DOI:10.31557/APJCB.2025.10.4.1031

REVIEW

Emerging Roles of lncRNA MSC-AS1 in Cancer: Molecular Mechanisms, Clinical Implications, and Therapeutic Potential

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Abstract

Overview: Long non-coding RNAs (lncRNAs) are key regulators of tumor biology, affecting proliferation, apoptosis, metastasis, and treatment resistance. Among them, Musculin Antisense RNA 1 (MSC-AS1) has attracted increasing attention for its oncogenic roles across multiple cancers. This review summarizes current knowledge on MSC-AS1, emphasizing molecular mechanisms, clinical relevance, and therapeutic potential. **Methods:** A comprehensive literature search of PubMed, Scopus, and Web of Science identified studies published 2015–2024 that investigated MSC-AS1 in cancer. Eligible articles examined its functional roles, implicated signaling pathways, regulatory interactions (e.g., lncRNA–miRNA–mRNA axes), and diagnostic, prognostic, or therapeutic implications. **Results:** Evidence consistently shows that MSC-AS1 is frequently upregulated in gastric, hepatic, pancreatic, and colorectal cancers. Mechanistically, MSC-AS1 contributes to tumor progression mainly through lncRNA–miRNA–mRNA regulatory networks, promoting malignant phenotypes and therapeutic resistance. Clinically, elevated MSC-AS1 expression correlates with poor prognosis, supporting its utility as a biomarker for diagnosis and prognosis and as a candidate target for precision oncology. **Conclusion:** MSC-AS1 functions as an oncogenic lncRNA across multiple gastrointestinal and hepatobiliary malignancies, driving disease through competitive regulatory networks and associating with adverse outcomes and resistance. Current evidence positions MSC-AS1 as a promising biomarker and a potential therapeutic target; future work should validate its clinical performance and evaluate targeted interventions against MSC-AS1-mediated pathways.

Keywords: LncRNA- MSC-AS1- Cancer biomarker- Precision oncology- Therapeutic resistance- Tumor progression

Asian Pac J Cancer Biol, **10 (4)**, 1031-1042 Submission Date: 08/24/2025 Acceptance Date: 10/02/2025

Introduction

Cancer is one of the most prevalent and deadly diseases, ranking first or second among noncommunicable diseases in terms of morbidity and mortality [1, 2]. Despite significant advances in cancer therapy over the past several decades, the survival rate, especially for those with advanced cancer and metastasis, remains poor [2]. Therefore, developing more effective clinical strategies and gaining a deeper understanding of the molecular mechanisms driving tumor growth are imperative [3, 4]. Among them, recent studies have highlighted that noncoding RNAs could be pivotal players in cancer pathogenesis [5]. Advances in epigenetic engineering,

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such as zinc finger–based control of immune genes, show how targeted gene regulation can be used therapeutically. Similar mechanisms of transcriptional and epigenetic modulation are also central to the oncogenic functions of lncRNAs like MSC-AS1 [6].

lncRNAs, which are RNA molecules longer than 200 nucleotides, have been found to play a crucial role in regulating various biological processes, including growth, chromatin dynamics, differentiation, progression, and gene expression [7, 8]. Unlike mRNAs, lncRNAs lack protein-coding capacity [9]. However, recent research using innovative molecular approaches has revealed the presence of small open reading frames (sORFs) in some lncRNAs, enabling them to interact with ribosomes and encode short peptides [10, 11]. Numerous investigations have demonstrated that lncRNAs function as principal regulators of the treatment response, onset, and tumor progression in cancer [12, 13]. For instance, lncRNA MALAT1 suppresses metastasis and shows an inverse correlation with breast cancer progression, underscoring its potential as a metastasis-inhibiting lncRNA [14]. Moreover, research revealed that the HOXB-AS3-encoded peptide inhibits colorectal cancer (CRC) development, and loss of this peptide is correlated with a worse prognosis for CRC [15]. MSC-AS1, a novel lncRNA molecule, has recently emerged as an important factor in tumor development [16-19]. A study found that MSC-AS1 overexpression promotes the development of liver cancer by increasing the expression of Phosphoglycerate Kinase 1 (PGK1) [20]. Another study revealed that MSC-AS1 regulates the miR-524-5p/NR4A2 axis, thereby promoting nasopharyngeal carcinoma [21]. Additionally, MSC-AS1 may enhance the differentiation of bone marrow mesenchymal stem cells (BMSCs) into osteoblasts [22]. It has also been shown to aggravate nasopharyngeal carcinoma by sponging miR-524-5p, leading to increased NR4A2 expression [21]. Furthermore, Hu et al. demonstrated that MSC-AS1 regulates the migration and proliferation of kidney renal clear cell carcinoma (KIRC) cells through the miR-3924/WNT5A/β-catenin axis [23].

This review aims to provide an in-depth overview of recent findings on the abnormal expression, molecular mechanisms, and clinical relevance of MSC-AS1 in various cancers.

Materials and Methods

This review aims to provide a comprehensive overview of the role of MSC-AS1 in various human cancers. To ensure broad coverage and minimize selection bias, no restrictions were applied regarding cancer type, experimental model, or publication date. A thorough search of the scientific literature was conducted using well-established databases, including PubMed, Scopus, Web of Science, and Google Scholar. The search strategy employed a combination of keywords such as "MSC-AS1," "long non-coding RNA," "cancer," "tumor progression," "prognostic biomarker," "chemoresistance," and "lncRNA–miRNA–mRNA axis." Studies published up to May 20, 2024, were considered. Only peer-reviewed articles written in English and focusing on the biological functions, molecular mechanisms, diagnostic and prognostic relevance, and therapeutic potential of MSC-AS1 were included in this review.

LncRNA biogenesis and function

RNA polymerase II (Pol II) is responsible for the transcription of lncRNAs, which are characterized by the addition of a 5′ methyl-cytosine cap and 3′ poly (A) tail [24]. These molecules can be classified based on their genetic origin into long intergenic, intronic, and exonic lncRNA, and based on transcriptional orientation as sense or anti-sense lncRNA. Additionally, they can be classified into macro and retained intron lncRNAs based on splicing-based classification [25]. LncRNAs are crucial in numerous physiological and pathological processes by either activating or suppressing gene expression [26]. Primarily, they function as transcriptional regulators through interactions with transcriptional complexes, chromatin remodeling, or by serving as scaffolds that recruit various molecules [27]. Moreover, lncRNAs regulate the expression of genes by interacting with DNA, RNA, and protein near enhancers or promoters of target genes [28]. These interactions occur via a variety of methods, such as guide, scaffold, decoy, and signal [26]. Enzymatically or regulatory active protein complexes are bound by guide lncRNAs, which then direct the complexes to specific target gene promoters or chromosomal areas to regulate downstream signaling pathways and expression of genes [8]. Moreover, lncRNAs may be related to pancreatic cancer (PC) via regulating various post-transcriptional protein molecules, promoting or suppressing gene transcription, or interacting with miRNA to regulate or increase its expression. In this manner, lncRNAs can act as regulators for cancer suppressors or proto-oncogene genes [29] (Figure 1 and 2).

LncRNAs in cancer

There is no doubt that cancer is a life-threatening disease that poses a major risk to human health. Since the coding genome accounts for less than 2 percent of all gene sequences, most cancer phenotypes are driven by mutations in non-coding regions [30]. lncRNAs have been demonstrated to have a significant effect on various cellular processes, including angiogenesis, differentiation, migration, and proliferation [31, 32]. Aberrant lncRNA expression is common in cancer and can act as factors that either promote or inhibit tumor growth. In oral cancers, for example, the lncRNA ELDR is overexpressed and activates the ILF3-cyclin E1 axis signaling. ELDR suppression markedly reduces the growth of oral cancer cells [33]. In colorectal cancer, it has been discovered that the lncRNA ZFAS1 stimulates tumor growth and metastasis while inhibiting apoptosis. Additionally, studies have indicated that ZFAS1 overexpression is associated with poor prognosis in patients with colorectal cancer [34]. LINC00460 has been shown to promote the growth of cervical cancer cells and suppress apoptosis by downregulating miRNA-503-5p to advance cervical cancer

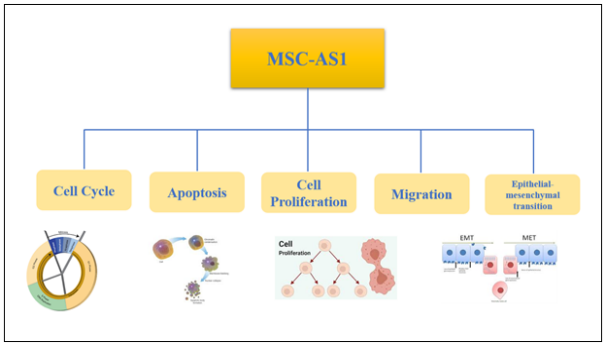

Figure 1. Role of MSC-AS1 in Key Cancer-Related Cellular Processes. This diagram summarizes the key cellular processes regulated by MSC-AS1 in cancer. MSC-AS1 modulates the cell cycle, suppresses apoptosis, and promotes cell proliferation. It also enhances cell migration and induces EMT. Together, these functions promote tumor growth, metastasis, and treatment resistance, highlighting MSC-AS1's oncogenic potential in various cancers.

progression. LINC00511 has been shown to upregulate MMP-13 and decrease miRNA-150 expression, driving invasion and proliferation [35, 36]. Conversely, lncRNA TUSC7 has been shown to sponge miRNA-23b to suppress epithelial-mesenchymal transition (EMT) and metastasis in CRC. TSLC8 lncRNA has also been shown to increase stability, leading to reduced colony formation and survival of CRC. Collectively, these findings indicate that lncRNAs have a bright future as cancer therapeutic targets [37-39].

MSC-AS1

MSC-AS1 is classified as an lncRNA that does not code for proteins but performs other cellular functions. It has been associated with several types of cancer, including laryngeal cancer, colorectal cancer, and gastric cancer. MSC-AS1 may also influence the ability of mesenchymal stem cells to differentiate into various tissues, such as bone, cartilage, and fat. Evidence suggests that MSC-AS1 affects cancer progression and stem cell function by modulating the expression of genes involved in the PI3K/Akt pathway, which is essential for cell survival, proliferation, and division (Figure 1). MSC-AS1 is classified as a long non-coding RNA (lncRNA) that does not code for proteins but performs other cellular functions. It has been associated with several types of cancer, including laryngeal cancer, colorectal cancer, and gastric cancer. MSC-AS1 may also influence the ability of mesenchymal stem cells to differentiate into various tissues, such as bone, cartilage, and fat. Evidence suggests that MSC-AS1 affects cancer progression and stem cell function by modulating the expression of genes involved in the PI3K/Akt pathway, which is essential for cell survival, proliferation, and division (Figure 1).

Numerous signals, including growth factors, cytokines, and hormones, can activate the PI3K/Akt pathway, which regulates various cellular functions such as angiogenesis, migration, metabolism, and cell death [16-18]. MSC-AS1 may influence the PI3K/Akt pathway by binding to and inhibiting microRNAs (miRNAs), which are small RNAs that suppress target gene expression by binding to messenger RNAs (mRNAs). For example, MSC-AS1 may bind to and inhibit miR-330-3p, which targets and reduces YAP1, a key factor in the PI3K/Akt pathway. By doing so, MSC-AS1 can increase YAP1 expression, enhancing the PI3K/Akt pathway. This promotes cancer cell survival and proliferation, as well as stem cell differentiation and function. Another mechanism by which MSC-AS1 affects cancer and stem cells is through a competing endogenous RNA (ceRNA) network. This network of interactions among lncRNAs, miRNAs, and mRNAs regulates gene expression at the post-transcriptional level. In a ceRNA network, lncRNAs act as sponges for miRNAs, thereby relieving repression of target mRNAs. For instance, MSC-AS1 may act as a sponge for miR-143-3p, which targets and reduces KRAS, another important factor in the PI3K/Akt pathway [40, 41].

Roles of MSC-AS1 in cancers

MSC-AS1 has been reported as an oncogene or tumor

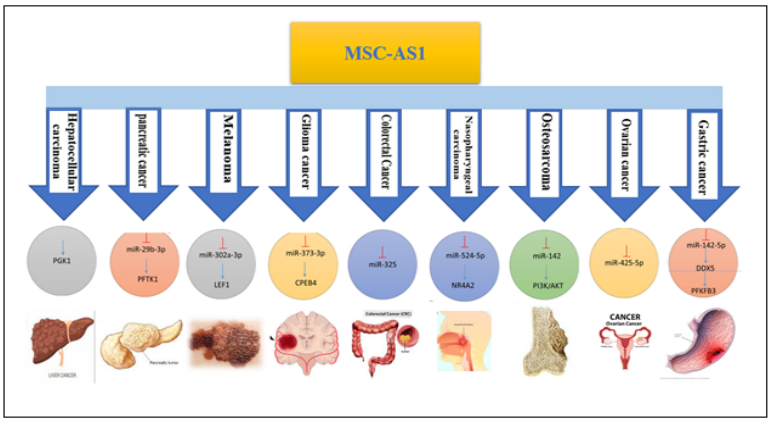

Figure 2. Molecular Targets and Regulatory Pathways of MSC-AS1 in Various Human Cancers. MSC-AS1 contributes to the progression of multiple cancers by regulating specific microRNA–mRNA axes. In hepatocellular carcinoma, MSC-AS1 upregulates PGK1; in pancreatic cancer, it modulates miR-29b-3p/PFTK1. Similar regulatory axes are observed in melanoma (miR-302a-3p/LEF1), glioma (miR-373-3p/CPEB4), colorectal cancer (miR-325), nasopharyngeal carcinoma (miR-524-5p/NR4A2), osteosarcoma (miR-142/PI3K/AKT), ovarian cancer (miR-425-5p), and gastric cancer (miR-142-5p/DDX5, PFKFB3). The figure summarizes the cancer-specific downstream targets and regulatory functions of MSC-AS1 in tumor biology.

Table 1. Aberrant Expression of MSC-AS1 Across Different Human Cancers in Tissue and Cell Line Models. Summary of MSC-AS1 expression patterns in cancer versus normal tissues and cell lines. "Upregulated" or "Downregulated" indicates differential expression in tumor samples or cancer cell lines relative to normal controls.

Tumor	Origin	Changes in Expression Level	Healthy Group	Illness Group	Ref
GC	Tissue	Upregulated	80 normal adjacent tissues	80 GC	[42]
	Cell	Upregulated	GES-1	MKN-45, AGS, SGC-7901, and MGC-803	[42]
GC	Tissue	Upregulated	27 normal adjacent tissues	27 GC	[41]
	Cell	Upregulated	-	-	[41]
GC	Tissue	Upregulated	40 normal adjacent tissues	40 GC	[43]
	Cell	Upregulated	GES-1	MGC-803, MKN-45 HGC-27, SGC-7901, and GES	[43]
HCC	Tissue	Upregulated	60 normal adjacent tissues	60 HCC	[20]
	Cell	Upregulated	HL-7702cells	HepG2, BEL-7404, SNU449 HUH- 7, and QGY-7701	[20]
HCC	Tissue	Upregulated	-	-	[44]
	Cell	Upregulated	L02	BEL7402, SMMC7721, Huh7, HepG2, MHCC97-H	[44]
PDAC	Tissue	Upregulated	45 normal adjacent tissues	45 PDAC	[16]
	Cell	Upregulated	-	PANC-1 and BxPC-3	[16]
OC	Tissue	Downregulated	25 normal adjacent tissues	25 OC	[45]
	cell	Downregulated	IOSE80	OVCAR3, A2780, SKOV3	[45]
LC	Tissue	Upregulated	37 normal adjacent tissues	37 LC	[40]
	Cell	Upregulated	-	-	[40]
CRC	Tissue	Upregulated	46 normal adjacent tissues	46 CRC	[46]
	Cell	Upregulated	NCM460	HT29, SW620, HCT116, and SW480	[46]
NPC	Tissue	Upregulated	34 normal adjacent tissues	34 NPC	[21]
	Cell	Upregulated	NP69 and NP460	SUNE1, CNE-2, 5-8F, CNE-1	[21]
Glioma	Tissue	Upregulated	25 normal adjacent tissues	50 Glioma	[47]
	cell	Upregulated	-	SHG-44, LN229, and 293T	[47]
Melanoma	Tissue	Upregulated	-	-	[48]
	Cell	Upregulated	HEMa-LP	A375, A2058, SK-MEL-5 and SKMEL-2	[48]
OS	Tissue	Downregulated	45 normal adjacent tissues	45 OS	[19]
	Cell	Downregulated	hFOB1.19	MG63, SOSP-9607, HOS, U2OS, and SaOS2	[19]

suppressor depending on the context, due to its diverse effects on tumor cell phenotypes (Figure 2).

Furthermore, an accumulating body of research suggests that MSC-AS1 plays a role in the processes of cell division, apoptosis, invasion and metastasis, and resistance to therapy in a variety of malignancies. The changes in the expression level of lncRNA in various cancers are presented in Table 1.

There has been evidence that the MSC-AS1 plays a crucial role in the development of several forms of cancer [41]. Several cancers have been associated with this compound, including OC, PC, Nasopharyngeal Cancer (NPC), and GC. The lncRNA-miRNA-mRNA network of MSC-AS1 has been demonstrated to modulate gemcitabine-induced apoptosis and cell proliferation in pancreatic cancer [16]. In PC, the lncRNA–miRNA–mRNA network of MSC-AS1 has been shown to modulate gemcitabine-induced apoptosis and cell proliferation [49]. Additionally, in ovarian cancer, MSC-AS1 has been shown to inhibit cancer progression by targeting miR-425-5p [45]. Furthermore, in gastric cancer, high expression of MSC-AS1 has been associated with a poor prognosis and might be used as a diagnostic biomarker and a predictor of unfavorable outcomes [41]. In NPC, MSC-AS1 promotes disease progression by sponging miR-524-5p and thereby upregulating NR4A2 expression [21]. Recent findings have revealed the involvement of MSC-AS1 in various tumor progressions. Research has indicated that MSC-AS1 may enhance the process of osteogenic differentiation in BMSCs [17]. In recent years, Hu et al have shown that MSC-AS1 regulates KIRC migration and cell proliferation through the miR3924-WNT5A-catenin axis [18].

Collectively, these findings underscore the critical role of MSC-AS1 in tumorigenesis and stem cell biology. They further suggest that MSC-AS1 may serve as a promising therapeutic target and prognostic biomarker. However, additional studies are required to elucidate the precise molecular mechanisms and validate its therapeutic potential.

The role of MSC-AS1 in cancer development and progression

Long non-coding RNAs (lncRNAs) have been extensively studied for their role in regulating gene expression, with important implications for diverse biological processes and diseases, including cancer. Among them, MSC-AS1 has emerged as a key regulator implicated in the pathogenesis of several cancer types. Multiple mechanisms have been identified to explain

its involvement in cancer progression, primarily through interactions with microRNAs (miRNAs) and modulation of gene expression (Table 2).

Results

Pancreatic Cancer

Approximately 64,050 new instances of PC are projected to arise globally in the United States in 2023 [50]. PC remains one of the deadliest cancers worldwide, largely because patients typically do not exhibit symptoms until advanced stages. Its incidence is higher in industrialized regions such as Europe, North America, and Australia, partly due to aging populations [23, 51, 52]. Non-coding RNAs (ncRNAs) play a crucial role in the progression and development of PC. Significantly, lncRNAs and microRNAs have particular relevance among them.

Sun et al. reported a significant correlation between the long non-coding RNA (lncRNA) MSC-AS1 and CDK14 in pancreatic ductal adenocarcinoma (PDAC) tissues, where MSC-AS1 was upregulated. Patients with higher MSC-AS1 expression had a poor prognosis. Suppressing MSC-AS1 reduced cell proliferation in BxPC-3 and Panc-1 cells. Additionally, the tumor suppressor miR-29b-3p was negatively correlated with MSC-AS1 levels; its reduced expression in PDAC patients was linked to unfavorable outcomes. Functional assays revealed that miR-29b-3p negatively regulates both MSC-AS1 and CDK14. Knockdown of MSC-AS1 led to decreased CDK14 protein levels, inhibited PDAC proliferation, and increased gemcitabine-induced apoptosis [16].

Gastric cancer

GC ranks among the five most common malignancies and represents a major cause of cancer-related mortality worldwide, irrespective of a country's level of development [52]. GC has a high fatality rate and poor prognosis [53]. ncRNAs play a crucial role in the progression and development of GC. Significantly, lncRNAs and microRNAs have particular relevance among them.

Jin et al. reported that MSC-AS1 was significantly overexpressed in GC tissues compared to adjacent non-tumor tissues and normal gastric mucosa. Elevated MSC-AS1 expression was associated with advanced tumor stage and poor prognosis. Functional assays showed that silencing MSC-AS1 suppressed GC cell proliferation and glycolytic activity, including lactate production, pyruvate production, and glucose consumption. Conversely, MSC-AS1 overexpression enhanced these processes. Mechanistically, MSC-AS1 promoted glycolysis by specifically upregulating PFKFB3, a key glycolytic enzyme, without affecting PKM2 or HK2. Restoration of PFKFB3 expression rescued glycolysis and proliferation in MSC-AS1–silenced cells [42].

Collectively, these findings indicate that MSC-AS1 promotes glycolysis and proliferation in GC cells by sustaining PFKFB3 expression, highlighting its potential as a therapeutic target in gastric cancer.

Yang et al. demonstrated that MSC-AS1 was significantly overexpressed in GC tissues compared to normal controls. Elevated MSC-AS1 expression promoted cell proliferation, cell cycle progression, and the release of inflammatory mediators such as TNF-α, IL-1β, and IL-6. Mechanistically, MSC-AS1 suppressed miR-142-5p expression in HGC-27 cells, a microRNA that targets DDX5. Overexpression of miR-142-5p reduced DDX5 activity, whereas this effect was abolished upon DDX5 mutation, confirming the specificity of this regulatory axis. Furthermore, miR-142-5p levels were significantly reduced in GC tissues and showed an inverse correlation with MSC-AS1 expression. Collectively, these findings suggest that MSC-AS1 functions as an oncogene in gastric cancer through modulation of the MSC-AS1/miR-142-5p/DDX5 pathway, highlighting its potential as a therapeutic target in GC [43].

Ovarian cancer

Ovarian cancer (OC) is one of the most lethal gynecologic malignancies worldwide and represents the leading cause of death among women with gynecologic cancers [45]. Patients are often diagnosed at an advanced stage, and diagnostic accuracy is low during the early stages [54]. Despite the progress made in treatment approaches for ovarian cancer, such as radiation, chemotherapy, and surgery, the rate of five-year survival for patients with this disease has remained unsatisfactory for an extended period [55-57]. The development and progression of OC are significantly influenced by ncRNAs. Among them, lncRNAs and microRNAs are of particular significance.

Zhao et al. observed that MSC-AS1 was downregulated in ovarian cancer cells and tissues, while miR-425-5p exhibited elevated expression. Overexpression of MSC-AS1 was found to significantly inhibit proliferation and induce apoptosis. Additionally, the study identified MSC-AS1 as a target and negative regulator of miR-425-5p, which partially reversed the tumor-suppressive effects of MSC-AS1. Collectively, these results suggest that MSC-AS1 acts as a tumor suppressor in OC by modulating the MSC-AS1/miR-425-5p axis, highlighting its potential as a therapeutic target [45].

Laryngeal cancer

There is a high morbidity and mortality rate associated with LC is a common type of head and neck cancer. In 2018, the global prevalence of LC accounted for 1% of all newly diagnosed cancer cases, while the fatality rate accounted for 1% of all cancer-related fatalities. The development and progression of LC are significantly influenced by ncRNAs [58].

Liu et al. found that MSC-AS1 lncRNA could be used as a biomarker for lung cancer (LC), and a ceRNA network involving MSC-AS1, miR-429, TGAV, and COL4A1 was constructed. Additionally, the MEblue module of a WGCNA network was related to the clinical stages of LC, with particular emphasis placed on the exploration of PI3K/Akt pathways. It was demonstrated by RT-qPCR that these genes were highly expressed in LC tissues, highlighting their importance for research [40].

Table 2. The Proposed Molecular Mechanism of lncRNA MSC-AS1 in Various Cancers

Disease	miR	Target	In vitro effect	Cell	In vivo effect	Animal	Ref
GC	-	PFKFB3	Knockdown of MSC-AS1 inhibited glucose consumption, proliferation, lactate production, and pyruvate production.	AGS, GES-1/MKN-45, MGC-803and SGC-7901	-	-	[42]
GC	miR-142-5p	DDX5	induce cell cycle progression, cell growth, and inflammation	MKN-45, GES-1/HGC-27SGC-7901, GES and MGC-803	-	-	[43]
HCC	-	PGK1	Knockdown of MSC-AS1 inhibits colony formation capacity, cell proliferation, and triggers cell apoptosis	HL-7702cells /HUH-7, BEL-7404, SNU449, HepG2, and QGY-7701	Decrease tumor volume and weight	nude mice	[20]
HCC	-	-	Knockdown of MSC-AS1 inhibits migration, cell proliferation, invasion and promotes apoptosis.	BEL7402, SMMC7721, Huh7, HepG2, MHCC97-H	-	-	[44]
PDAC	miR-29b-3p	PFTK1	Knockdown of MSC-AS1 inhibits cell proliferation, migration, and promotes apoptosis and invasion.	PANC-1 and BxPC-3	-	-	[16]
OC	miR-425-5p	-	Promote apoptosis and inhibit cell proliferation,	OVCAR3, A2780, SKOV3	-	-	[45]
CRC	miR-325	TRIM14	Knockdown of MSC-AS1 inhibits invasion, migration, and cell proliferation	NCM460/HT29, SW620, HCT116, and SW480	-	-	[46]
NPC	miR-524-5p	NR4A2	Knockdown of MSC-AS1 promotes apoptosis and inhibits cell proliferation	NP69 and NP460/SUNE1, CNE-2, 5-8F, CNE-1	-	-	[21]
Glioma	miR-373-3p	CPEB4	Knockdown of MSC-AS1 promotes apoptosis, TMZ sensitivity, and inhibits cell proliferation	LN229/ TR and SHG-44/TR	reducing tumor volume and weight	nude mice	[47]
Melanoma	miR-302a-3p	LEF1	Knockdown of MSC-AS1 inhibits migration, cell proliferation, and EMT	HEMa-LP /A375, A2058, SK-MEL-5 and SKMEL-2	Decrease tumor growth	nude mice	[48]
OS	miR-142	PI3K/AKT	migration, cell proliferation, promote apoptosis, and invasion	hFOB1.19/MG63, SOSP-9607, HOS, U2OS, and SaOS2	reduce tumor volume and weight	nude mice	[19]

Hepatocellular carcinoma

According to the World Health Organization, HCC is a major contributor to global cancer-related deaths. Annually, more than 500,000 new cases of HCC are documented [59, 60]. ncRNAs have significant involvement in the development and advancement of HCC. Notably, lncRNAs and microRNAs have special importance among them [61].

Cao et al. reported a notable increase in MSC-AS1 expression in both HCC tissues and cells. Inhibition of MSC-AS1 in the BEL-7404 and HepG2 cell lines resulted in a significant reduction in colony formation and cell proliferation, while simultaneously inducing apoptosis. Additionally, the cell cycle of BEL-7404 and HepG2 cells was effectively arrested in the G1 phase, leading to a marked decrease in cell migration and invasion. In vivo experiments further demonstrated that the suppression of MSC-AS1 impeded HCC growth by activating phosphoglycerate kinase 1 (PGK1). The data indicated that

silencing MSC-AS1 in HCC cells was associated with a decrease in PGK1 expression. Collectively, these findings suggest that MSC-AS1 plays a critical role in promoting HCC development by enhancing PGK1 expression [20].

Kou et al. discovered that the expression of MSC-AS1 was significantly higher in HCC cells than in comparison with L02 cells. As compared to the blank and NC-siRNA groups, the colonization and proliferation of HCC cells were inhibited; however, the rate of apoptosis was significantly higher in the MSC-AS1 siRNA group. A significant reduction in wound healing rates and invasion rates was observed in the MSC-AS1 siRNA group when compared to the blank and NC-siRNA groups. These findings suggest that MSC-AS1 exhibited increased expression in HCC cells, and suppressing its expression may inhibit migration, cell proliferation, invasion, and enhance apoptosis in HCC cells [44].

Colorectal Cancer

According to the World Health Organization (WHO), CRC was projected to cause over 1.93 million deaths worldwide in 2020, making it the third leading cause of cancer-related mortality. The incidence and mortality rates of CRC are influenced by several risk factors, including poor dietary habits, obesity, and physical inactivity [62-65]. ncRNAs play a crucial role in the progression and development of HCC. Significantly, lncRNAs and microRNAs have particular relevance among them.

He et al. reported that the expression levels of TRIM14 and MSC-AS1 were elevated in tissues containing CRCs, whereas miR-325 exhibited reduced expression in these tissues. Functional experiments indicated that the suppression of MSC-AS1 led to decreased migration, invasion, and proliferation of cancer cells. Furthermore, miR-325 was identified as the specific microRNA targeted by MSC-AS1, with TRIM14 being the gene regulated by miR-325. It was also demonstrated that MSC-AS1 counteracted the inhibitory effects of miR-325 on cell growth and TRIM14 expression. Consequently, MSC-AS1 was shown to activate miR-325, thereby enhancing TRIM14 expression and promoting CRC progression. These findings suggest that MSC-AS1 could be a promising therapeutic target for the treatment of CRC [46].

Nasopharyngeal carcinoma

NPC is an aggressive malignancy of the head and neck that arises from the epithelial lining of the Yao et al. reported that MSC-AS1 expression was significantly elevated in both NPC cells and patient-derived tissues. Functional assays demonstrated that MSC-AS1 inhibited apoptosis, promoted cell proliferation, induced epithelial–mesenchymal transition (EMT), and enhanced invasive capacity. Mechanistically, MSC-AS1 acted as a sponge for miR-524-5p, thereby upregulating NR4A2 expression. Notably, overexpression of NR4A2 reversed the suppressive effects of MSC-AS1 knockdown on NPC progression, confirming the oncogenic role of NR4A2 in NPC cells. Collectively, these findings indicate that MSC-AS1 promotes NPC development through the miR-524-5p/NR4A2 axis and may represent a promising therapeutic target for lncRNA-based interventions in NPC [21].

Glioma cancer

Glioma is a prevalent kind of brain cancer, making up around 40-50% of tumors that occur inside the skull [66]. Despite advancements in medical treatment techniques, the median survival duration for patients with glioma remains below one year [67]. ncRNAs play a crucial role in the progression and development of Glioma. Significantly, lncRNAs and microRNAs have particular relevance among them [68].

Li et al. found that MSC-AS1 expression was elevated in glioma tissues and cells that exhibited resistance to temozolomide (TMZ). Suppression of MSC-AS1 led to decreased resistance to TMZ and increased cell death. The influence of miR-373-3p was found to be reversible by silencing this microRNA, which directly targeted CPEB4 and affected the PI3K/Akt signaling pathway. Furthermore, knocking down miR-373-3p reversed the effects of CPEB4 or MSC-AS1 suppression on TMZ sensitivity. The study indicated that the PI3K/Akt pathway regulates the miR-373-3p/CPEB4 axis through MSC-AS1 knockdown, ultimately inhibiting the growth of TMZ-resistant glioma cells. Overall, MSC-AS1 inhibition suppressed glioma growth and enhanced TMZ sensitivity both in vitro and in vivo, highlighting its potential as a therapeutic target [47].

Melanoma

Melanoma is one of the most aggressive and lethal forms of skin cancer, and its incidence and mortality rates continue to rise despite considerable preventive efforts [69]. Early detection and treatment of melanoma might somewhat decrease the occurrence rate [70]. ncRNAs have significant involvement in the development and advancement of melanoma. Notably, lncRNAs and microRNAs have special importance among them.

Ma et al. demonstrated that the expression levels of MSC-AS1 and lymphoid enhancer-binding factor 1 (LEF1) were elevated in melanoma cell lines, while the expression of microRNA 302a-3p (miR-302a-3p) was reduced. Their study revealed that silencing MSC-AS1 inhibited migration, cell proliferation, and EMT in vitro, as well as tumor growth in vivo. Additionally, MSC-AS1 was found to modulate LEF1 expression by functioning as a sponge that recruits insulin-like growth factor 2 mRNA-binding protein 2 (IGF2BP2) and miR-302a-3p. The tumor progression rescue facilitated by the overexpression of LEF1 was hindered by the knockdown of MSC-AS1. Collectively, these findings indicate that the MSC-AS1/miR-302a-3p/IGF2BP2/LEF1 axis plays a crucial role in melanoma progression and that MSC-AS1 may represent a promising biomarker and therapeutic target in melanoma [48].

Osteosarcoma

Osteosarcoma (OS) is the most common primary malignant bone tumor, characterized by multiple genetic abnormalities and the uncontrolled proliferation of mesenchymal cells that produce immature bone or malignant osteoid [71, 72]. ncRNAs play a crucial role

in the progression and development of OS. Significantly, lncRNAs and microRNAs have particular relevance among them.

Zhang et al. demonstrated that silencing MSC-AS1 led to decreased proliferation, invasion, and migration of OS cells, while increasing apoptosis. Additionally, the suppression of MSC-AS1 heightened the susceptibility of OS cells to cisplatin (DDP). Their findings indicated that MSC-AS1 knockdown resulted in reduced levels of CDK6 and miR-142 expression, which subsequently decreased the protein expression of pPI3K/t-PI3K and pAKT/t-AKT. Furthermore, the suppression of MSC-AS1 impeded the progression of osteosarcoma in vivo by enhancing miR-142 levels, lowering CDK6 expression, and inactivating the PI3K/AKT signaling pathway. these findings highlight MSC-AS1 as a potential therapeutic target and suggest novel treatment strategies for osteosarcoma [19].

MSC-AS1 as a promising diagnostic biomarker in cancer prognosis

Early cancer detection is critical for effective treatment, yet current diagnostic methods often lack the specificity and sensitivity required for reliable early-stage identification [73]. This highlights the need for novel biomarkers that can improve early diagnosis and prognosis. Recent investigations have identified MSC-AS1 as a promising diagnostic and prognostic biomarker across several cancer types [41]. ncRNAs play a crucial role in the progression and development of hepatocellular carcinoma (HCC). Significantly, lncRNAs and microRNAs have particular relevance among them. MSC-AS1 is elevated in PDAC tissues, associated with a worse prognosis. Silencing of MSC-AS1 suppresses cell proliferation, but the elevated expression of miR-29b-3p is associated with improved prognosis. In gastric cancer, increased MSC-AS1 levels are substantially correlated with T stage, histological type, and grade, TP53 status, and PIK3CA status. Elevated MSC-AS1 expression forecasts reduced overall survival and progression-free interval, with its independent association with overall survival validated by multivariate analysis. Zhang et al. discovered that MSC-AS1 lncRNA is markedly elevated in OS tissues relative to surrounding normal bone tissues and correlates with worse prognosis. Increased MSC-AS1 levels were detected in osteosarcoma cell lines relative to normal osteoblasts. Likewise, MSC-AS1 levels are elevated in NPC tissues, with heightened levels associated with advanced tumor grade and worse prognosis.

SUN et al. found that MSC-AS1 expression was increased in pancreatic ductal adenocarcinoma (PDAC) tissues. Elevated MSC-AS1 levels were linked to worse prognosis in PDAC patients. Silencing MSC-AS1 in Panc-1 and BxPC-3 cells led to a significant reduction in cell proliferation. Furthermore, miR-29b-3p, which is known for its tumor-suppressing role, was predicted to bind to both MSC-AS1 and CDK14. Unlike MSC-AS1, elevated levels of miR-29b-3p were correlated with improved prognosis in patients with PDAC [16]. A different study revealed that MSC-AS1 expression was significantly elevated in GC tissues compared to non-tumor tissues. Additionally, higher MSC-AS1 levels were observed in GC cell lines relative to normal gastric mucosal GES-1 cells. Data from The Cancer Genome Atlas (TCGA) also indicated that elevated MSC-AS1 expression is strongly associated with advanced poor prognosis and tumor stages in GC patients [42].

Another study showed that MSC-AS1 levels were higher in gastric cancer. They showed that a significant association between elevated MSC-AS1 expression and factors such as histological classification, histological grade, T stage, and the status of TP53 and PIK3CA. Moreover, they revealed that patients with high MSC-AS1 expression had worse overall survival and shorter progression-free intervals. Additionally, multivariate survival analysis confirmed that MSC-AS1 expression independently predicted overall survival [41].

Zhang et al. revealed that MSC-AS1 lncRNA levels were significantly higher in OS tissues than in the surrounding normal tissues. The analysis suggested that increased MSC-AS1 expression correlated with worse prognosis in OS patients [19]. Likewise, in nasopharyngeal carcinoma (NPC), elevated MSC-AS1 expression is associated with advanced tumor grade and poor prognosis. Collectively, these findings support the role of MSC-AS1 as a clinically relevant biomarker for cancer diagnosis and prognosis across multiple tumor types.

MSC-AS1 in cancer chemotherapy

Chemotherapy remains one of the most widely used and effective treatment strategies for various cancers; however, its efficacy is often limited by the emergence of drug resistance. Although the mechanisms underlying this resistance are not fully understood, alterations within the tumor microenvironment (TME) are considered major contributors [74]. MSC-AS1 has been found to enhance chemotherapy resistance in various types of cancer, including glioma. In particular, MSC-AS1 levels are elevated in temozolomide (TMZ)-resistant cells and tissues. Patients with high MSC-AS1 expression tend to have shorter overall survival. Furthermore, reducing MSC-AS1 via knockdown impairs cell viability, proliferation, and sensitivity to TMZ in resistant glioma cells [47].

In gastric cancer, MSC-AS1 promotes cell proliferation and inflammatory mediator secretion while enhancing cisplatin resistance through the miR-142-5p/DDX5 axis [43]. MSC-AS1 interacts with miRNAs like miR-142-5p, miR-373-3p, and miR-425-5p to regulate chemotherapy resistance genes [45, 47]. MSC-AS1 promotes fatty acid oxidation (FAO) and stemness in gastric cancer cells, contributing to 5-FU and oxaliplatin resistance. MSC-AS1 influences cell cycle progression, apoptosis, and expression of proliferation markers like PCNA and Ki-67 to modulate chemosensitivity [45]. Collectively, these findings identify MSC-AS1 as a critical regulator of chemotherapy resistance in diverse cancers. Targeting MSC-AS1 and its downstream signaling pathways may provide a promising strategy to overcome resistance and improve the effectiveness of chemotherapeutic agents.

In conclusion, cancer research continues to evolve with emphasis on targeted therapies, epigenetic mechanisms, and environmental influences on tumor development across various types like ovarian, oral, and hepatocellular cancers. Biosensing advancements and regulatory networks further aid in diagnosis and treatment, highlighting nanotechnology's broad potential in combating cancer [75-95]. lncRNAs are increasingly recognized as key regulators of tumor development, and MSC-AS1 has consistently demonstrated a strong association with tumor aggressiveness across multiple cancer types. Elevated MSC-AS1 expression correlates with adverse clinical features, including higher histological grade, larger tumor size, and reduced overall survival. Functional studies further support its oncogenic potential, showing that silencing MSC-AS1 significantly impairs cancer cell proliferation, invasion, and metastasis both in vitro and in vivo. These findings highlight MSC-AS1 as a promising candidate for prognostic biomarker development and therapeutic intervention. Although initial studies suggest its potential for early cancer detection, current evidence is insufficient for clinical application. Further validation through large-scale clinical trials and mechanistic studies is required to fully elucidate its diagnostic value, therapeutic feasibility, and underlying molecular pathways. Future investigations of MSC-AS1 may not only clarify lncRNA-driven mechanisms in tumorigenesis but also facilitate the development of innovative RNA-based biomarkers and precision therapies tailored to specific cancer subtypes.

Conflicts of Interest

The authors state that they have no competing interests or financial relationships relevant to this work.

Declaration

This manuscript was prepared without the use of any artificial intelligence (AI) tools or technologies.

Funding

Not applicable

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