

Decoding long non-coding RNAs: Friends and foes in cancer development (Review)

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Abstract. Cancer remains a formidable adversary, challenging medical advancements with its dismal prognosis, low cure rates and high mortality rates. Within this intricate landscape, long non-coding RNAs (lncRNAs) emerge as pivotal players, orchestrating proliferation and migration of cancer cells. Harnessing the potential of lncRNAs as therapeutic targets and prognostic markers holds immense promise. The present comprehensive review delved into the molecular mechanisms underlying the involvement of lncRNAs in the onset and progression of the top five types of cancer. By meticulously examining lncRNAs across diverse types of cancer, it also uncovered their distinctive roles, highlighting their exclusive oncogenic effects or tumor suppressor properties. Notably, certain lncRNAs demonstrate diverse functions across different cancers, confounding the conventional understanding of their roles. Furthermore, the present study identified lncRNAs exhibiting aberrant expression patterns in numerous types of cancer, presenting them as potential indicators for cancer screening and diagnosis. Conversely, a subset of

lncRNAs manifests tissue-specific expression, hinting at their specialized nature and untapped significance in diagnosing and treating specific types of cancer. The present comprehensive review not only shed light on the intricate network of lncRNAs but also paved the way for further research and clinical applications. The unraveled molecular mechanisms offer a promising avenue for targeted therapeutics and personalized medicine, combating cancer proliferation, invasion and metastasis.

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1. Introduction

Cancer stands as one of the most perilous diseases, with its incidence and fatality rates consistently occupying the top positions among non-communicable diseases (1). In 2020, the world witnessed ~19.3 million fresh cases of cancer and nearly 10.0 million cancer-related fatalities (2). There have been significant advancements in cancer treatment, leading to substantial successes in recent decades. Nevertheless, the prognosis remains grim for the majority of cancer patients, particularly those in advanced stages with metastasis, as their survival rates continue to be low (3). Hence, there is an urgent need to gain deeper insights into the molecular mechanisms that control the development and progression of tumors and to devise more efficient clinical tactics for treating cancer.

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Traditionally, long non-coding RNA (lncRNA) was thought of as mere background noise in genomic transcription (4). However, recent research has uncovered that lncRNA indeed serves a crucial role in governing gene expression. This includes functions such as gene suppression, modifying chromatin structure, influencing epigenetic gene activation, regulating transcription, post-transcriptional modifications and even affecting translation processes (5-8). Consequently, lncRNA is actively involved in various biological processes such as cell proliferation, cell cycle regulation, immune regulation and programmed cell death (apoptosis) (9-11).

Cancer, among other human diseases, is closely associated with lncRNAs (12). Irregular levels of lncRNA expression can play a pivotal role in the development of various types of cancer, serving as a significant regulatory factor in their onset with a predictive potential (8). lncRNAs can perform diverse biological functions in different types of cancers, such as regulating gene expression, metabolism, immunity, influencing cell proliferation, controlling apoptosis and affecting tumor metastasis (13-16). These versatile molecules can act as oncogenes, promoting cancer growth, or tumor suppressors, inhibiting tumor progression, or both depending on the specific context and type of cancer. The present study provided a comprehensive discussion of how lncRNAs contribute to both cancer-promoting and cancer-inhibiting processes in the top five types of cancer with the highest incidence rates. Additionally, it offered a summary of the oncogenic and suppressive roles of lncRNAs across all types of cancer.

2. Overview of the top five types of cancer

Breast cancer (BC), the leading cause of mortality in women, surpassed lung cancer (LC) in prevalence in 2020, resulting in over 685,000 fatalities (2). Nearly 680 million women worldwide were estimated to have suffered from BC in 2018 (2). LC, the second most common tumor globally (2), claims ~1.6 million lives annually (17). It is primarily categorized into small-cell LC (SCLC) and non-small cell LC (NSCLC) (18), with NSCLC accounting for 80% of cases (19). Early diagnosis of LC is challenging due to its asymptomatic nature (20). Gastric cancer (GC), the fifth most common cancer and the fourth most fatal, maintains high mortality rates worldwide (2). Diagnosis and treatment involve techniques such as endoscopic biopsies, CT scans and laparoscopic staging (21). Despite a gradual decline in the incidence of GC over the past few decades, the 5-year overall survival rate for GC patients remains low, partly because GC patients display no symptoms in the early stages (21). Prostate cancer (PCa) is a common malignant tumor in elderly men and ranks as the second most common cancer and the fifth leading cause of mortality in men worldwide (2). Metastatic diseases, particularly bone metastasis, contribute to the mortality rate. Treatment resistance to androgen deprivation therapy and chemotherapy drugs poses a significant challenge (22,23). Colorectal cancer (CRC), the most prevalent gastrointestinal tract cancer, ranks third in terms of incidence and second in mortality (2). Sporadic CRC develops slowly through the adenoma-cancer sequence and is associated with long-term colorectal inflammation. Early detection remains challenging, despite the use of endoscopy and biopsy (24).

The significance of lncRNAs in the progression and development of BC, LC, GC, PCa, CRC and other types of cancer has been demonstrated in various studies (25-28). These lncRNAs have been found to play essential roles in cancer-related mechanisms, functioning as either oncogenes or tumor suppressors (Fig. 1). Consequently, there is considerable potential for lncRNAs to serve as diagnostic indicators and therapeutic targets. Further exploration of lncRNAs may result in advancements in early detection, personalized treatment strategies and overall management of various types of cancer.

3. lncRNAs as oncogenes in the top five types of cancer

BC. Several lncRNAs including, lncRNA-CDC6 (25), SNHG₁ (29) and MALATA1 (30) have been implicated in the proliferation and metastasis of cancer cells during the progression and development of BC (Table I). When Kong *et al* (25) sequenced BC sample tissues from the TCGA database, they discovered that the expression of lncRNA-CDC6 was significantly upregulated and the expression level was positively linked with the BC stage. The proliferation and metastasis of MB-231 and MCF-7 cells were inhibited by the suppression of lncRNA-CDC6, which was connected to the arrest of BC cells in the G₁ phase (25). At the same time, overexpression of lncRNA-CDC6 was demonstrated to promote the proliferation and metastasis of BC cells (25). Further experiments by the authors revealed that lncRNA-CDC6 may bind to micro(miR)-215, which would then promote the proliferation and metastasis of MCDA-MB-231 and MCF-7 cells (25) (Fig. 2). A study has also shown an association between low expression of the miRNA-215, which is related to BC and a poor clinical outcome in BC patients (31).

Up to 50% of tumor-associated macrophages (TAMs) exist in BC. TAMs can differentiate into M1 and M2 cells (32). Studies have found that M2 cells are the main cells in BC tissues and are implicated in BC progression (33,34). The STAT signaling pathway is an important pathway to drive M2 macrophage polarization (29). According to Zong *et al* (29) the expression level of small nucleolar RNA host gene 1 (SNHG₁) was related to the polarization of M2 macrophages. By enhancing STAT6 phosphorylation in the STAT pathway, lncRNA-SNHG₁ may facilitate M2 macrophage polarization, ultimately promoting metastasis in BC cells (29) (Fig. 2).

The lncRNA Metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) plays a crucial role in regulating tumor progression across various cancers. In BC, MALAT1 interacts with miR-570-3p, resulting in the promotion of BC cell proliferation and metastasis (30). This interaction underscores the significant effect of MALAT1 on BC progression (30). According to Yue *et al* (30), the expression level of MALAT1 in BC tissues and cell lines (MCF-7, SK-BR-3, MDA-MB-468, MDA-MB-231, T-47d and MDA-MB-453) were higher compared with that in normal tissues. Bioinformatics analysis and luciferase reporter gene experiments revealed that MALAT1 binds to miR-570-3p, reducing its expression. This interaction promotes BC proliferation and metastasis (30) (Fig. 2). However, the specific targets of miR-570-3p downstream of this regulation remain poorly understood, warranting further investigation.

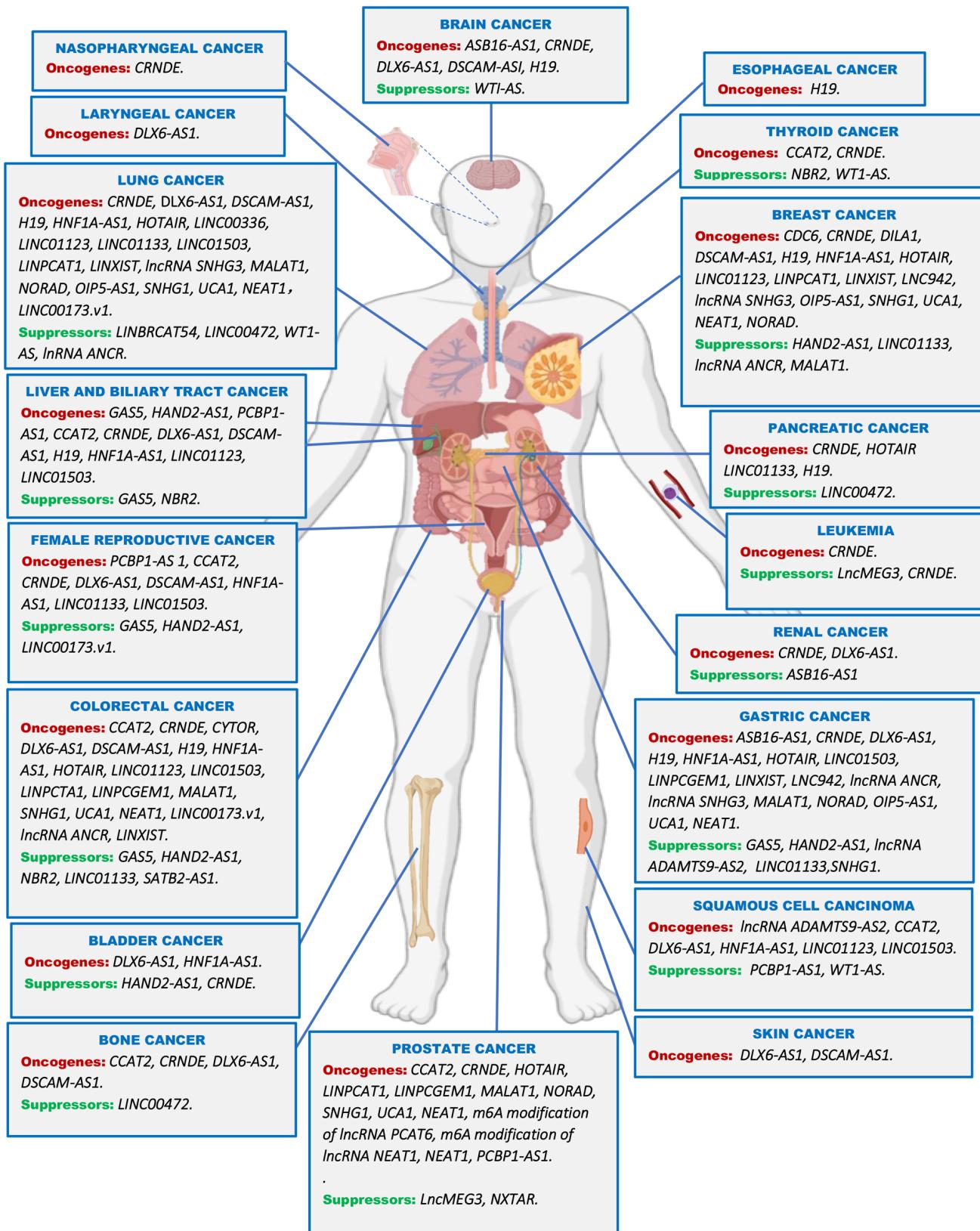


Figure 1. A central schematic illustrating the lncRNAs associated with various types of cancer. lncRNAs can act as oncogenes, promoting cancer growth, or tumor suppressors, inhibiting tumor progression, depending on the specific context and cancer type. lncRNA, long non-coding RNA.

The lncRNA LOXL1-AS1 is highly expressed in BC cell lines (MCF-7, MDAMB-231, BT549 and SKBR-3) compared with normal a breast tissue cell line (HBL100) (35). Silencing LOXL1-AS1 expression leads to the inhibition of BC cell

proliferation, migration and invasion (35). miR-143-3p, a known tumor suppressor in various types of cancer such as triple-negative breast cancer (36), plays a role here. Decreasing the expression of miR-143-3p counteracts the inhibitory effect

Table I. The oncogenic roles of lncRNAs in the top five types of cancer.

First author, year	Type of cancer	lncRNA	Species	Expression	Target Spot	Effect	(Refs.)
Kong <i>et al.</i> , 2019	Breast cancer	CDC6	Human MCF-10A, MCF-10AT, MCF-10CA1A, MCF-10CA1H cell lines	↑	miR-215/CDC6	Proliferation and metastasis of BC cells	(25)
Zong <i>et al.</i> , 2021		SNHG ₁	Human BC cell line MCF-7 cells and mouse macrophage cell line RAW264.7 cells	↑	STAT6 protein	Polarization of M2 macrophages in BC	(29)
Zhang <i>et al.</i> , 2021			Tissue samples from BC patients, BC cell lines MCF-7 and MDA-MB-231 and normal epithelial cell line MCF-10A, mice Human BC cell lines (MCF-7, SK-BR3, MDA-MB-468, MDA-MB-231, T-47d and MDA-MB-453) and normal mammary epithelial cell lines (MCF-10A)	↑	miR-381/EZH2	DDP resistance in BC cells	(97)
Yue <i>et al.</i> , 2021		MALAT1	Human BC cell lines (MCF-7, SK-BR3, MDA-MB-468, MDA-MB-231, T-47d and MDA-MB-453)	↑	miR-570-3p	Proliferation and migration of BC cells	(30)
Li <i>et al.</i> , 2019		LOXL1-AS1	Human BC cell line (MCF-7, MDA-MB-231 and BT549 SKBR-3) and Human breast epithelial normal cells (HBL-100)	↑	miR-143-3p	Proliferation, migration and invasion	(35)
Du <i>et al.</i> , 2020		DLX6-AS1	Human breast fibroblast CCD-1095SK and human triple negative BC cell lines HCC1599, MDA-MB-231, HCC1806 and HS578 T	↑	miR-199b-5p/Paxilin	Proliferation, EMT and DDP resistance in BC cells	(98)
Liu <i>et al.</i> , 2020		CYTOR	Human BC cell line MCF7	↑	miR-125a-5p/SRF	Tamoxifen resistance in BC cells	(99)
Shi <i>et al.</i> , 2020		DILA1	Human MCF-7, T47D BC cell lines and 293T cell lines	↑	Thr286/Cyclin D1	Tamoxifen resistance in BC cells	(100)
Yu <i>et al.</i> , 2021		OIP5-AS1	Human BC cell lines SKBR3 and BT474	↑	miR-381-3p/HMGB3	and proliferation	(101)
Jen <i>et al.</i> , 2017	Lung cancer	MALAT1	Human lung adenocarcinoma cell line A549 and CL1-0 and normal bronchial epithelial cell line BEAS-2B	↑	4-Oct	Trastuzumab resistance in BC cells	(39)
Hua <i>et al.</i> , 2019		LINC01123	NSCLC tissue and its adjacent normal lung tissue	↑	miR-199a-5p	Proliferation, migration	(42)
Wang <i>et al.</i> , 2019		LINC00336	Lung cancer cell line, clinical samples of patients with lung adenocarcinoma	↑	ELAV1	Inhibition of ferroptosis and proliferation	(45)
Chen <i>et al.</i> , 2020		LINC00173-v1	Endothelial cells and lung squamous cell carcinoma cells	↑	miR-511-5p/VEGFA	Proliferation and migration of vascular endothelial cells and tumorigenesis of SQC cells	(102)

Table I. Continued.

First author, year	Type of cancer	lncRNA	Species	Expression	Target Spot	Effect	(Refs.)
Zeng <i>et al.</i> , 2020		Linc00173	Human SCLC cell lines NCI-H69, NCI-H446 and the drug resistant H69AR purchased from the American Type Culture Collection (ATCC, USA), cisplatin-resistant NCIH446DDP cell line.	↑	miR-218/Etk axis	DDP resistance in SCLC cell	(103)
Hua <i>et al.</i> , 2021		XIST	Human normal lung epithelial cell lines BEAS-2B and three lung cancer cell lines, A549, H460 and SKMES-1	↑	miR-101-3p	Glycolysis and swelling	(104)
Xu <i>et al.</i> , 2020			Human A549 and H1299 cells	↑	SMAD2	DDP resistance	(105)
Zhang <i>et al.</i> , 2020	Colorectal cancer	H19	Human CRC cells HCT116, SW480 and DLD1/female BALB/c nude mice	↑	H19/hnRNPA2B1/ EMT axis	EMT and CRC metastasis	(48)
Ding <i>et al.</i> , 2018			Human HT29, HCT116, SW480 and SW620 cells and normal colorectal mucosa cell line (NCM460)	↑	H19/miR-29b-3p/ PGRN/Wnt signal	EMT	(51)
Zhang <i>et al.</i> , 2018		NEAT1	Human HCT116 and SW1116 cells/male BALB/c nude mice	↑	NEAT1/DDX5/Wnt/ β-catenin axis	CRC cell proliferation, migration and invasion	(52)
Zhuang <i>et al.</i> , 2020			Colon cancer cell lines (SW620 HT-29, HCT 116, LoVo and SW480) and normal colon epithelial cells (NCM460)	↑	NEAT1/miR-185-5p/ IGF2 axis	NEAT1/miR-185-5p/ IGF2 axis	(106)
Wang <i>et al.</i> , 2020			Patient samples, SW480 and HCT116 cells, normal colorectal epithelial cells (NCM460) and male BALB/c-nude mice.	↑	Inc-NEAT1/ miR-150-5p/CPSF4 axis	5-FU resistance, inhibition of CRC cell apoptosis and promoting CRC cell invasion.	(107)
Zhu <i>et al.</i> , 2020			Human CRC tissue, human HCT116 and SW480 cells	↑	NEAT1/ALDH1/ c-Myc	5-Fu resistance	(108)
Bian <i>et al.</i> , 2016		UCA1	Patients with CRC, cell lines (HEK-293T, HCT8, HCT116, HT29, LoVo and SW480)	↑	UCA1/miR-204-5p/ CREB1	Proliferation, inhibition of apoptosis of CRC cells and 5-FU resistance of CRC	(109)
Chen <i>et al.</i> , 2020		CCAT2	Patient sample CRC	↑	CCAT2/BOP1 axis	5-FU and OxoPt resistance	(110)
Ding <i>et al.</i> , 2017		CRNDE	Human CRC cell lines (DLD1, HCT116, SW480 and LOVO cells) and the human colonic epithelial cells HCoEpiC	↑	CRNDE/EZH2/ DUSP5/CDKN1A	Proliferation and CRC metastasis	(111)
Li <i>et al.</i> , 2017		HOTAIR	Human CRC cell lines (HT29, SW480 and FHC cells)	↑	Axis of HOTAIR/ miR-218/NF-κB or HOTAIR/ PCAT1/FKBP51	5-FU resistance	(112)
Shang <i>et al.</i> , 2019	Prostate cancer	LINPCAT1	Surgical specimen of human prostate tissue and nude mice	↑		Cancer cell proliferation	(28)

Table I. Continued.

First author, year	Type of cancer	lncRNA	Species	Expression	Target Spot	Effect	(Ref.s.)
He <i>et al.</i> , 2014		LINPCGEM1	Mice, human non-cancerous RWPE-1 cells, HEK293T cells and LNCaP cells	↑	miR-145	Cancer cell proliferation and colony formation	(55)
Lang <i>et al.</i> , 2021		N6-m ⁶ PCAT6	Human prostate tissue, nude mice and mice	↑	PCAT6/IGF2BP2/IGFIR axis	Cancer cell invasion, migration, proliferation and tumor growth	(59)
Wen <i>et al.</i> , 2020		N6-m ⁶ LncNEAT1	Human prostate cancer specimens, patient samples, mice, nude mice	↑	CYCLINL1/CDK19/NEAT-1	Carcinogenesis in metastatic bone prostate cancer	(61)
Hu <i>et al.</i> , 2021		NORAD	Human PCA cell lines (22Rv1, DU145 and PC-3) and mice	↑	NORAD/miR-541-3p/PKM2	Proliferation and migration of prostate cancer cells	(65)
Mo <i>et al.</i> , 2021		NEAT1	Human prostate epithelial cell line RWPE-1, human low metastatic MDA-PCa-2PPCA cell line, human PCA bone metastasis related cell line, mouse	↑	SFPQ/PTBP2	Participate in the osteogenic differentiation of human bone marrow mesenchymal stem cells	(66)
Zhang <i>et al.</i> , 2020		DSCAM-AS1	PCA cell line 22Rv1, nude mice	↑	FOXA1 and ERα	Pedigree-specific carcinogenesis regulated by FOXA1	(57)
Zhang <i>et al.</i> , 2021	Gastric cancer	PCBP1-AS1	CRPC patients, LNCaP and C4-2 cells and mice	↑	AR\AR-V7	Proliferation, migration and cancer growth	(113)
Xie <i>et al.</i> , 2021		lncRNA SNHG3	Human GES-1 Gastric Epithelial Cells, MGC-803, AGS, BGC-823 and HGC-27 Cell Lines and BALB/c Nude Mice GC Cell Lines	↑	miR-139-5p/MYB axis	Upregulation of MYB drives GC proliferation, migration and invasion	(67)
Ma <i>et al.</i> , 2021		Linc01503	Human MKN-74, NCI-N87 and SGC-7901GC cell lines	↑	EGR1 protein	GC cell proliferation and metastasis	(72)
Xie <i>et al.</i> , 2020		lncRNA ANCR	Patient sample human GC cell and TAMs, nude mouse	↑	FOXO1 protein	GC cell metastasis and invasion	(73)
Jiang <i>et al.</i> , 2022		HNF1A-AS1	Human GC cell lines HGC-27, MKN-45, AGS, NCI-N87, human embryonic kidney (HEK) 293T cells, immortalized gastric mucosal epithelial cell line GES-1 and BALB/c mouse GC cell lines	↑	miR-30b-5p/EIF5A2 axis	EMT, enhanced 5-FU resistance of GC cells	(114)
Xin <i>et al.</i> , 2021		lncRNA CRNDE	Human GC cell line SGC7901 and mouse GC cell line MFC	↑	PI3K/AKT pathway	PI3K/Akt pathway, reduced the sensitivity of GC cells to DDP	(115)
Zhu <i>et al.</i> , 2022		LINC00942	Human GC cell line, SGC7901, BGC823, human 293T cell line, SGC7901, BGC823 (SGC-R and BGC-R) and nude mice GC cell line	↑	MSI2 protein	Enhance the stability of c-Myc mRNA expression, promote GC chemoresistance	(116)

Table I. Continued.

First author, year	Type of cancer	lncRNA	Species	Expression	Target Spot	Effect	(Refs.)
Fu <i>et al</i> , 2021	ASB16-AS1	Human GC cell lines (AGS, MKN-45, HGC-27 and MKN-7)	↑	miR-3918, miR-4676-3p	NF-κB pathway, enhance the stemness and cisplatin resistance of GC cells		(117)

lncRNA, long non-coding RNA; BC, breast cancer; miR, microRNA; DDP, cisplatin; EMT, epithelial-mesenchymal transition; LC, lung cancer; NSCLC, non-small cell LC; SCLC, small cell LC; CRC, colorectal cancer; 5-FU, fluorouracil; OxPt, oxaliplatin; PCA, prostate cancer GC, gastric cancer; TAMs, tumor-associated macrophages.

of LOXL1-AS1 silencing on BC cell proliferation (35). Low LOXL1-AS1 expression promotes BC tumor suppression by upregulating the expression of directly bound miR-143-3p (35) (Fig. 2). This suggests a crucial regulatory pathway involving LOXL1-AS1 and miR-143-3p in BC that warrants further investigation (35).

LC. In recent years, it has been found that a number of lncRNAs are involved in the proliferation and metastasis of LC (Table I). MALAT1 is a lncRNA initially noted by Ji *et al* (26) in 2003 through subtractive hybridization during their investigation of human NSCLC metastasis. This particular lncRNA has since gained significant attention due to its association with LC and has become one of the most extensively researched lncRNAs in the field (37). Octamer-binding transcription factor 4 (Oct4), a product of the Pou5f1 gene and part of the POU-domain transcription factor family, plays a crucial role in preserving the pluripotent state of both embryonic stem cells and cancer stem cells (38). The expression of Oct4 in cancer cells can indicate a dedifferentiated or stem cell-like state, which may contribute to the aggressiveness and metastatic potential of certain tumors, including LC. Jen *et al* (39) performed unbiased ChIP-seq sequencing in A549 and CL1-0 cells and the overexpression of Oct4 showed that this transcription factor could activate the transcription of MALAT1 by directly binding to the MALAT1 enhancer region (Fig. 3). In LC, MALAT1 does not alter alternative splicing but actively modulates gene expression including a set of metastasis-associated genes (40). According to Gutschner *et al* (40) suppressing MALAT1 in human lung tumor cells by genomically integrating RNA destabilizing elements using zinc finger nucleases led to a reduction in cell migration ability and a decreased formation of tumor nodules in a mouse xenograft model.

A study found that LC cells maintain growth by increasing glucose uptake and lactic acid release, a unique metabolic phenotype of LC cells (41). Hua *et al* (42) identified 364 differentially expressed genes between NSCLC tissues with high uptake of 18F-FDG and adjacent normal lung tissues by RNA sequencing, among which LINC01123 was the most significant lncRNA. Functional analysis showed that LINC01123 enhanced the proliferation and aerobic glycolysis of NSCLC cells (42). RNA immunoprecipitation and luciferase analysis confirmed that LINC01123 promoted the transcription of c-myc by competitively binding to miR-199a-5p and isolating it from c-myc mRNA, thus promoting the glycolysis and proliferation of LC cells (42) (Fig. 3).

Ferroptosis is a recently discovered cell death mode different from apoptosis (43). A study has shown that LC cells fight against ferroptosis by regulating lipid metabolism through lymphoid-specific helicase (LSH) (44). Wang *et al* (45) found that lncRNA LINC00336 was abnormally upregulated by sequencing the RNA of LC cells and examining clinical samples of numerous patients with lung adenocarcinoma. LSH can enhance the expression of the RNA binding protein known as Elav-like RNA binding protein 1 (ELAVL1) by suppressing the activity of p53 in relation to iron-mediated cell death (45). At the same time, ELAVL1 can promote its expression by stabilizing the transcription level of LINC00336 (45). Overexpressing

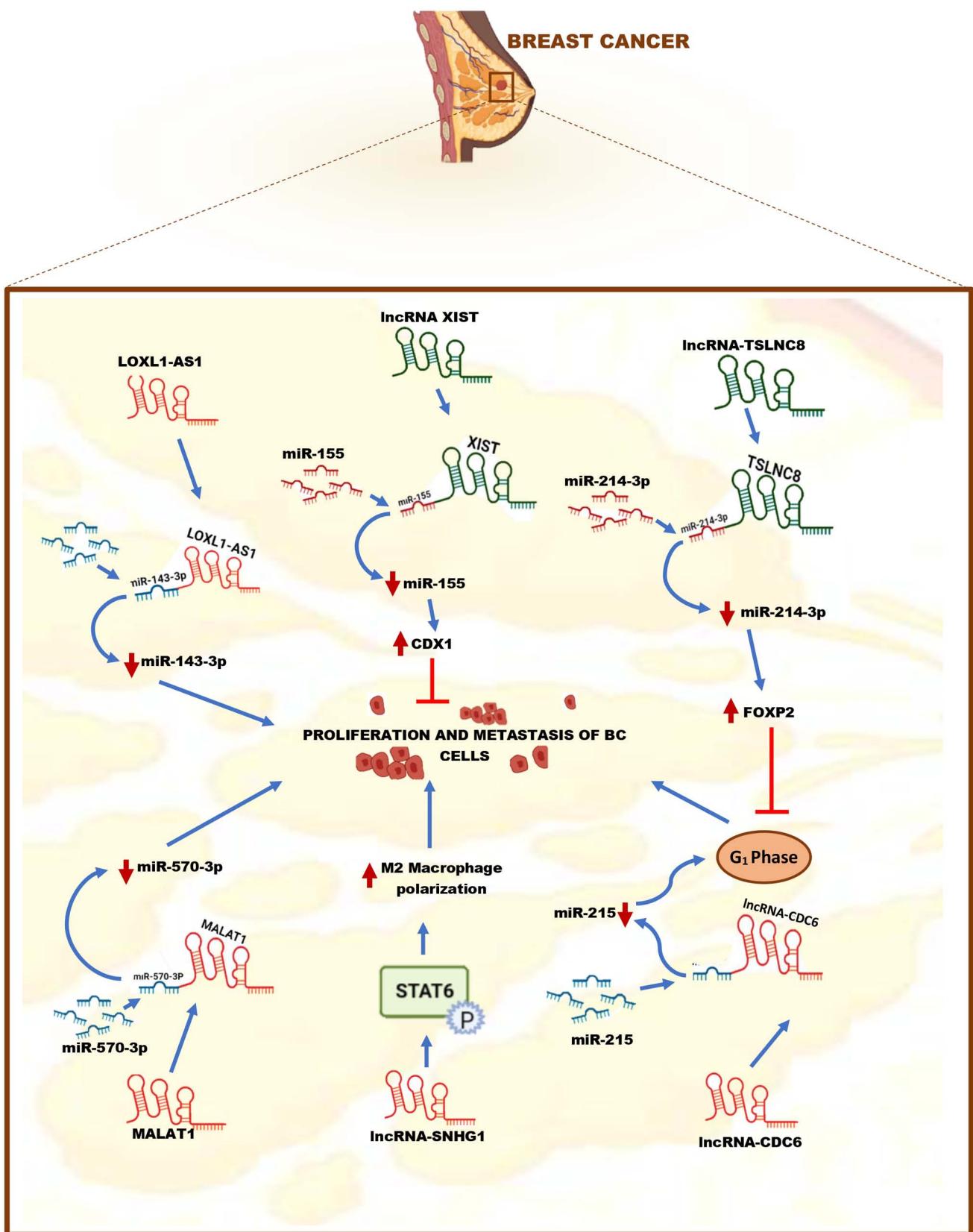


Figure 2. The mechanism of lncRNAs in BC. lncRNAs, such as MALAT1, lncRNA-SNHG1, lncRNA-CDC6 and LOXL1-AS1 could enhance the proliferation and metastasis of BC cells, whereas lncRNAs, including lncRNA XIST and lncRNA-TSLNC8 could inhibit the development of BC via the downregulation of miR-155 and miR-214-3p, respectively. lncRNA, long non-coding RNA; BC, breast cancer; miR, microRNA.

LINC00336 as a competitive endogenous RNA adsorbed miR 6852 and reduced its activity, thus upregulating the expression of cystathionine- β -synthase (CBS), the target gene

of miR6852 (45) (Fig. 3). CBS serves as an indicator of the sulfur pathway in ferroptosis and an increase in its expression suggests the inhibition of ferroptosis in LC cells (45-47).

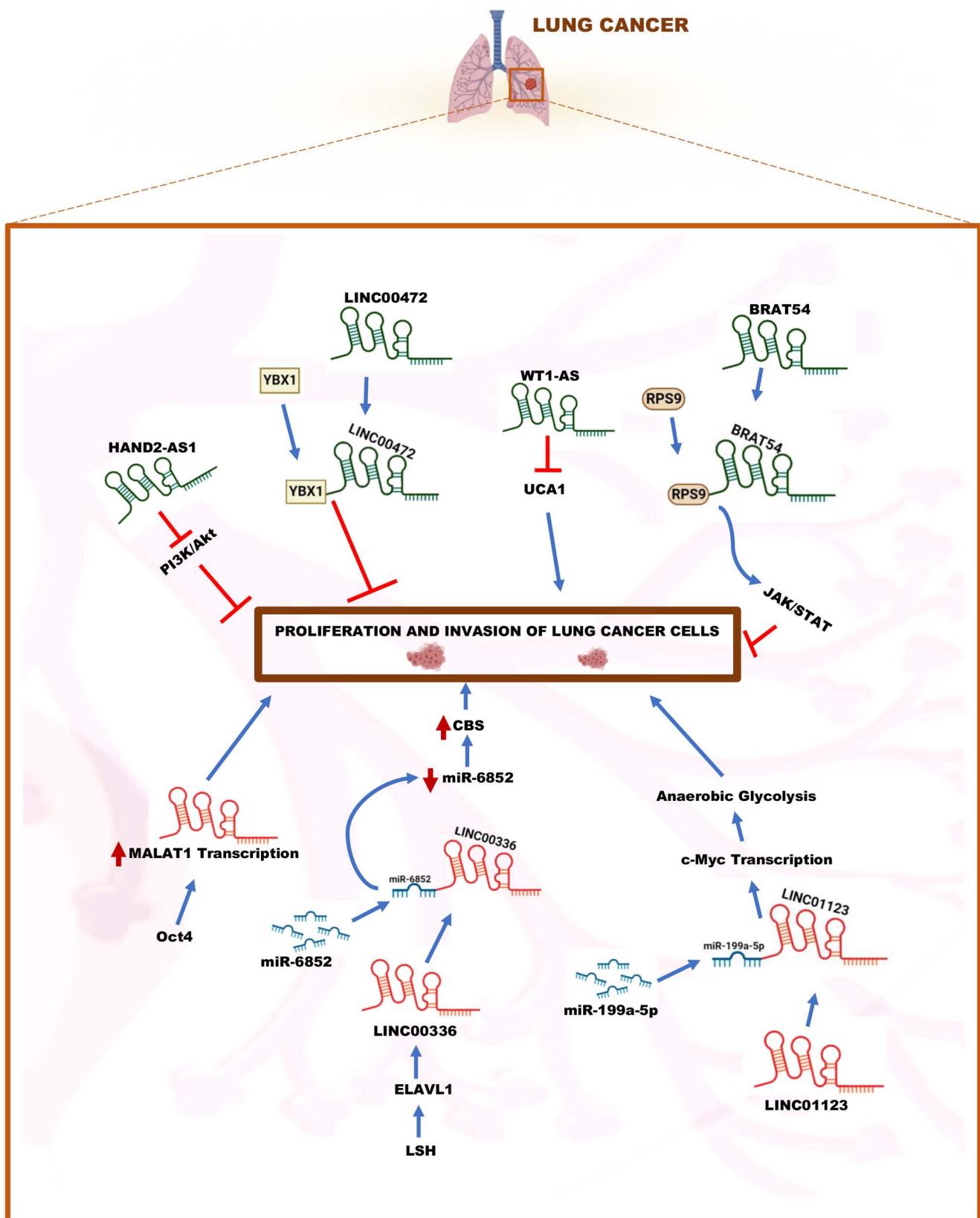


Figure 3. The mechanism of lncRNAs in LC. lncRNAs, such as MALAT1, LINC00336 and LINC01123 could act as oncogenes and promote the proliferation and invasion of LC cells, whereas lncRNAs, including HAND2-AS1, LINC00472, WT1-AS and BRAT54 could serve as suppressors during the development of LC. lncRNA, long non-coding RNA; LC, lung cancer; miR, microRNA.

CRC. A number of lncRNAs have been implicated in the proliferation, metastasis, invasion and epithelial-mesenchymal transition (EMT) of CRC cells (Table I) (27,48). H19 is an

early-discovered lncRNA initially identified as a carcinogenic embryonic transcript. It is located on chromosome 11p15.5 and is exclusively expressed from the maternal allele (27).

Zhang *et al* (48) found that the overexpression of H19 was related to distant metastasis of CRC and poor prognosis of patients by database and reverse transcription-quantitative (RT-q) PCR sequencing analysis. Heterogeneous nuclear ribonucleoprotein (hnRNP A2B1) is a protein reportedly associated with CRC metastasis and EMT (49). RNA pull-down analysis found that hnRNP A2B1 could combine with H19 in CRC cancer cells HCT116 (48). Immunoprecipitation reaction further found that H19 can specifically bind to hnRNP A2B1 protein and translocate H19 from the nucleus to the cytoplasm, stabilize Raf-1 mRNA, activate the Raf-ERK signal pathway and promote the proliferation, metastasis and EMT of CRC cancer cells (48). Granular precursor protein (PGRN) is a protein that promotes the occurrence and proliferation of epithelial ovarian cancer cells (50). Ding *et al* (51) found that H19 can promote the expression of PGRN by downregulating miR-29b-3p which ultimately promote the occurrence and increase of EMT through the Wnt signal pathway in CRC (Fig. 4).

Additionally, a study by Zhang *et al* (52) found that abnormal expression of lncRNA NEAT1 was related to CRC development. They discovered that NEAT1 activated the Wnt/β-catenin signal pathway, stabilizing the expression of the DEAD box p68 RNA helicase (DDX5) through targeted binding, acetylation and thiolation of DDX5 (52) (Fig. 4).

PCa. Some lncRNAs have been shown to promote the proliferation, invasion and migration of PCa cells (Table I). A study by Shang *et al* (28) revealed a high expression of LINPCAT1 in tissue samples of castrated refractory PCa (CRPC) patients. Subsequent animal experiments in nude mice with LINPCAT1 knockout showed that LINPCAT1 activated AKT and NF-κB pathways by promoting phosphorylation levels of AKT and NF-κB (p65) (28). FK506 binding protein 51 (FKBP51) is a molecular chaperone that interacts with the nuclear factor IκB kinase α subunit (IKKα) and participates in NF-κB activation (53). In addition, FKBP51 acts as a scaffold protein for AKT interaction with a domain-rich leucine repeat protein phosphatase (PHLPP) (54). The enhanced PHLPP activity combined with FKBP51 can play a negative role in AKT signal transduction by binding to AKT (54). Low expression of FKBP51 can reduce the activity of PHLPP and phosphorylate AKT (S437) to activate its pathway (28). Highly expressed LINPCAT1 can competitively bind to FKBP51 and replace the position of PHLPP, ultimately inhibiting the negative regulation of PHLPP on AKT signaling (28). Moreover, the binding of PCAT1 to FKBP51 further stabilizes the FKBP51/IKKα complex, resulting in increased NF-κB signaling and ultimately promoting the growth of CRPC (28) (Fig. 5). LINPCAT1 may be a viable target for treating CRPC, as evidenced by the preclinical mouse model of decreasing CRPC development after targeting PCAT1 (28).

Research based on the interplay between lncRNA LINPCGEM1 and miR-145 (55) has shown that the mutual suppression of LINPCGEM1 and miR-145 has a role in regulating the proliferation of LNCaP cells. Elevated levels of miR-145 have the potential to hinder the *in vitro* proliferation and invasion of PCa cells by directly binding to a specific sequence within the 3' untranslated region (UTR) of LINPCGEM1, leading to a reduction in LINPCGEM1

expression (55). Thus, high expression of LINPCGEM1 can downregulate the expression of miR-145 to promote the growth and proliferation of PCa cells (55) (Fig. 5).

The positive feedback loop formed by lncRNAs and other protein expression levels can promote PCa progression. Forkhead box (FOX) A1 is a key transcription factor in the occurrence and development of PCa, driving the malignant transformation of normal prostate epithelial cells (56). Zhang *et al* (57) found that FOXA1 expression was upregulated through public CHIP-seq experiments and LINDSCAM-AS1 regulated by FOXA1 was explicitly expressed in PCa. DSCAM-AS1 can bind to Y box binding protein 1 (YBX1), a DNA- and RNA-binding protein, and enhance its recruitment in the FOXA1 and estrogen receptor (ER) α initiation region (57). This may result in the formation of PCa and increase the transcription of FOXA1 and ER (57). FOXA1 and ER overexpression can increase the upregulation of LINDSCAM-AS1, generating a positive feedback loop (57) (Fig. 5). Finally, xenograft experiments also revealed that the knockout of DSCAM-AS1 can inhibit the formation of PCa (57).

Bone metastasis is one of the leading causes of death in PCa patients (58) and lncRNA can promote bone metastasis in PCa. Lang *et al* (59) discovered that N6-methyladenosine (m6A) modified PCa-related transcript 6 (lncRNAPCAT6), which was considerably enhanced in PCa tissues, by sequencing PCa tissue samples from the TCGA database. Functional analysis experiments verified that PCAT6 could promote PCa growth and bone metastasis by regulating the cell cycle (59). Type I insulin-like growth factor receptor (IGF1R) is expressed in prostate cells and promotes bone metastasis of PCa (60). PCAT6 experiences an increase in expression following m6A modification mediated by methyltransferase-like 3 (METTL3). This modification process leads to the regulation of IGF1R mRNA stability through the formation of PCAT6/IGF2BP2/IGF1R complex. As a result, it enhances the stability of IGF1R mRNA, elevates the levels of IGF1R and ultimately stimulates the invasion and migration of PCa cells (Fig. 5). These effects are brought about through the activation of the IGF/IGF1R signaling pathway, contributing to the promotion of PCa bone metastasis (60).

Bone-specific expression protein (CYCLINL1) was found to be expressed in cultured primary prostate cells and patient-derived xenografts of patients with bone metastasis (61). In the cancer genome map data set, NEAT1-1 expression was higher in PCa than in normal tissues (61). The m6A-modified nuclear-rich transcript 1 (lncNEAT1) (61) acts as a binding bridge between CYCLINL1 and prostate-specific expression protein (CDK19), activating CYCLINL1 to form the CYCLINL1/CDK19 complex that is recruited to the RUNX2 promoter, a key protein for bone and prostate metastasis (62-64). The formed LINNEAT1/CYCLINL1/CDK19 complex enhances PolII Ser2 phosphorylation and finally promotes bone metastasis of PCa (61) (Fig. 5). Related lncRNA may also promote PCa cell bone metastasis by binding mRNA to release extracellular vesicles (65) and affect the microenvironment of bone metastasis (66).

GC. In GC, numerous lncRNAs have been associated with the growth and advancement of cancer cells (Table I).

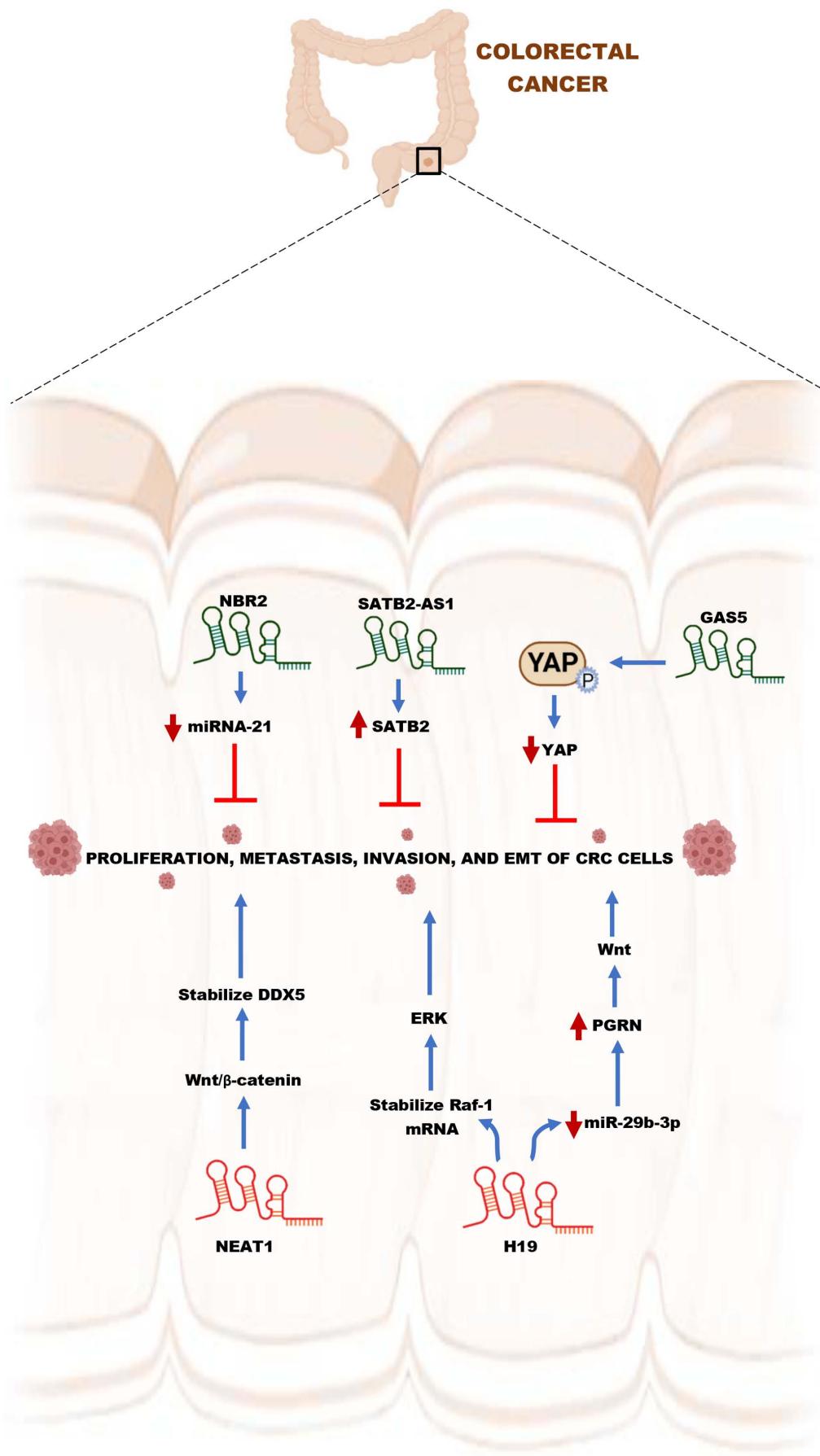


Figure 4. The mechanism of lncRNAs in colorectal cancer. lncRNAs, including NEAT1 and H19 could act as oncogenes and enhance the proliferation, metastasis, invasion and EMT of CRC cells. By contrast, SATB2-AS1, NBR2 and GAS5 can serve as suppressors via the modulation of SATB2, miRNA-21 and YAP, respectively, subsequently inhibiting the proliferation, metastasis, invasion and EMT of CRC cells. lncRNA, long non-coding RNA; EMT, epithelial-mesenchymal transition; CRC, colorectal cancer; miR, microRNA.

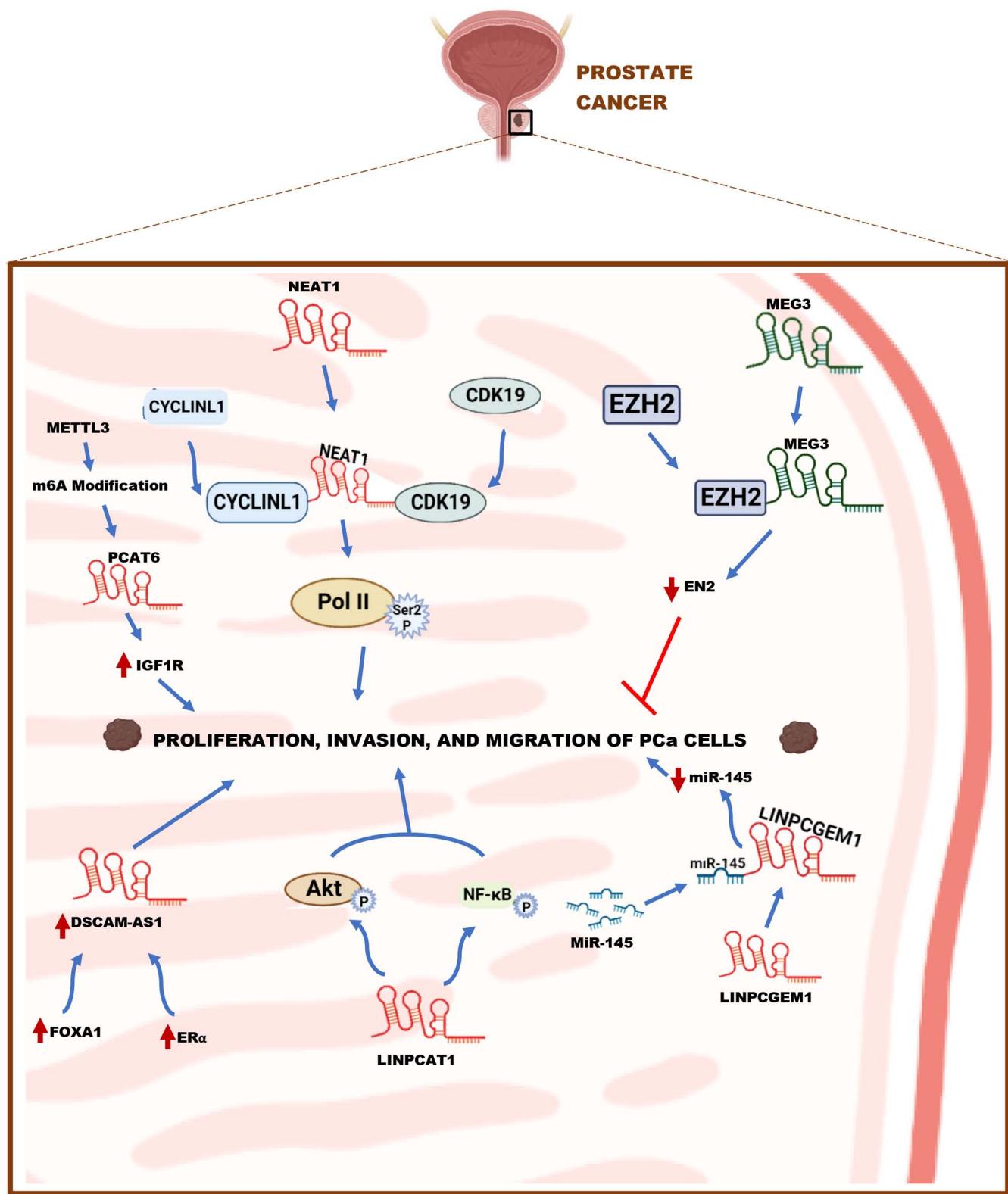


Figure 5. Mechanism of lncRNAs in PCa. Increase expression of lncRNAs, such as DSCAM-AS1, LINPCAT1, LINPCGEM1, PCAT6 and NEAT1 could promote the proliferation, invasion and migration of PCa cells, whereas overexpression of MEG3 could inhibit the progression of PCa via the downregulation of EN2. lncRNA, long non-coding RNA; PCa, prostate cancer; miR, microRNA.

Xie *et al* (67) found that the expression of lncRNA SNHG3 was upregulated in BGC-823 and AGS cell lines transfected with pcDNA3.1-SNHG3 plasmid by gene sequencing. SNHG3 overexpression can increase the proliferation ability of GC cells and enhance the migration and invasion activity by

reducing the G₀/G₁ phase and increasing the relative frequency of S phase and G₂ phase cells (67). miR-139-5p has been shown to inhibit the progression of bladder cancer (68), GC (69) and CRC (70). MYB, a target gene of miR-139-5p, is connected with GC cell proliferation and MYB expression is inversely

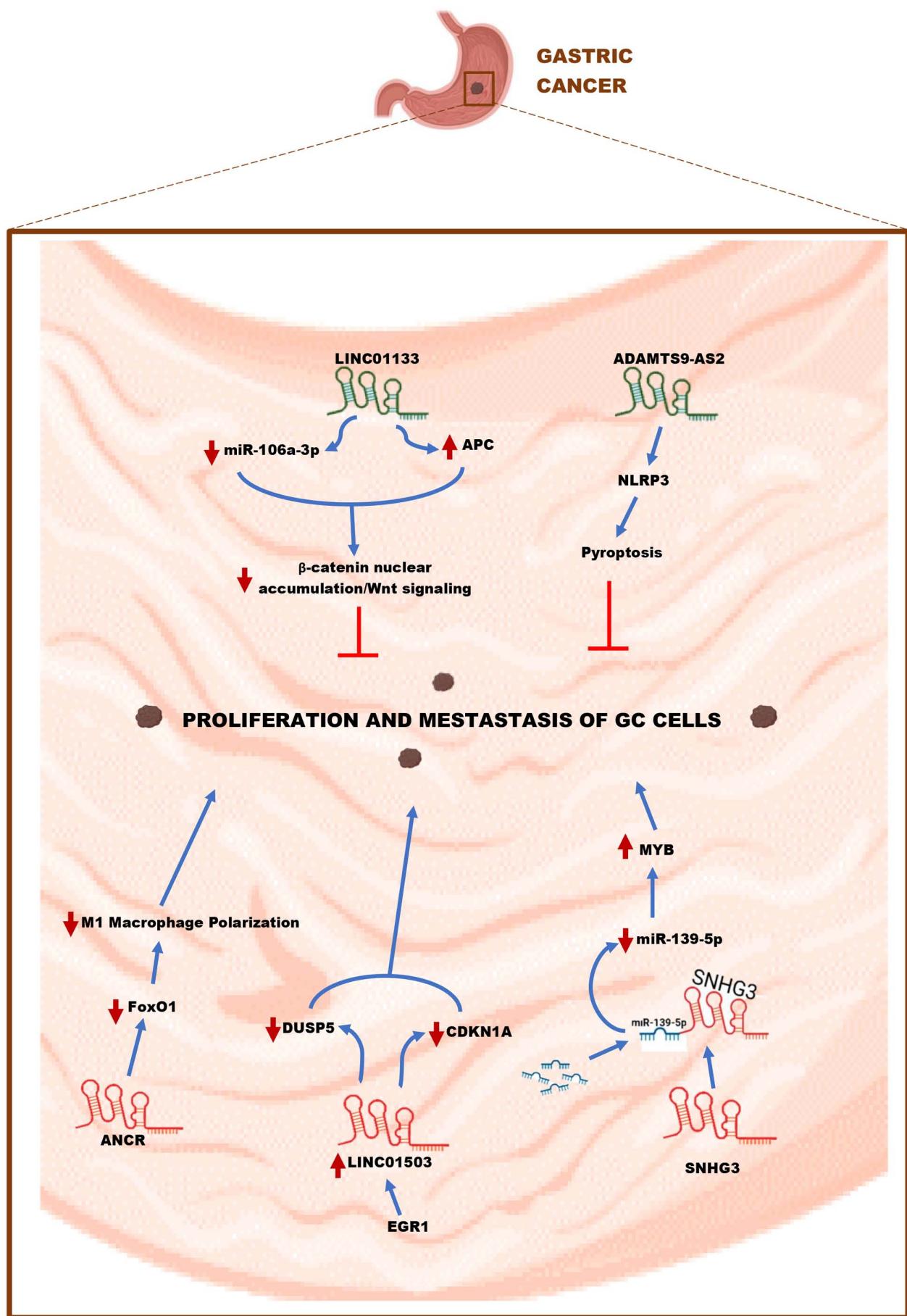


Figure 6. Mechanism of lncRNAs in GC. lncRNAs, including ANCR, LINC01503 and SNHG3 could act as oncogenes and enhance the proliferation and metastasis of GC cells. In contrast, LINC01133 and ADAMTS9-AS2 could serve as suppressors by inhibiting the proliferation and metastasis of GC cells. GC: gastric cancer; miR, microRNA.

correlated with miR-139-5p expression (67). High SNHG3 expression can reduce miR-139-5p to promote MYB expression, which in turn drives GC cell proliferation, migration and invasion (67) (Fig. 6).

LINC01503 is a new lncRNA located on human chromosome 19, which was first discovered as an oncogene in invasive squamous cell carcinoma (SCC) (71). Ma *et al* (72) studied whether overexpression of LINC01503 is related to GC progression. The public data analysis results of GEO and TCGA datasets showed that LINC01503 was overexpressed in GC patient tissue samples and gene sequencing showed that the expression level of this gene was upregulated in GC cells (72). Downregulation of LINC01503 expression increases the number of GC cells in G₀/G₁, which is connected to cell cycle arrest in G₀/G₁ (72). Early growth response protein 1 (EGR1) is an upstream target effector of LINC01503 (72). The binding of EGR1 to LINC01503 can activate the transcription of LINC01503 (72). The upregulation of LINC01503 mediated by EGR1 promotes the methylation of histone inhibitory chromatin marker (H3K27) and the demethylation of histone 3 tetra-amino acid in GC cells (72). It also inhibits the transcription of dual specific phosphatase 5 and cyclin 1 dependent kinase inhibitor 1A, subsequently downregulating their expressions in an epigenetic manner, promoting the transition of GC cells to the G₀/G₁ phase and ultimately enhancing the proliferation and metastasis of GC cells (72) (Fig. 6). Xie *et al* (73) found that lncRNA anti-differentiation RNA (ANCR) is highly expressed in GC tissues. It has been reported that recombinant Forkhead box O1 protein (FOXO1) can promote macrophages to produce inflammatory factors and polarization to M1 macrophages, thereby playing an anti-tumor role (74-76). Overexpression of the lncRNA ANCR can decrease the level of FOXO1 protein, inhibit the polarization of macrophages to M1, and reduce the production of inflammatory factors by M1 macrophages, thereby indirectly promoting the metastasis and invasion of GC cells (73) (Fig. 6). The molecular mechanisms underlying the involvement of numerous lncRNAs in the growth of GC cells are still in progress.

4. lncRNAs as tumor suppressors in the top five types of cancer

BC. lncRNAs are also capable of suppressing the proliferation, migration and invasion of BC cells (Table II). lncRNA XIST is a transcript of chromosome Xq13.2 located in the X inactivation center, affecting the reactivation of X-linked genes (77). XIST is underexpressed in BC tissue samples and cells (78). RT-qPCR results of MCF-7 and MDA-MB-231 cells transfected with pc-XIST showed that overexpression of XIST could inhibit cell proliferation, migration and invasion (78). miR-155 is a potential BC oncogene (79). The overexpression of XIST can directly bind to miR-155 and inhibit its expression, subsequently upregulating the miR-155 downstream target CDX1 and inhibiting the proliferation, migration and invasion of BC cells (78) (Fig. 2).

In addition, the expression of lncRNA TSLNC8 is downregulated in breast cancer tissues and cells (80). Upregulated TSLNC8 can block the proliferation of BC cells, which is related to its inhibition of cell G₁/S phase progression (80). TSLNC8 interacts with miR-214 and overexpression of

TSLNC8 inhibits downstream miR-214-3p expression, upregulating Forkhead box P2 (FOXP2) expression and ultimately inhibiting BC cell proliferation (80) (Fig. 2).

LC. A number of studies have shown that lncRNAs, such as LINBRAT54 (81), WT1-AS (82) and LINC00472 (83) can also inhibit the growth of LC cells and tissues (Table II). After a comprehensive microarray investigation of lncRNAs in preoperative and postoperative plasma samples of NSCLC patients, Yang *et al* (81) identified LINBRAT54 as a tumor suppressor that can reduce NSCLC proliferation *in vitro* and *in vivo*. A study also revealed that BRAT54 can directly bind to ribosomal protein S9 (RPS9) to activate the Janus tyrosine kinase/activator (JAK/STAT) and calcium signaling pathways to inhibit proliferation and invasion of NSCLC cells, ultimately promoting apoptosis of these cells (81) (Fig. 3). Gao *et al* (84) detected the expression of lncRNA in lung tissues and serum of NSCLC patients and healthy controls by RT-qPCR. They discovered that the expression level of lncRNA HAND2-AS1 in tumor tissues was lower compared with healthy tissues and that its downregulation influenced LC proliferation. HAND2-AS1 can inhibit the proliferation and promote the apoptosis of NSCLC cells by inactivating the PI3K/Akt pathway, thus inhibiting the growth of tumors (84) (Fig. 3).

Wan *et al* (82) took the lung tissues of 66 patients with NSCLC for RNA sequencing and found that Wilms tumor 1 antisense RNA (WT1-AS) was downregulated in NSCLC, which was related to the low survival rate of NSCLC patients but was not associated with clinical stage. Overexpression of WT1-AS inhibited the proliferation and migration of NSCLC cells (82). Urinary tract cancer-related 1 (UCA1) is mostly upregulated in LC (82). Correlation analysis found that the expression level of UCA1 negatively correlated with the expression level of WT1-AS in NSCLC and non-cancerous tissues (82). Its overexpression increased the proliferation, EMT, migration and invasion of NSCLC cells and was inhibited by WT1-AS (82). Gene sequencing results of H1993 and H1581 cells transfected with UCA1 and WT1-AS1 showed that the overexpression of UCA1 had little effect on the expression of WT1-AS1; however, the decrease in proliferation and migration of NSCLC cells mediated by overexpression of WT1-AS1 might be achieved by reducing the expression of UCA1 (82) (Fig. 3). Deng *et al* screened and identified lncRNA LINC00472 by using published expression profile data from lung adenocarcinoma and integrating bioinformatics analysis and proved that this lncRNA could bind with YBX1 to regulate cell hardness and inhibit the migration and invasion of lung adenocarcinoma, thus playing a role as a tumor suppressor (83) (Fig. 3).

CRC. lncRNAs including lncRNA GAS5, SATB2-AS1 and NBR2 have been shown to limit the growth of CRC cells (Table II). Biosphere interference and RNA fluorescence *in situ* hybridization study demonstrate that lncRNA GAS5 can bind to the WW domain of Yes-related protein (YAP) (85). YAP is the main participant of the Hippo YAP signaling pathway, which can regulate cell proliferation and apoptosis (85).

lncRNA GAS5 interacts with YAP to cause its translocation from the nucleus to the cytoplasm, which in turn results in the phosphorylation and degradation of YAP. This inhibits YAP

Table II. Suppressive roles of lncRNAs in the top five types of cancer.

First author, year	Cancer	lncRNA	Species	Expression	Target Spot	Effect	(Refs.)
Qin <i>et al.</i> , 2019	Breast cancer	TSLNC8	BC cell lines (MDA-MB-231, HCC1559, BT-549, UACC-812 and MDA-MB-453) and Human BC tissues	↓	miR-214-3p	Inhibits G ₁ /S phase progression	(80)
Zheng <i>et al.</i> , 2018		XIST	Human BC cells (MCF-7, ZR-75-1, HCC1937, MDA-MB-231, MDA-MB-468, MDA-MB-453) and normal breast epithelial cell line MCF-10 A	↓	miR-155/CDX	Inhibits proliferation, migration and invasion	(78)
Yang <i>et al.</i> , 2021	Lung cancer	LINBRCAT54	Plasma samples from NSCLC patients	↓	RPS9	Inhibits proliferation, invasion and promote apoptosis	(81)
Wan <i>et al.</i> , 2021		WT1-AS	Tissue samples of NSCLC patients	↓	UCA1	Reduces proliferation and migration	(82)
Deng <i>et al.</i> , 2020		LINC00472	Lung adenocarcinoma A549 and PC-9 cell lines, Human normal lung epithelial cells (BEAS-2B)	↓	YBX1	Inhibits cancer cell migration and invasion	(83)
Ni <i>et al.</i> , 2019	Colorectal cancer	GASS5	Human DLD1, LOVO, SW480, SW620, LS174T, HCT116, RKO and HT29 cells	↓	The lncRNA GAS5-YAP-YTHDF3 axis	Inhibits proliferation and invasion	(85)
Xu <i>et al.</i> , 2019		SATB2-AS1	Human CRC cell lines HCT-116, HT-29, SW-620, HCT-8, SW-480 and DLD-1	↓	SATB2-AS1/WDR5/GADD45A/SATB2 axis	Inhibits metastasis	(87)
Bai <i>et al.</i> , 2020		NBR2	Human CRC tissue, human CRC cell line RKO, HT115	↓	NBR2/miRNA-21 axis	Reduces migration and invasion	(88)
Zhou <i>et al.</i> , 2018		HAND2-AS1	patient sample, CRC cell line, mouse	↓	HAND2-AS1/miR-1275/KLF14 axis	Reduces 5-FU resistance, cell proliferation, migration and invasion	(118)
Zhou <i>et al.</i> , 2020	Prostate cancer	LncMEG3	Human prostate cells, nude mice	↓	EZH2	Reduces cancer cell vitality, migration and invasion	(91)
Ghildiyal <i>et al.</i> , 2022		NXTAR	Prostate, mouse, normal human prostate cell line	↓	AR\AR-V7	Inhibits proliferation of cancer cells	(119)
Ren <i>et al.</i> , 2020	Gastric cancer	lncRNA ADAMTS9-AS2	GES-1, DDP-sensitive GC (CS-GC) cell lines (SGC7901, MKN74, NUGC-4, HGC-27 and BGC-823) and DDP-resistant GC (CR-GC) cell lines (SGC7901/DDP and BGC-823/DDP)	↓	miR-223-3p/NLRP3 axis	Reduces pyroptosis and sensitivity of cancer cells to cisplatin	(95)

Table II. Continued.

First author, year	Cancer	lncRNA	Species	Expression	Target Spot	Effect	(Refs.)
Yang <i>et al.</i> , 2018		LINC01133	Human GC cell lines (SUN-216, BGC-823, AGS, BGC-803, NUGC4, MKN74, MKN45, SGC-7901 and HGC-27), nonmalignant gastric mucosal epithelial cell line GES-1 and human embryonic kidney (HEK) 293FT cell lines	↓ miR-106a-3p/ APC axis	miR-106a-3p/ APC axis	Inhibits Wnt/β-Catenin pathway, EMT and GC cell metastasis	(96)

lncRNA, long non-coding RNA; BC, breast cancer; miR, microRNA; LC, lung cancer; NSCLC, non-small cell LC; DDP, cisplatin; EMT, epithelial-mesenchymal transition; CRC, colorectal cancer; 5-FU, fluorouracil; GC, gastric cancer.

signal transduction, ultimately preventing the growth of CRC cells (85) (Fig. 4). Special AT-rich binding protein (SATB2) is a nuclear gene protein. As an important transcription factor, it plays a vital role in biological development, gene expression regulation and chromatin remodeling (86). SATB2-AS1 is an antisense RNA located on chromosome 2q33 of SATB2 (87). According to Xu *et al* (87), silencing lncRNA SATB2-AS1 can significantly reduce the RNA and protein levels of SATB2. By recruiting WD repeat domain 5 (WDR5), a growth arrest and DNA damage indigenous protein, SATB2-AS1 can increase the expression of SATB2 and ultimately prevent CRC cells from metastasizing (87) (Fig. 4). In addition, lncRNA NBR2 has been shown to inhibit CRC metastasis and invasion by downregulating the level of miRNA-21 (88) (Fig. 4). Future treatment targets for CRC are expected to be these lncRNAs and their associated miRNAs (89,90).

PCa. Some lncRNAs have also been shown to slow the course of PCa (91) (Table II). Using RT-qPCR sequencing, Zhou *et al* (91) discovered that the expression of lncRNA MEG3 was downregulated in PCa cells, but western blotting revealed that the expression of EN railed-2 (EN2) was elevated in PCa cells. EN2 is a well-known carcinogenic gene (92,93). PCa cells transfected with MEG3 demonstrate that overexpression of MEG3 inhibited cancer cell growth, whereas overexpression of EN2 reverses this effect (91). MEG3 in the nucleus can bind to EZH2, causing EN2 to undergo H3K27 trimethylation, thereby inhibiting the proliferation of PCa (91) (Fig. 5).

GC. lncRNA can also prevent GC progression (Table II). Pyroptosis is a type of programmed cell death that is caused by the activation of the NOD-like receptor hot protein domain-associated protein 3 inflammasome (NLRP3) (94). Ren *et al* (95) discovered that overexpression of the lncRNA ADAMTS9-AS2 activated NLRP3, induced pyroptosis in cisplatin (DDP)-treated cells, increased the cytotoxicity of high-dose DDP on GC cells and ultimately prevented GC cell growth (Fig. 6). By contrast, using pyroptosis inhibitors Z-VAD-FMK and NSA to treat GC cells treated with high-dose DDP can abolish the inhibitory effect of overexpressed lncRNA ADAMTS9-AS2 on GC cell growth and increase GC cell development (95).

In a study by Yang *et al* (96) the colon adenomatous polyposis gene (APC) was used as the main study object. It was found that overexpression of LINC01133 lowered miR-106a-3p expression in GC samples and eight elevated mRNAs were seen in cells inhibited by AGS-miR-106a-3p. The overexpression of LINC01133 elevated the production of APC mRNA, indicating that the control of miR-106a-3p and APC was primarily responsible for the suppression of GC metastasis by LINC01133 overexpression (96). To determine whether the Wnt signaling pathway is involved in the regulation of GC metastasis by LINC01133/miR-106a-3p, the authors conducted a comprehensive bioinformatics analysis and Gene Ontology bioprocess enrichment analysis and found that 93 mRNAs were potential targets of miR-106a-3p (including the APC gene) (96). These genes are mainly enriched in the Wnt signaling and cell migration pathways and the low expression of LINC01133 affects the Wnt signaling pathway (96). The

Table III. lncRNAs playing a dual role in cancer development.

lncRNA	Effect	Type of cancer
GAS5	Oncogene	Cholangiocarcinoma (120)
	Suppressor	Colorectal cancer (85), gastric cancer (121), cervical cancer (122), liver cancer (123), ovarian cancer (124)
HAND2-AS1	Oncogene	Liver cancer (125)
	Suppressor	Breast cancer (126), colorectal cancer (118,127), gastric adenocarcinoma (128), cervical cancer (129), bladder cancer (130), lung cancer (84)
lncRNA ADAMTS9-AS2	Oncogene	Squamous cell carcinoma of tongue (131)
	Suppressor	Gastric cancer (95)
PCBP1-AS1	Oncogene	Liver cancer (132), cervical cancer (133), prostate cancer (113)
	Suppressor	Vulvar squamous cell carcinoma (134)
ASB16-AS1	Oncogene	Glioma (135), gastric cancer (117)
	Suppressor	Clear cell renal cell carcinoma (136)
CRNDE	Oncogene	Colorectal cancer (110,137), pancreatic cancer (138), cervical cancer (139), ovarian cancer (140), Wilms' tumor (141), hepatocellular carcinoma (142,143), papillary thyroid cancer (144), non-small cell lung cancer (145), prostate cancer (146), osteosarcoma (147), gastric cancer (115,148), breast cancer (149), acute myeloid leukemia (150), medulloblastoma (151), intrahepatic cholangiocarcinoma (152), glioma (153,154), myeloma (155), melanoma (156), gallbladder carcinoma (157)
	Suppressor	Chronic lymphocytic leukemia (158)
LINC00173.v1	Oncogene	Lung cancer (102), colorectal cancer (159)
	Suppressor	Cervical cancer (160)
LINC01133	Oncogene	Lung cancer (161), cervical cancer (162), epithelial ovarian cancer (163), pancreatic cancer (164)
	Suppressor	Breast cancer (165), colorectal cancer (166), gastric cancer (96,167)
lncRNA ANCR	Oncogene	Gastric cancer (73), colorectal cancer (168)
	Suppressor	Breast cancer (169), lung cancer (170)
MALAT1	Oncogene	Colorectal cancer (171,172), lung cancer (39,173), prostate cancer (174,175), gastric cancer (176,177), breast cancer (30)
	Suppressor	Breast cancer (178,179), colon cancers (178)

lncRNA, long non-coding RNA.

enhanced transcriptional activity of the gene plasmid TOP/FOP weakens the activity of the Wnt signaling pathway and enhances the EMT and metastasis of GC cells (96). β -catenin is involved in GC cell adhesion through the catenin-cadherin complex and the Wnt signaling pathway (96). It can also reduce the dependence of the LINC01133/miR-106a-3p/APC axis on the Wnt pathway and promote GC cell migration (96). In a nutshell, LINC01133 overexpression can downregulate miR-106a-3p and promote APC gene expression, inhibit β -catenin nuclear accumulation and Wnt signaling pathway in GC cells and ultimately prevent GC cell metastasis (96) (Fig. 6). To verify the reliability and correctness of the aforesaid research, they must be supplemented with several clinical experiments.

5. lncRNAs acting as both oncogenes and tumor suppressors during cancer development

A number of lncRNAs have been shown to display a dual role as both oncogenes and tumor suppressors in different types

of cancer. This duality of such lncRNAs makes them essential characters in the complex story of cancer development. Based on literature, the present study identified 10 lncRNAs demonstrating this dual role in cancer research, including GAS5, HAND2-AS1, lncRNA ADAMTS9-AS2, PCBP1-AS1, ASB16-AS1, CRNDE, LINC00173.v1, LINC01133, lncRNA ANCR and MALAT1, which has been condensed in Table III. Due to their contrasting roles in various cancers, as diagnostic markers, they must closely match the type of cancer and propose that they are not suitable as therapeutic targets for cancer.

6. Conclusion and prospects

Over the last decade, research into the role of lncRNAs in cancer diagnosis and treatment has steadily increased, becoming an emerging focus in cancer diagnosis and treatment. The development and metastasis of tumors are linked to the aberrant expression of lncRNAs. Overall, the oncogenic and suppressive

roles of lncRNAs in various cancers were reviewed as displayed in Fig. 1. Based on the two aforementioned roles of lncRNAs in cancers, distinct strategies for treating different types of cancer must be employed based on the lncRNAs involved. The discovery of several lncRNAs, their widespread expression patterns in various types of cancer, their tumor specificity and their stability in circulating body fluids (plasma and urine) provides a new basis for developing cancer diagnostics and treatments. Although the structure and function of lncRNAs need to be further explored, these molecules seem very promising to develop new diagnoses and targeted treatment strategies, which offers new paradigms for cancer research and may become a major treatment strategy for cancer in the near future.

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Availability of data and materials

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Authors' contributions

RT and JY were responsible for conceptualization, resources and original draft preparation. HS, JA-A and QZ were responsible for original draft preparation, data collection, analysis, reviewing and editing. DY, KL, AS and JZ were responsible for reviewing and editing. All authors read and approved the final manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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