] Bhan A, Soleimani M and Mandal SS. Long noncoding RNA and cancer: a new paradigm. Cancer Res 2017; 77: 3965-3981.

[11] Huarte M. The emerging role of lncRNAs in cancer. Nat Med 2015; 21: 1253-1261.

[12] Takata M, Pachera E, Frank-Bertoncelj M, Kozlova A, Jüngel A, Whitfield ML, Assassi S, Calcagni M, de Vries-Bouwstra J, Huizinga TW, Kurreeman F, Kania G and Distler O. OTUD6B-AS1 might be a novel regulator of apoptosis in systemic sclerosis. Front Immunol 2019; 10: 1100.

[13] Messemaker TC, Chadli L, Cai G, Goelela VS, Boonstra M, Dorjée AL, Andersen SN, Mikkers HMM, van't Hof P, Mei H, Distler O, Draisma HHM, Johnson ME, Orzechowski NM, Simms RW, Toes REM, Aarbiou J, Huizinga TW, Whitfield ML, DeGroot J, de Vries-Bouwstra J and Kurreeman F. Antisense long non-coding RNAs are deregulated in skin tissue of patients with systemic sclerosis. J Invest Dermatol 2018; 138: 826-835.

[14] Wang Z, Xia F, Feng T, Jiang B, Wang W and Li X. OTUD6B-AS1 inhibits viability, migration, and invasion of thyroid carcinoma by targeting miR-183-5p and miR-21. Front Endocrinol (Lausanne) 2020; 11: 136.

[15] Wang YW, Liu C, Chen YD, Yang B, Chen X, Ma G, Tian YR, Bo X and Zhang K. An angiogenesis-related lncRNA signature predicts the immune microenvironment and prognosis of breast cancer. Aging (Albany NY) 2023; 15: 7616-7636.

[16] Lv W, Wang Y, Zhao C, Tan Y, Xiong M, Yi Y, He X, Ren Y, Wu Y and Zhang Q. Identification and validation of m6A-related lncRNA signature as potential predictive biomarkers in breast cancer. Front Oncol 2021; 11: 745719.

[17] Li PP, Li RG, Huang YQ, Lu JP, Zhang WJ and Wang ZY. LncRNA OTUD6B-AS1 promotes paclitaxel resistance in triple negative breast cancer by regulation of miR-26a-5p/MTDH pathway-mediated autophagy and genomic instability. Aging (Albany NY) 2021; 13: 24171-24191.

[18] Kong S, Xue H, Li Y, Li P, Ma F, Liu M and Li W. The long noncoding RNA OTUD6B-AS1 enhances cell proliferation and the invasion of hepatocellular carcinoma cells through modulating GSKIP/Wnt/β-catenin signalling via the sequestration of miR-664b-3p. Exp Cell Res 2020; 395: 112180.

[19] Zhang Z, Ye B, Lin Y, Liu W, Deng J and Ji W. LncRNA OTUD6B-AS1 overexpression promoted GPX4-mediated ferroptosis to suppress radioresistance in colorectal cancer. Clin Transl Oncol 2023; 25: 3217-3229.

[20] Wang W, Cheng X and Zhu J. Long non-coding RNA OTUD6B-AS1 overexpression inhibits the proliferation, invasion and migration of colorectal cancer cells via downregulation of microRNA-3171. Oncol Lett 2021; 21: 193.

[21] Wang G, Zhang ZJ, Jian WG, Liu PH, Xue W, Wang TD, Meng YY, Yuan C, Li HM, Yu YP, Liu ZX, Wu Q, Zhang DM and Zhang C. Novel long noncoding RNA OTUD6B-AS1 indicates poor prognosis and inhibits clear cell renal cell carcinoma proliferation via the Wnt/β-catenin signaling pathway. Mol Cancer 2019; 18: 15.

[22] Hou H, Yu R, Zhao H, Yang H, Hu Y, Hu Y and Guo J. LncRNA OTUD6B-AS1 induces cisplatin resistance in cervical cancer cells through up-

regulating cyclin D2 via miR-206. Front Oncol 2021; 11: 777220.
[23] Li N and Zhan X. Identification of clinical trait-related lncRNA and mRNA biomarkers with weighted gene co-expression network analysis as useful tool for personalized medicine in ovarian cancer. EPMA J 2019; 10: 273-290.
[24] Rothzerg E, Ho XD, Xu J, Wood D, Märtson A and Kõks S. Upregulation of 15 antisense long non-coding RNAs in osteosarcoma. Genes (Basel) 2021; 12: 1132.
[25] Wang Y, Yang T, Han Y, Ren Z, Zou J, Liu J and Xi S. lncRNA OTUD6B-AS1 exacerbates As(2)O(3)-induced oxidative damage in bladder cancer via miR-6734-5p-mediated functional inhibition of IDH2. Oxid Med Cell Longev 2020; 2020: 3035624.
[26] Bartha Á and Győrffy B. TNMplot.com: a web tool for the comparison of gene expression in normal, tumor and metastatic tissues. Int J Mol Sci 2021; 22: 2622.
[27] Xu Z, Jiang S, Ma J, Tang D, Yan C and Fang K. Comprehensive analysis of ferroptosis-related lncRNAs in breast cancer patients reveals prognostic value and relationship with tumor immune microenvironment. Front Surg 2021; 8: 742360.
[28] Luo Z, Nong B, Ma Y and Fang D. Autophagy related long non-coding RNA and breast cancer prognosis analysis and prognostic risk model establishment. Ann Transl Med 2022; 10: 58.
[29] Shi GJ, Zhou Q, Zhu Q, Wang L and Jiang GQ. A novel prognostic model associated with the overall survival in patients with breast cancer based on lipid metabolism-related long non-coding RNAs. J Clin Lab Anal 2022; 36: e24384.
[30] Han X, Chen Y, Xie J and Wang Y. Characteristics of m(6)A-related LncRNAs in breast cancer as prognostic biomarkers and immunotherapy. J Cancer 2023; 14: 2919-2930.
[31] Liu Z, Ren C, Cai J, Yin B, Yuan J, Ding R, Ming W, Sun Y and Li Y. A novel aging-related prognostic lncRNA signature correlated with immune cell infiltration and response to immunotherapy in breast cancer. Molecules 2023; 28: 3283.
[32] Yu H, Liu Y, Zhang W, Peng Z, Yu X and Jin F. A signature of cuproptosis-related lncRNAs predicts prognosis and provides basis for future anti-tumor drug development in breast cancer. Transl Cancer Res 2023; 12: 1392-1410.
[33] Ma B, Wang S, Wu W, Shan P, Chen Y, Meng J, Xing L, Yun J, Hao L, Wang X, Li S and Guo Y. Mechanisms of circRNA/lncRNA-miRNA interactions and applications in disease and drug research. Biomed Pharmacother 2023; 162: 114672.
[34] Xu J, Xu J, Liu X and Jiang J. The role of lncRNA-mediated ceRNA regulatory networks in pancreatic cancer. Cell Death Discov 2022; 8: 287.
[35] Paraskevopoulou MD and Hatzigeorgiou AG. Analyzing MiRNA-LncRNA interactions. Methods Mol Biol 2016; 1402: 271-286.
[36] Rajakumar S, Jamespaulraj S, Shah Y, Kejamurthy P, Jaganathan MK, Mahalingam G and Ramya Devi KT. Long non-coding RNAs: an overview on miRNA sponging and its co-regulation in lung cancer. Mol Biol Rep 2023; 50: 1727-1741.
[37] Das S, Vera M, Gandin V, Singer RH and Tutucci E. Intracellular mRNA transport and localized translation. Nat Rev Mol Cell Biol 2021; 22: 483-504.
[38] Noh JH, Kim KM, McClusky WG, Abdelmohsen K and Gorospe M. Cytoplasmic functions of long noncoding RNAs. Wiley Interdiscip Rev RNA 2018; 9: e1471.
[39] Bridges MC, Daulagala AC and Kourtidis A. LNCcation: lncRNA localization and function. J Cell Biol 2021; 220: e202009045.
[40] Statello L, Guo CJ, Chen LL and Huarte M. Gene regulation by long non-coding RNAs and its biological functions. Nat Rev Mol Cell Biol 2021; 22: 96-118.
[41] Han P and Chang CP. Long non-coding RNA and chromatin remodeling. RNA Biol 2015; 12: 1094-1098.
[42] Tang J, Wang X, Xiao D, Liu S and Tao Y. The chromatin-associated RNAs in gene regulation and cancer. Mol Cancer 2023; 22: 27.
[43] Tang Z, Kang B, Li C, Chen T and Zhang Z. GEPIA2: an enhanced web server for large-scale expression profiling and interactive analysis. Nucleic Acids Res 2019; 47: W556-W560.
[44] Badowski C, He B and Garmire LX. Blood-derived lncRNAs as biomarkers for cancer diagnosis: the good, the bad and the beauty. NPJ Precis Oncol 2022; 6: 40.
[45] Zhang W, Wang Q, Yang Y, Zhou S, Zhang P and Feng T. The role of exosomal lncRNAs in cancer biology and clinical management. Exp Mol Med 2021; 53: 1669-1673.
[46] Huang JY, Wang SY, Lin Y, Yi HC and Niu JJ. The diagnostic performance of lncRNAs from blood specimens in patients with hepatocellular carcinoma: a meta-analysis. Lab Med 2021; 52: 64-73.
[47] Lai H, Li Y, Zhang H, Hu J, Liao J, Su Y, Li Q, Chen B, Li C, Wang Z, Li Y, Wang J, Meng Z, Huang Z and Huang S. exoRBase 2.0: an atlas of mRNA, lncRNA and circRNA in extracellular vesicles from human biofluids. Nucleic Acids Res 2022; 50: D118-D128.
[48] Su K, Wang N, Shao Q, Liu H, Zhao B and Ma S. The role of a ceRNA regulatory network based

on lncRNA MALAT1 site in cancer progression. Biomed Pharmacother 2021; 137: 111389.
[49] Zhang Y, Xu Y, Feng L, Li F, Sun Z, Wu T, Shi X, Li J and Li X. Comprehensive characterization of lncRNA-mRNA related ceRNA network across 12 major cancers. Oncotarget 2016; 7: 64148-64167.
[50] Ding Y, Li M, Tayier T, Zhang M, Chen L and Feng S. Bioinformatics analysis of lncRNA–associated ceRNA network in melanoma. J Cancer 2021; 12: 2921-2932.
[51] Shi Y, Yang D and Qin Y. Identifying prognostic lncRNAs based on a ceRNA regulatory network in laryngeal squamous cell carcinoma. BMC Cancer 2021; 21: 705.
[52] Ye L and Jin W. Identification of lncRNA-associated competing endogenous RNA networks for occurrence and prognosis of gastric carcinoma. J Clin Lab Anal 2021; 35: e24028.
[53] Wang P, Guo Q, Hao Y, Liu Q, Gao Y, Zhi H, Li X, Shang S, Guo S, Zhang Y, Ning S and Li X. LnCeCell: a comprehensive database of predicted lncRNA-associated ceRNA networks at single-cell resolution. Nucleic Acids Res 2021; 49: D125-D133.
[54] Huebner K, Procházka J, Monteiro AC, Mahadevan V and Schneider-Stock R. The activating transcription factor 2: an influencer of cancer progression. Mutagenesis 2019; 34: 375-389.
[55] Amarah A, Elsabagh AA, Ouda A, Karen O, Ferih K, Elmakaty I and Malki MI. Emerging roles of activating transcription factor 2 in the development of breast cancer: a comprehensive review. Precis Clin Med 2023; 6: pbad028.
[56] Boice A and Bouchier-Hayes L. Targeting apoptotic caspases in cancer. Biochim Biophys Acta Mol Cell Res 2020; 1867: 118688.
[57] Olsson M and Zhivotovsky B. Caspases and cancer. Cell Death Differ 2011; 18: 1441-1449.
[58] Wen X, Lin ZQ, Liu B and Wei YQ. Caspase-mediated programmed cell death pathways as potential therapeutic targets in cancer. Cell Prolif 2012; 45: 217-224.
[59] Kolenko VM, Uzzo RG, Bukowski R and Finke JH. Caspase-dependent and -independent death pathways in cancer therapy. Apoptosis 2000; 5: 17-20.
[60] Watson G, Ronai ZA and Lau E. ATF2, a paradigm of the multifaceted regulation of transcription factors in biology and disease. Pharmacol Res 2017; 119: 347-357.
[61] Vlahopoulos SA, Logotheti S, Mikas D, Giarika A, Gorgoulis V and Zoumpourlis V. The role of ATF-2 in oncogenesis. Bioessays 2008; 30: 314-327.
[62] Chen LL. Linking long noncoding RNA localization and function. Trends Biochem Sci 2016; 41: 761-772.
[63] Xu J, Xu J, Liu X and Jiang J. The role of lncRNA-mediated ceRNA regulatory networks in pancreatic cancer. Cell Death Discov 2022; 8: 287.
[64] Marchal I. Discovering the crucial function of long noncoding RNAs. Nat Biotechnol 2024; 42: 1793.
[65] Zhang J, Zhu H, Li L, Gao Y, Yu B, Ma G, Jin X and Sun Y. New mechanism of LncRNA: in addition to act as a ceRNA. Noncoding RNA Res 2024; 9: 1050-1060.
[66] Ala U. Competing endogenous RNAs, non-coding RNAs and diseases: an intertwined story. Cells 2020; 9: 1574.
[67] Kartha RV and Subramanian S. Competing endogenous RNAs (ceRNAs): new entrants to the intricacies of gene regulation. Front Genet 2014; 5: 8.
[68] De Martino S, Iorio E, Cencioni C, Aiello A, Spallotta F, Chirico M, Pisanu ME, Grassi C, Pontecorvi A, Gaetano C, Nanni S and Farsetti A. MALAT1 as a regulator of the androgen-dependent choline kinase A gene in the metabolic rewiring of prostate cancer. Cancers (Basel) 2022; 14: 2902.
[69] Yu S, Guo J, Yang D, Yan X, Zhang Z, Wei P and Qiu L. The ATF4-regulated LncRNA MALAT1 promotes odontoblastic differentiation of human dental pulp stem cells via histone demethylase JMJD3: an in vitro study. Int Endod J 2024; 57: 50-63.
[70] Sun H, Lin DC, Cao Q, Pang B, Gae DD, Lee VKM, Lim HJ, Doan N, Said JW, Gery S, Chow M, Mayakonda A, Forscher C, Tyner JW and Koeffler HP. Identification of a novel SYK/c-MYC/MALAT1 signaling pathway and its potential therapeutic value in ewing sarcoma. Clin Cancer Res 2017; 23: 4376-4387.
[71] Fuschi P, Carrara M, Voellenkle C, Garcia-Manteiga JM, Righini P, Maimone B, Sangalli E, Villa F, Specchia C, Picozza M, Nano G, Gaetano C, Spinetti G, Puca AA, Magenta A and Martelli F. Central role of the p53 pathway in the noncoding-RNA response to oxidative stress. Aging (Albany NY) 2017; 9: 2559-2586.
[72] Battistelli C, Cicchini C, Santangelo L, Tramontano A, Grassi L, Gonzalez FJ, de Nonno V, Grassi G, Amicone L and Tripodi M. The Snail repressor recruits EZH2 to specific genomic sites through the enrollment of the lncRNA HOTAIR in epithelial-to-mesenchymal transition. Oncogene 2017; 36: 942-955.
[73] Ma Q, Yang L, Tolentino K, Wang G, Zhao Y, Litzenburger UM, Shi Q, Zhu L, Yang C, Jiao H, Zhang F, Li R, Tsai MC, Chen JA, Lai I, Zeng H, Li L and Chang HY. Inducible lncRNA transgenic mice reveal continual role of HOTAIR in promoting breast cancer metastasis. Elife 2022; 11: e79126.

[74] Wu L, Murat P, Matak-Vinkovic D, Murrell A and Balasubramanian S. Binding interactions between long noncoding RNA HOTAIR and PRC2 proteins. Biochemistry 2013; 52: 9519-9527.
[75] Kuo FC, Neville MJ, Sabaratnam R, Wesolowska-Andersen A, Phillips D, Wittemans LBL, van Dam AD, Loh NY, Todorčević M, Denton N, Kentistou KA, Joshi PK, Christodoulides C, Langenberg C, Collas P, Karpe F and Pinnick KE. HOTAIR interacts with PRC2 complex regulating the regional preadipocyte transcriptome and human fat distribution. Cell Rep 2022; 40: 111136.