REVIEW

Cancer Medicine *Open Access* WILEY

Long non-coding small nucleolar RNA host genes in digestive cancers

Huan Yang[1] (iD) | Zheng Jiang[2] | Shuang Wang[2,3] | Yongbing Zhao[2,3] |
Xiaomei Song[2,3] | Yufeng Xiao[1] | Shiming Yang[1] (iD)

[1]Department of Gastroenterology, Xinqiao Hospital, Army Medical University, Chongqing, China

[2]Department of Gastroenterology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

[3]Department of Gastroenterology, People's Hospital of Changshou Chongqing, Chongqing, China

Correspondence
Yufeng Xiao and Shiming Yang, Department of Gastroenterology, Xinqiao Hospital, Army Military Medical University, Chongqing, China.
Email: jackshawxyf@163.com (Y. X.) and shimingyang@yahoo.com (S. Y.)

Funding information
National Natural Science Foundation of China, Grant/Award Number: 81602173; Chongqing Basic Science and Advanced Technology Research Program, Grant/Award Number: cstc2015jcyjBX0021

Abstract

Although long noncoding RNAs (lncRNAs) do not have protein coding capacities, they are involved in the pathogenesis of many types of cancers, including hepatocellular carcinoma, cervical cancer, and gastric cancer. Notably, the roles of lncRNAs are vital in nearly every aspect of tumor biology. Long non-coding small nucleolar RNA host genes (lnc-SNHGs) are abnormally expressed in multiple cancers, including urologic neoplasms, respiratory tumors, and digestive cancers, and play vital roles in these cancers. These host genes could participate in tumorigenesis by regulating proliferation, migration, invasion and apoptosis of tumor cells. This review focuses on the overview of the roles that lnc-SNHGs play in the formation and progression of digestive cancers.

KEYWORDS

cancer, digestive, LncRNA, SNHG

1 | INTRODUCTION

Various studies have shown that the carcinogenic effects of genes are mainly exerted by transcription and protein encoding of genes.[1-3] However, recent studies have shown that less than 2% of the human genome is coding genes, and over 90% of the genes are noncoding genes that play regulatory roles in most systems.[4] Noncoding RNA (ncRNA) can regulate gene expression at different levels such as epigenetic modification, transcription and posttranscription.[5-7] NcRNAs can be divided into short ncRNAs, midsize ncRNAs and lncRNAs according to the length of their nucleotides.[8] Their lengths are 50, 50-200, and more than 200 nucleotides, respectively.[9]

Long noncoding RNAs (lncRNAs) are longer than 200 nucleotides, which participate in the development of tumors in many ways.[10-12] LncRNAs can directly or indirectly interact with target genes at the transcriptional level.[13] At the same time, they can regulate histone modification and chromatin remodeling,[14,15] as well as affect other RNA generations.[16] Additionally, they can act as competitive endogenous RNAs (ceRNAs) or precursors to small RNA molecules.[17,18]

Small nucleolar RNA host genes (SNHGs) are host genes for snoRNAs. Primary RNA transcripts of host genes (including all exons and introns with their snoRNAs) are spliced to many exons and introns. Exons can play roles in the cytoplasm, and the removed introns that contain snoRNAs are processed

further to mediated series of functions in the nucleolus (Figure 1). SnoRNAs consist of 60-300 nucleotides and are mainly located in the nucleolus. They can be directly related to the posttranscriptional modification of some spliceosomal RNAs and ribosomal RNAs, and play crucial roles in the procession of useful ribosomes. Host genes include coding genes and noncoding genes. Long non-coding small nucleolar host genes are one of the classes of SNHGs. Most snoRNAs are located in the introns of their host genes.[19] Some scientists proposed that they might be regulated by host genes through cotranscription,[19] but studies have also shown that the biological properties of host genes are independent of their snoRNA genes.[20,21]

In the human genome, there are 232 host genes, including 15 non-protein coding small nucleolar host genes,[22] while recent studies have revealed increasing lnc-SNHG members in cancers. Previously, researchers recognized that non-coding snoRNA host genes contained only short, conservative, open reading frames without any known functions. However, recent studies have overturned this assumption. Long non-coding small nucleolar host genes are found to be involved in the development of various diseases, including cancer progression, cell apoptosis and survival.[21] Scientists have investigated many lnc-SNHGs in multiple cancers. For instance, Lan et al described that the inhibition of *NUAK1* by *MIR-145a-5p* could inhibit the AKT pathway and reduce nasopharyngeal tumor cell invasion. However, *SNHG1* impaired the capacity of *MIR-145a-5p* to increase *NUAK1* and promoted nasopharyngeal carcinoma distant metastasis.[23] Wang et al also discovered that *SNHG1* could inhibit *MIR-302/372/373/520*'s influence on TGFB1/SMAD3 and RAB11A/Wnt signaling pathway to promote pituitary tumor cell growth, migration and metastasis.[24] Researches have also shown that most lnc-SNHG members play vital roles in digestive cancer progression. Li et al proposed that *SNHG5* could upregulate CTNNB1, MYC and CCND1 expression to activate the Wnt signaling pathway and then induce Epithelial-mesenchymal transition (EMT) to promote liver cancer cell invasion.[25] *SNHG17* bound with EZH2 and inhibited the expression of *CDKN2B* and *CDKN1C* to promote gastric cancer cell cycle progression.[26] However, since the biofunctions, molecular mechanisms and potential pathways of SNHGs in digestive cancers are complicated, and they have not yet been clearly defined. Thus, we try to review them here for a better clarification.

2 | LNC-SNHGS IN DIGESTIVE CANCERS

In 1997, Mark et al first reported the small nucleolar RNA host gene *SNHG1* as the host gene of *SNORD22*. They detected the location of *SNHG1* in chromosome 11q13 and *SNORD22* in the nucleolus. There was little protein coding ability for the host gene of *SNORD22*.[27] Subsequently, *SNHG3*,[28] *GAS5*,[29] *SNHG5*[30] were reported in succession, and hundreds of the genes have been researched to date. The Lnc-SNHG family includes many members, in which the most associated with digestive cancers are *SNHG1*, *GAS (SNHG2)*, *SNHG3*, *SNHG5*, *SNHG6*, *SNHG7*, *SNHG8*, *SNHG9*, *SNHG12*, *DANCR (SNHG13)*, *SNHG14*, *SNHG15*, *SNHG16*, *SNHG17*, *SNHG18* and *SNHG20*. Multiple molecular regulatory mechanisms of each SNHG member are involved in different human cancers. Some SNHGs can act as sponges of microRNAs to inhibit the roles of microRNAs in tumorigenesis and affect tumor progression.[23,31,32] On the other hand, they can also bind proteins to influence target genes or impact tumorigenesis via different signaling pathways, including the EMT, Wnt, PIK3CA, NF-κB, and TP53 signaling pathways.[33-35] Moreover, the relationship with transcriptional activation also participates in the progression.[36] The biological effects are mainly exerted through the above mechanisms. However, additional studies are needed to learn more about the regulation and control of SNHG members. Here, according to the reported results, we have constructed a table describing each SNHG member's alternative name, relative snoRNAs, chromosome location, subcellular location, related pathways and associated digestive cancers types (Table 1).
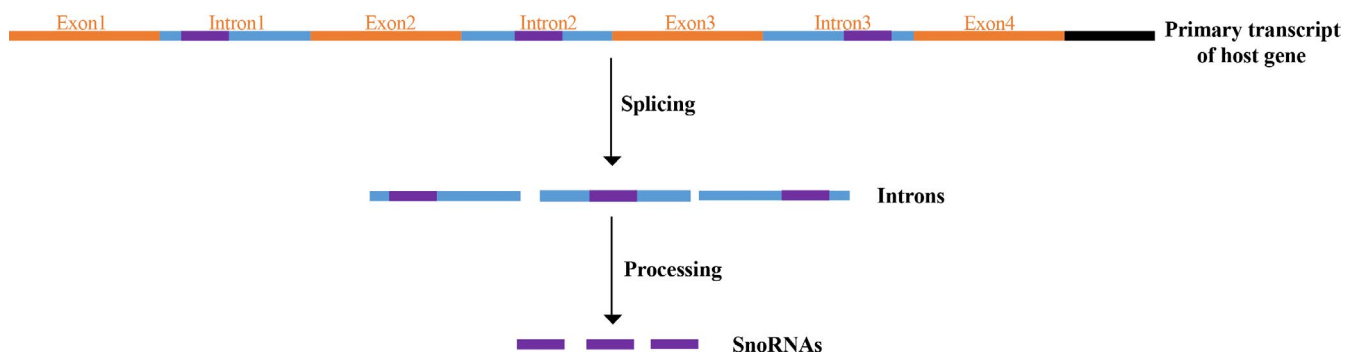

FIGURE 1 Primary RNA transcripts of host genes are spliced to many exons and introns. The removed introns that contain snoRNAs are processed further to mediated series of functions in the nucleolus

3 | BIOLOGICAL FUNCTIONS AND MECHANISMS OF SNHGS IN DIGESTIVE CANCERS

3.1 | SNHGs in colorectal cancer

Among the causes of death from malignant tumors, colon cancer ranks the fourth in China.[37] Although surgical resection is radical, the recurrence rate is still high. Moreover, some patients lost the chances of surgery when they are diagnosed. It is increasingly important to study the treatment of related genes in colon cancer. Higher *SNHG1* expression indicated a poor prognosis in colon cancer. *SNHG1* was determined to be an independent indicator for the poor prognosis of colorectal cancer.[38,39] *SNHG1* is located in both cytoplasm and nucleus. But different researchers have different conclusions about whether *SNHG1* mainly exists in the nucleus or cytoplasm. Bai J et al and Tian T et al showed that *SNHG1* was mainly located in the cytoplasm.[40,41] *SNHG1* could sponge *MIR-497/MIR-195-5p* to influence EMT to facilitate cancer cell migration and invasion,[40] and sponge *MIR-145* to increase the expression of *MIR-145*'s targets, to promote colorectal cancer cell proliferation.[41] On the contrary, Xu et al confirmed the presence of *SNHG1* mainly in the nucleus by performing in situ hybridization and nuclear slurry separation experiments. In the nucleus, *SNHG1* combined with protein EZH2 to decrease the epigenetic impact of *KLF2* and *CDKN2B*.[42] Additionally, downregulation of *SNHG1* could promote apoptosis and reduce the size and weight of tumors in vivo.[38] Yuan Shen et al[33] also found that *SNHG1* could undergo nuclear residency on activation of doxorubicin, and nuclear-resident *SNHG1* competitively binds HNRNPC to weaken the association between HNRNPC and TP53, and to increase TP53's expression level, transcriptional activity and phosphorylation, leading to TP53-dependent apoptosis of colon cancer cells.[33] *SNHG1* also accelerated colorectal cancer tumorigenesis by affecting MYC, CTNNB1, MMP9, and activated the Wnt signaling pathway.[33]

SNHG2, known as *GAS5*, is a tumor suppressor gene that has been thoroughly studied previously. Downregulation of *GAS5* was significantly connected with high malignant level and lymphatic metastasis.[43] Reduced *GAS5* facilitated colon cancer cell migration, proliferation and invasion.[44] Downregulated *GAS5* also promoted the cell cycle in the G0/G1 stage and prevented apoptosis. Increased *GAS5* was an independent marker of a longer overall survival and better prognosis.[43,45]Yuan et al found that co-overexpressed *GAS5* and *SNORD44* could significantly repress tumor growth and they could induce cancer cells apoptosis in both vivo and vitro.[46] The overexpression of *GAS5* could suppress colon cancer cells proliferation and promote apoptosis by inhibiting the expression of *MIR-182-5p* and *MIR-221*, but upregulating *FOXO3a*.[43,44]

SNHG3 acted as an oncogene and accelerated cancer cell growth in tumorigenesis.[47] In colorectal cancer, *SNHG3* could augment the expression of *MYC* and *MYC*'s target genes *CCNB1*, *CCND2*, *CDK4* and *E2F1*. Combining the results of GSE54632 database and starBase2.1, Huang et al found that *MIR-182-5p* was the only gene that could target *MYC* and at the same time, be sponged by *SNHG3*. *SNHG3* obstructed *MIR-182-5p's* suppression on *MYC* to promote tumor growth.[47]

SNHG5 sponged *MIR-132-3p* and positively regulated *CREB5* to inhibit colon cancer cell apoptosis but promoted cancer cell proliferation, migration and invasion.[48] The upregulation of *SNHG5* led to the increased mRNA expression of *SPATS2*, and *SNHG5* played this role by decreasing the effect of the protein STAU1 on *SPATS2* to promote colon cancer proliferation.[49] Li and Li et al verified that the expression of *SNHG6* in colon cancer tissues was higher than that in normal tissues.[50,51] *SNHG6* could induce EZH2 to bind with the promoter of *CDKN1A* and inhibit the *CDKN1A* function, leading to the growth of cancer cells.[51] In the cytoplasm, *SNHG6* sponged *MIR760* and upregulated its target gene *FOXC1* to promote colon cancer cell proliferation, migration and invasion.[52] *SNHG7* was located in the cell cytoplasm in colon cancer and was highly expressed in colon cancer tissues.[32] Although several mRNAs, including *B3GLCT*, *FUT2*, *MFNG*, *MGAT4A*, *GALNT1*, *GALNT5*, *GALNT7*, *ST3GAL5*, and *ST6GALNAC2* were related, *GALNT7* was the most commonly associated with *SNHG7*. The overexpression of *SNHG7* and *GALNT1* could enhance cell proliferation and invasion. Additionally, *GALNT1* was the direct target gene of *MIR216B*, and *SNHG7* could act as a ceRNA to sponge *MIR216B*, and rescue *GALNT1* to facilitate colon cancer cell invasion. Li Y et al further pointed out that the PIK3CA/AKT/MTOR signaling pathway might play a crucial role in the mechanism induced by *SNHG7*.[53] *SNHG7* also could sponge *MIR216B*, to increase *GALNT1* and activate EMT to promote colorectal cancer cell migration and invasion.[32] Wang et al put forward that *SNHG12* augmented colon cancer proliferation, cell cycle progression and inhibited apoptosis by inhibiting the related proteins CDK4, CDK6 and CCND1, and suppressing CASP3.[54] Shorter overall survival rate and disease-free survival rate were correlated with higher *DANCR* expression. It was determined as an individual poor prognosis factor in colon cancer.[55,56] DANCR could upregulate colon cancer cell proliferation and migration ability by sponging *MIR577* and increase the expression of *HSPB1*.[56] Huang et al and Zhang et al concluded that *SNHG15* and *SNHG16* were both highly expressed in colon cancer samples.[57-59] *SNHG15* could only increase the protein level of SNAI2 but not the mRNA level through preventing SNAI2's ubiquitin.[58] Wnt signaling pathway and ceRNA mechanism might participate in the progression of *SNHG16*.[59] *SNHG17* could bind with EZH2 and regulate *CDKN1C* to promote cell proliferation.[60]

TABLE 1 SNHG members in digestive cancers

SNHG member	Aliases	SnoRNAs	Chromosomal location	Main subcellular location	Related digestive cancer types	Interactions and related genes	Related pathway	Related cell bio-functions	Role	References
SNHG1	LINC00057, NCRNA00057, U22HG, UHG, lncRNA16	SNORD22, SNORD25, SNORD26, SNORD27, SNORD28, SNORD29, SNORD30, SNORD31	11q12.3	Cytoplasm	Colon cancer; gastric cancer; liver cancer; esophageal cancer; cholangiocarcinoma; pancreatic cancer	MIR497/MIR-195-5p, MIR145, EZH2, KLF2, CDKN2B, HNRNPC, TP53, MYC, CTNNB1, MMP9, MIR140, ADAM10, DNMT1, TP53, BAX, FAS, CDKN1A, DNMT1, MIR195, MIR338, CST3, CASP8/3	EMT; TP53 pathway; AKT signaling pathway; Wnt signaling pathway; NOTCH signaling pathway	Proliferation, cycle, apoptosis, migration, invasion	Oncogene	[6,7,23,24,33,38-42,64,65,83-86,102,112,120]
GAS5	SNHG2, NCRNA00030,	SNORD74, SNORD77, SNORD75, SNORD76, SNORD44, SNORD78, SNORD79, SNORD80, SNORD47, SNORD81	1q25.1	Cytoplasm	Colon cancer; gastric cancer; liver cancer; esophageal cancer; pancreatic cancer	MIR-182-5p, MIR-221, FOXO3a, MIR222, MIR23A, MT2A, YBX1, CDKN1A, MIR21, CDH1, VIM, MIR301A, MIR-181c-5p, MIR-32-5p, PTEN	PTEN/AKT/ MTOR pathway; EMT; Wnt signaling pathway; NF-kB pathway	Proliferation, cell cycle, apoptosis, migration, invasion	Antioncogene/ oncogene	[29,34,36,43-46,66,67,87-90,103-105,113,114]
SNHG3	U17HG; RNU17C; RNU17D; U17HG-A; U17HG-AB; NCRNA00014	SNORA73A, SNORA73B	1p35.3	Cytoplasm	Colon cancer; liver cancer	CCNB1, CCND2, CDK4, E2F1, MIR-182-5p, MYC, MIR128, CD151	EMT	Invasion, proliferation	Oncogene	[47,91,92]
SNHG5	C6orf160, LINC00044, NCRNA00044, U50HG	SNORD50A, SNORD50B	6q14.3	Cytoplasm	Colon cancer; gastric cancer; liver cancer;	MIR-132-3p, CREB5, SPATS2, STAU1, METAse, MIR20, BECN1, ATG5, ATG7, LC3-II/LC3-I, MIR32,KLF4,MTA2,MMP2, MMP9, EGFR, CDH1, CDKN1A, MIR-26a-5p, GSK3B,CTNNB1,MYC, CCND1	Wnt signaling pathway; EMT	Apoptosis, proliferation, migration	Antioncogene/ oncogene	[25,31,48,49,68,69]
SNHG6	HBII-276HG, NCRNA00058, U87HG	SNORD87	8q13.1;	Cytoplasm	Colon cancer; gastric cancer; liver cancer; esophageal cancer	EZH2, CDKN1A, MIR760, FOXC1, MIR-101-3p, ZEB1, CDH2, EZH2, CDKN1B, MAPK1, MAPK8, MAPK14, TP53, EZH2, CDKN1A, MIR-101-3p, UPF1	EMT; JNK signaling pathway; TGFB1/SMAD signaling pathway;	Proliferation, apoptosis, migration, invasion	Oncogene	[50-52,70,71,107,108]
SNHG7	NCRNA00061	SNORA17A, SNORA17B	9q34.3	Cytoplasm	Colon cancer; gastric cancer; liver cancer; esophageal cancer;	B3GLCT, FUT2, MFNG, MGAT4A, GALNT1, GALNT5, GALNT7, ST3GAL5, ST6GALNAC2, MIR216B, CDKN2B, CDKN2A	PIK3CA/AKT/ MTOR signaling pathway; EMT	Proliferation, migration, invasion, apoptosis, cell cycle progression	Oncogene	[32,53,72,93,106]

(Continues)

TABLE 1 (Continued)

SNHG member	Aliases	SnoRNAs	Chromosomal location	Main subcellular location	Related digestive cancer types	Interactions and related genes	Related pathway	Related cell bio-functions	Role	References
SNHG8	*LINC00060, NCRNA00060*	*SNORA24*	4q26	Cytoplasm	Liver cancer	*MIR149*	—	Proliferation, cell cycle, apoptosis, migration, invasion	Oncogene	[94]
SNHG9	*NCRNA00062*	*SNORA78*	16p13.3	—	Pancreatic cancer	—	—	Proliferation	Antioncogene	[115]
SNHG12	*C1orf79; PNAS-123; LINC00100: ASLNC04080; NCRNA00100*	*SNORA44, SNORA61, SNORA16A, SNORD99*	1p35.3	Cytoplasm	Colon cancer; gastric cancer; liver cancer;	*CDK4, CDK6, CCND1, CASP3, MIR-199a/b-5p, MIR320, MIR-199a/b-5p*	NF-κB signaling pathway	Proliferation, cell cycle, apoptosis	Oncogene	[54,73,74,95]
DANCR	*AGU2; ANCR; SNHG13; KIAA0114; lncRNA-ANCR*	*SNORA26*	4q12	—	Colon cancer; gastric cancer; liver cancer	*MIR577, HSPB1, NPTN-IT1, EZH2, HDAC3, CTNNB1*	—	Proliferation, invasion, migration	Oncogene	[55,56,75,76,96]
SNHG14	*115HG, IC-SNURF-SNRPN, LNCAT, NCRNA00214, U-UBE3A-ATS, UBE3A-AS, UBE3A-AS1, UBE3A-ATS, UBE3AATS*	*SNORD115-(1 ~ 48), SNORD116-(1 ~ 30), SNORD (64,107,108)*	15q11.2	Cytoplasm	Gastric cancer	*MIR-145, SOX9*	PIK3CA/AKT/MTOR signaling pathway	Migration, invasion, apoptosis	Oncogene	[77]
SNHG15	*C7orf40, MYO1GUT, Linc-Myo1g*	*SNORA9*	7p13	Nucleus	Colon cancer; gastric cancer; pancreatic cancer	*SNAI2, MMP2, MMP9, EZH2, CDKN2B, KLF2*	—	Proliferation, invasion, growth, migration, apoptosis	Oncogene	[57,58,78,116,117]
SNHG16	*Nbla10727, Nbla12061, ncRAN*	*SNORD1A, SNORD1B, SNORD1C*	17q25.1	Cytoplasm	Colon cancer; gastric cancer; esophageal cancer; liver cancer	*MIR-140-5p, MYC, CTNNB1, CCND1, ZEB1*	Wnt signaling pathway	Proliferation, migration, invasion, cell cycle, apoptosis	Antioncogene/oncogene	[59,97,109,110]
SNHG17	*9430008C03Rik*	*SNORA71A, SNORA71B, SNORA71C, SNORA71D*	20q11.23	Nucleus	Colon cancer; gastric cancer	*EZH2, CDKN1C, CDKN2B*	—	Proliferation, cell cycle	Oncogene	[26,60]
SNHG18	—	*SNORD123*	5p15.31	—	Liver cancer	—	—	—	—	—
SNHG20	*C17orf86, LINC00338, NCRNA00338, SCARNA16HG*	*SCARNA16*	17q25.2	Cytoplasm	Colon cancer; gastric cancer; liver cancer	*MIR-495-3p, ZFX*	EMT	Proliferation, invasion, cell cycle	Oncogene	[35,61,79,98]

SNHG20 promoted cancer cell proliferation, migration and invasion, but the flow cytometry results showed that _SNHG20_ was only related to cell cycle progression and had no relationship with cell apoptosis.[61]

3.2 | SNHGs in gastric cancer

Gastric cancer is the third leading cause of death worldwide.[62,63] As described previously in colon cancer tissues, the patients also showed the short life time when the expression of _SNHG1_ was significantly high. Knocking down the expression of _SNHG1_ could reduce the tumor size and suppress cell proliferation and colony formation. Similarly, _SNHG1_ also sponged miRNA in the cytoplasm. _SNHG1_ inhibited the expression of _MIR140_ and upregulated the expression of _ADAM10_ to increase the ability of proliferation and invasion of gastric cancer cells.[64] Additionally, _SNHG1_ could also promote the proliferation of gastric cancer cells by upregulating the expression of _DNMT1_.[65]

GAS5, a tumor inhibitor gene, inhibits gastric cancer cell proliferation, blocks the cell cycle and promotes cell apoptosis.[34,36,66] Li Y et al and Liu X et al showed that _GAS5_ sponged _MIR222_ and _MIR23A_ in gastric cancer tumorigenesis.[34,67] Li et al further studied that _GAS5_ could bind _MIR222_ and regulate the PTEN/AKT/MTOR pathway to decrease gastric cancer proliferation.[34] Another study verified that _GAS5_ combined with the 3'UTR of _MIR23A_ and inhibited the effect of _MT2A_ to impair gastric cancer progression.[67] Additionally, the downregulation of _GAS5_ could only obstruct the protein level of transcriptional activator Y-box binding protein 1 (YBX1), but not reduce its mRNA level. Downregulated _GAS5_ interacted with YBX1 to reduce the expression of CDKN1A and promote the cell cycle.[36] In accordance with _GAS5_, _SNHG5_ could also facilitate gastric cancer cell apoptosis.[68] Moreover, it could reduce cancer cell proliferation and migration.[31] The subcellular location of _SNHG5_ was mainly in the cytoplasm.[69] _SNHG5_ was found to be the target gene of L-methionine-α-deamino-γ-mercaptomethanelyase (METase). Increased METase promoted gastric cancer cell apoptosis by upregulating the expression of _SNHG5_. Upregulated _SNHG5_ reduced _MIR20A_ and led to the overexpression of the apoptosis proteins BECN1, ATG5, ATG7 resulting in increased proportion of LC3-II/LC3-I.[68] Additionally, _SNHG5_ could sponge _MIR32,_ and _MIR32_ could reduce the migration and proliferation effects of _SNHG5_ on gastric cancer cells. Conversely, when _MIR32_ inhibited its target gene _KLF4_, the overexpression of _SNHG5_ could partially prevent _MIR32_ function.[31] Moreover, Zhao et al found that upregulation of _SNHG5_ could prevent MTA2 locating to the nucleus from the cytoplasm, and inhibit gastric cancer cell migration and invasion.[69] They also found that when _SNHG5_ was overexpressed, the protein levels of MMP2, MMP9 and EGFR were reduced, while CDH1 and CDKN1A were upregulated.[69]

In gastric cancer, _SNHG6_ was significantly highly expressed in gastric cancer tissues and in serum.[70,71] Yan K et al suggested that high expression of _SNHG6_ was related to the tumor grade and lymph node metastasis, which predicted a poor prognosis for patients.[70] Yan et al and Li et al both proposed that _SNHG6_ existed not only in the cytoplasm but also in the nucleus, and the proportion in the cytoplasm was nearly 67.5%-80%. It participated in both transcriptional and posttranscriptional regulation.[70,71] In the cytoplasm, _SNHG6_ could suppress _MIR-101-3p_, upregulate _ZEB1_ and _CDH2_, and accelerate EMT progression.[70] In the nucleus, _SNHG6_ could recruit EZH2 to the promoter of _CDKN1B_ to play the transcriptional regulatory role.[70] In another study, downregulation of _SNHG6_ could augment the phosphorylation level of MAPK1, MAPK8 and MAPK14, while increasing the expression of TP53 and decreasing the expression of EZH2. Reduced _SNHG6_ enhanced the expression of _CDKN1A_ via the JNK signaling pathway to participate in tumor growth.[71] Down-regulated _SNHG7_ could arrest gastric cancer cell cycle progression in the G0-G1 period probably because it augmented the expression of CDKN2B and CDKN2A.[72] Yang et al and Zhang et al raised the idea that not only _SNHG12_ accelerated gastric cancer cell proliferation and invasion, but it also determined the adverse events prediction.[73,74] _SNHG12_ could sponge _MIR-199a/b-5p_ and _MIR320_ to promote tumorigenesis.[73,74] _DANCR_ and _SNHG14_ were also upregulated in gastric cancer and could promote cancer cell proliferation, invasion and migration.[75-77] Mao et al described that _DANCR_ could also regulate another lncRNA. They found _DANCR_ inhibited the expression of _NPTN-IT1_ by binding with EZH2 and HDAC3.[76] _SNHG14_ suppressed the inhibition of _MIR-145_ on _SOX9_, and activated the PIK3CA/AKT/MTOR signaling pathway to accelerate cell proliferation and invasion.[77] _SNHG15_ was expressed at a higher level in cancer tissues, with expression increased by over 1.5-fold compared to the normal tissues. It promoted cell invasion and migration by increasing MMP2 and MMP9.[78] _SNHG17_ bound with EZH2 and inhibited the expression of _CDKN2B_ and _CDKN1C_ to promote gastric cancer cell cycle progression in the G0/G1 phase.[26] Liu et al further proposed that _SNHG20_ could facilitate gastric cancer cell proliferation and invasion.[35] Another study showed _SNHG20_ was located in the cytoplasm, and _SNHG20_ interacted with _MIR-495-3p_ to upregulate _ZFX_, and promoted gastric tumor growth and invasion.[79]

3.3 | SNHGs in liver cancer

The morbidity and mortality of liver cancer are still high in the world.[80,81] α-fetoprotein (AFP) was a crucial factor in predicting the occurrence and recurrence; however, Gao et al found that the high expression of *SNHG1* in the blood plasm was superior to AFP to distinguish liver cancer from the control group, and the combination of *SNHG1* and AFP could further improve the ability of distinguishing hepatic cancer.[82] Gao et al pointed out that upregulated *SNHG1* was associated with advanced tumor, TNM stage and AFP level, but did not correlate with age and smoking status.[82] *SNHG1* promoted liver cancer cell cycle and inhibited apoptosis by suppressing the expression of *TP53*'s target genes, including *BAX*, *FAS*, and *CDKNIA*.[83] Li et al further found that *SNHG1* reduced *TP53* by binding the protein DNMT1, and the overexpression of *TP53* could partially impair the effect of *SNHG1* on cancer tumorigenesis.[84] Other scientists researched the impact of *SNHG1* on sorafenib resistance.[85] Overexpression of *SNHG1* could significantly enhance the sorafenib resistance of liver cancer.[85] Moreover, *SNHG1* sponged *MIR195* to promote cancer cell proliferation and metastasis.[86]

On the contrary, reduced expression of *GAS5* was associated with poor differentiation, advanced TNM stage, tumor size, lymph node metastasis and acted an independent poor prognosis marker for liver cancer.[87,88] *GAS5* could downregulate *MIR21* to prevent cancer cell migration and invasion.[89] Chang et al indicated that *GAS5* repressed cell proliferation by means of reducing VIM, increasing CDH1 and influencing EMT pathway.[90]

The overexpression of *SNHG3* predicted high rates of larger tumor size, portal vein tumor thrombus, sorafenib resistance and relapse.[91,92] It directly combined with *MIR128* to upregulate the expression *CD151*, and activated EMT to promote cell invasion.[91] Li found that the overexpression of *SNHG5* inhibited the suppressive influence of *MIR-26a-5p* on *GSK3B* to promote liver cancer tumorigenesis. Additionally, when *SNHG5* increased *GSK3B* expression, CTNNB1, MYC, and CCND1 were upregulated to activate the Wnt signaling pathway and then induced EMT to promote cancer cell invasion.[25] Cui et al analyzed several datasets from TCGA and GEO database. They found two significantly differentially expressed lncRNAs, named *PVT1* and *SNHG7*. Cell biofunction experiments verified that *SNHG7* could increase cell invasion ability,[93] which implied that *SNHG7* acted as an oncogene to promote tumorigenesis. Dong et al regarded that *SNHG8* promoted liver cancer tumorigenesis and pulmonary metastasis via sponging *MIR149*.[94] *SNHG12* was the host gene of four small nucleolar RNAs—*SNORA44*, *SNORA61*, *SNORA16A* and *SNORD99*. *SNHG12* was expressed at a significantly higher level in cancerous tissues than in normal tissues. But the change of the expression of *SNHG12* did not cause expression fluctuation in the four small nucleolar RNAs.[95] *SNHG12* located mainly in the cytoplasm. Its high expression was related to tumor size, TNM stage, vascular invasion, and relapse and predicted a poor prognosis but was not involved in the AFP level, portal vein tumor thrombosis, tumor differentiation, gender and age. *SNHG12* promoted liver cancer cell proliferation and invasion, and resulted in a marked reduction in apoptosis.[95] *SNHG12* also sponged *MIR-199a/b-5p*, which directly targeted the key markers of the NF-κB signaling pathway.[95] Similar to *SNHG1*, the high expression level of *DANCR* might be a more advanced marker than AFP to identify hepatic cancer no matter in the sensitivity or specificity. *DANCR* might promote cancer cell proliferation and invasion by inhibiting protein CTNNB1.[96] On the contrary, Xu et al showed that *SNHG16* acted as an antioncogene in hepatocellular carcinoma. *SNHG16* was expressed at a lower level in the cancerous tissue than normal tissue, and *SNHG16* could alleviate 5-FU resistance.[97] Liu J et al showed that *SNHG20* played an oncogenic role in liver cancer, and promoted the EMT pathway in cancer progression.[98]

3.4 | SNHGs in esophageal cancer

Esophageal cancer is a common digestive system tumor[99] with the number of cases increasing annually; more than 300,000 people die from this cancer each year.[100] In 2016, the numbers of new cases and fatal cases of esophageal cancer in the United States were approximately 16 910 and 15 910, respectively,[101] indicating the increased morbidity and mortality of esophageal cancer. The discovery of long noncoding RNAs provides further clinical idea for the diagnosis and treatment of esophageal cancer. *SNHG1* was significantly upregulated in esophageal cancer tissues. It also promoted the proliferation, cloning, and invasion of esophageal cancer cells.[6,102] *SNHG1* could activate the NOTCH and EMT pathway to augment cancer cell invasion and growth, while *SNHG1* sponged *MIR338* to increase the expression of CST3 and to downregulate CASP8/3.[6,102] Regarding *GAS5*, in contrast to other digestive cancers types, Li W et al showed that *GAS5* no longer acted as a tumor suppressor gene but acted as an oncogene in esophageal cancer. It could sponge *MIR301A* to affect Wnt and NF-kB signaling pathways to promote cancer cell proliferation, migration and invasion but reduced cell apoptosis.[103] However, Ke et al insisted that *GAS5* was an anticancer gene in esophageal tumor. Overexpression of *GAS5* significantly impeded tumorigenesis via EMT.[104] Huang et al verified the influences of *GAS5* on proliferation, invasion and migration, which was consistent with Ke K's opinions.[105] *SNHG6* and *SNHG7* were both expressed higher in esophageal cancer tissues than normal tissues, and promoted cancer cell proliferation and metastasis.[106-108] Xu et al suggested that CDKN2B and CDKN2A were partially connected to *SNHG7* in the proliferation and metastasis progression.[106] Additionally, reduced *SNHG16*

resulted in the downregulation of key markers of the Wnt signaling pathway, such as MYC, CTNNB1, and CCND1.[109] Furthermore, *SNHG16* showed a positive correlation with *ZEB1* to promote esophageal cancer tumorigenesis by sponging MIR-140-5p.[110]

3.5 | SNHGs in pancreatic cancer

The incidence of pancreatic cancer ranks the eleventh worldwide. The incidence and mortality of pancreatic cancer in developed countries are higher than those in developing countries. In 2012, approximately 338 000 people had pancreatic cancer, and the number of deaths exceeded 331 000. Li et al found that *SNHG1* not only promoted pancreatic cancer tumorigenesis, but also was differently expressed in gemcitabine-resistant and gemcitabine-sensitive pancreatic cells, which suggested that *SNHG1* could play an important role in tumor therapy. The phosphatidylinositol 3-kinase-AKT signaling pathway might affect this drug resistance.[111] Cui et al suggested that *SNHG1* could upregulate the key markers of the NOTCH signaling pathway to affect pancreatic cancer proliferation and invasion.[112] Additionally, *SNHG1* also played a crucial role in pancreatic ductal adenocarcinoma. The PIK3CA/AKT signaling pathway was activated when *SNHG1* was overexpressed.[39] Gao et al put forward that *GAS5* reduced the drug resistance of cancer cells through regulating *MIR-181c-5p* and Hippo pathway.[113] Moreover, *GAS5* could downregulate *MIR-32-5p* and increase the PTEN protein level.[114] *SNHG9* was expressed at a lower level in cancer tissues and serum than in normal tissues, and there were negative correlations with cancer stage, lymph node metastasis, disease prognosis. *SNHG9* played an antioncogenic role and decreased pancreatic cancer cell proliferation.[115] *SNHG15* was mainly located in the nucleus; high expression of *SNHG15* predicted a poor differentiation of pancreatic cancer. In the nucleus, *SNHG15* could bind with EZH2 to the promoter of *CDKN2B* and *KLF2* to inhibit their expression.[116,117]

3.6 | SNHGs in other digestive cancer types

Cholangiocellular carcinoma is a type of tumor with high invasive character.[118] The survival time of most patients is only 2 years after the diagnosis.[119] Yang et al[120] researched The Cancer Genome Atlas CCA, RNA Sequencing data and Gene Expression Omnibus GSE76297 and concluded that *SNHG1* was expressed at a higher level in cholangiocarcinoma tissues than in normal tissues. Upregulated *SNHG1* could promote cholangiocarcinoma cell proliferation, migration, and cell cycle but reduce apoptosis,[121,122] and the interaction between *SNHG1* and EZH2 could target *CDKN1A* to promote the biological behavior of cholangiocarcinoma.[120]

4 | SMALL NUCLEOLAR HOST GENES AND SNORNAS

SnoRNAs could be regulated by their host genes, copy number variation, and DNA methylation.[19] Some scientists pointed out that the host genes may affect the expression of snoRNAs by cotranscription[19]; however, other scholars reported that the functions of some SNHG members were independent of their snoRNAs.[21] Moreover, recent studies have shown that some snoRNAs are also related to cancer tumorigenesis.[21] Scholars have reported that some snoRNAs can produce smaller products during nucleolytic processing, and these products, like microRNAs, can play important roles in tumor progression.[123] Some researchers call these products as sno-miRNAs.[124] Long noncoding RNAs can sponge microRNAs in the cytoplasm, but it is still unclear whether there is a potential pathway by which lnc-SNHGs and snoRNAs jointly regulate microRNAs, which is worthy of further exploration.

5 | CONCLUSION

It has been shown that the irregular expression status of SNHGs is significantly related to digestive tumors stage, metastasis, infiltration, and poor prognosis in cancers. SNHGs also act as prognostic factors in most malignant tumors. Many studies have implied that SNHG members regulate the development of tumor diseases by the means of mediating its sponge miRNAs, activating different signaling pathways, and regulating the expression of key markers. However, these studies are just preliminary discussions; further mechanistic studies on SNHG members and snoRNAs will be required in the future.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

S-M Y, Y-F X and HY designed the study and drafted the manuscript. HY wrote the paper. ZJ revised the paper. X-M S, SW and Y-B Z received and reviewed the manuscript. All authors read and approved the manuscript and agree to be accountable for all aspects of the research.

ORCID

Huan Yang https://orcid.org/0000-0003-3051-5964

Shiming Yang https://orcid.org/0000-0002-5911-8746

REFERENCES

1. Pandey A, Bahl C, Sharma S, Singh N, Behera D. Functional role of CyclinD1 polymorphism (G870A) in modifying susceptibility and overall survival of north indian lung cancer patients. *Tumori J*. 2018;tj.5000707.

2. Wroblewska JP, Mull J, Wu CL, et al. SF3B1, NRAS, KIT, and BRAF mutation; CD117 and cMYC expression; and tumoral pigmentation in sinonasal melanomas: an analysis with newly found molecular alterations and some population-based molecular differences. *Am J Surg Pathol*. 2019;43(2):168-177.

3. Youssef O, Fawzy A, Elshimy R, Almangush A, Mahmoud AM, Loay I. Expression of plasma miRNA-221 in colorectal carcinoma patients and its diagnostic significance in comparison with p53 expression. *Clin Lab*. 2018;64(9):1527-1533.

4. Isaac C, Patel TR, Zovoilis A. Non-coding RNAs in virology: an RNA genomics approach. *Biotechnol Genet Eng Rev*. 2018;34(1):90-106.

5. Fawzy MS, Abu AlSel BT, Al Ageeli E, Al-Qahtani SA, Abdel-Daim MM, Toraih EA. Long non-coding RNA MALAT1 and microRNA-499a expression profiles in diabetic ESRD patients undergoing dialysis: a preliminary cross-sectional analysis. *Arch Physiol Biochem*. 2018;1-11. https://doi.org/10.1080/13813455.2018.1499119. [Epub ahead of print]

6. Yan Y, Fan Q, Wang L, Zhou Y, Li J, Zhou K. LncRNA Snhg1, a non-degradable sponge for miR-338, promotes expression of proto-oncogene CST3 in primary esophageal cancer cells. *Oncotarget*. 2017;8(22):35750-35760.

7. Li J, Zhang Z, Xiong L, et al. SNHG1 lncRNA negatively regulates miR-199a-3p to enhance CDK7 expression and promote cell proliferation in prostate cancer. *Biochem Biophys Res Commun*. 2017;487(1):146-152.

8. Esteller M. Non-coding RNAs in human disease. *Nat Rev Genet*. 2011;12(12):861-874.

9. Fatica A, Bozzoni I. Long non-coding RNAs: new players in cell differentiation and development. *Nat Rev Genet*. 2014;15(1):7-21.

10. Yuan JH, Yang F, Wang F, et al. A long noncoding RNA activated by TGF-beta promotes the invasion-metastasis cascade in hepatocellular carcinoma. *Cancer Cell*. 2014;25(5):666-681.

11. Li L, Zhang L, Zhang Y, Zhou F. Increased expression of LncRNA BANCR is associated with clinical progression and poor prognosis in gastric cancer. *Biomed Pharmacother*. 2015;72:109-112.

12. Chen J, Fu Z, Ji C, et al. Systematic gene microarray analysis of the lncRNA expression profiles in human uterine cervix carcinoma. *Biomed Pharmacother*. 2015;72:83-90.

13. Jiang W, Liu Y, Liu R, Zhang K, Zhang Y. The lncRNA DEANR1 facilitates human endoderm differentiation by activating FOXA2 expression. *Cell Rep*. 2015;11(1):137-148.

14. Yang F, Deng X, Ma W, et al. The lncRNA Firre anchors the inactive X chromosome to the nucleolus by binding CTCF and maintains H3K27me3 methylation. *Genome Biol*. 2015;16:52.

15. Xiao T, Liu L, Li H, et al. Long noncoding RNA ADINR regulates adipogenesis by transcriptionally activating C/EBPalpha. *Stem Cell Reports*. 2015;5(5):856-865.

16. Pefanis E, Wang J, Rothschild G, et al. RNA exosome-regulated long non-coding RNA transcription controls super-enhancer activity. *Cell*. 2015;161(4):774-789.

17. Salmena L, Poliseno L, Tay Y, Kats L, Pandolfi PP. A ceRNA hypothesis: the Rosetta Stone of a hidden RNA language? *Cell*. 2011;146(3):353-358.

18. Wilusz JE, Sunwoo H, Spector DL. Long noncoding RNAs: functional surprises from the RNA world. *Genes Dev*. 2009;23(13):1494-1504.

19. Gong J, Li Y, Liu C-J, et al. A pan-cancer analysis of the expression and clinical relevance of small nucleolar RNAs in human cancer. *Cell Rep*. 2017;21(7):1968-1981.

20. Askarian-Amiri ME, Crawford J, French JD, et al. SNORD-host RNA Zfas1 is a regulator of mammary development and a potential marker for breast cancer. *RNA*. 2011;17(5):878-891.

21. Williams GT, Farzaneh F. Are snoRNAs and snoRNA host genes new players in cancer? *Nat Rev Cancer*. 2012;12(2):84-88.

22. Herter EK, Stauch M, Gallant M, Wolf E, Raabe T, Gallant P. snoRNAs are a novel class of biologically relevant Myc targets. *BMC Biol*. 2015;13:25.

23. Lan X, Liu X. LncRNA SNHG1 functions as a ceRNA to antagonize the effect of miR-145a-5p on the down-regulation of NUAK1 in nasopharyngeal carcinoma cell. *J Cell Mol Med*. 2018.

24. Wang H, Wang G, Gao Y, et al. Lnc-SNHG1 activates the TGFBR2/SMAD3 and RAB11A/Wnt/beta-catenin pathway by sponging MiR-302/372/373/520 in invasive pituitary tumors. *Cell Physiol Biochem*. 2018;48(3):1291-1303.

25. Li Y, Guo D, Zhao Y, et al. Long non-coding RNA SNHG5 promotes human hepatocellular carcinoma progression by regulating miR-26a-5p/GSK3beta signal pathway. *Cell Death Dis*. 2018;9(9):888.

26. Zhang G, Xu Y, Wang S, et al. LncRNA SNHG17 promotes gastric cancer progression by epigenetically silencing of p15 and p57. *J Cell Physiol*. 2019;234(4):5163-5174.

27. Frey MR, Wu W, Dunn JM, Matera AG. The U22 host gene (UHG): chromosomal localization of UHG and distribution of U22 small nucleolar RNA. *Histochem Cell Biol*. 1997;108(4–5):365-370.

28. Pelczar P, Filipowicz W. The host gene for intronic U17 small nucleolar RNAs in mammals has no protein-coding potential and is a member of the 5'-terminal oligopyrimidine gene family. *Mol Cell Biol*. 1998;18(8):4509-4518.

29. Smith CM, Steitz JA. Classification of gas5 as a multi-small-nucleolar-RNA (snoRNA) host gene and a member of the 5'-terminal oligopyrimidine gene family reveals common features of snoRNA host genes. *Mol Cell Biol*. 1998;18(12):6897-6909.

30. Tanaka R, Satoh H, Moriyama M, et al. Intronic U50 small-nucleolar-RNA (snoRNA) host gene of no protein-coding potential is mapped at the chromosome breakpoint t(3;6)(q27;q15) of human B-cell lymphoma. *Genes Cells*. 2000;5(4):277-287.

31. Zhao L, Han T, Li Y, et al. The lncRNA SNHG5/miR-32 axis regulates gastric cancer cell proliferation and migration by targeting KLF4. *FASEB J*. 2017;31(3):893-903.

32. Shan Y, Ma J, Pan Y, Hu J, Liu B, Jia L. LncRNA SNHG7 sponges miR-216b to promote proliferation and liver metastasis of colorectal cancer through upregulating GALNT1. *Cell Death Dis*. 2018;9(7):722.

33. Shen Y, Liu S, Fan J, et al. Nuclear retention of the lncRNA SNHG1 by doxorubicin attenuates hnRNPC-p53 protein interactions. *EMBO Rep*. 2017;18(4):536-548.

34. Li Y, Gu J, Lu H. The GAS5/miR-222 axis regulates proliferation of gastric cancer cells Through the PTEN/Akt/mTOR pathway. _Dig Dis Sci_. 2017;62(12):3426-3437.

35. Liu J, Liu L, Wan JX, Song Y. Long noncoding RNA SNHG20 promotes gastric cancer progression by inhibiting p21 expression and regulating the GSK-3beta/ beta-catenin signaling pathway. _Oncotarget_. 2017;8(46):80700-80708.

36. Liu Y, Zhao J, Zhang W, et al. lncRNA GAS5 enhances G1 cell cycle arrest via binding to YBX1 to regulate p21 expression in stomach cancer. _Sci Rep_. 2015;5:10159.

37. Zhai X, Xue Q, Liu Q, Guo Y, Chen Z. Colon cancer recurrenceassociated genes revealed by WGCNA coexpression network analysis. _Mol Med Rep_. 2017;16(5):6499-6505.

38. Sun X, Wang Z, Yuan W. Down-regulated long non-coding RNA SNHG1 inhibits tumor genesis of colorectal carcinoma. _Cancer Biomark_. 2017;20(1):67-73.

39. Zhang Y, Zhang R, Luo G, Ai K. Long noncoding RNA SNHG1 promotes cell proliferation through PI3K/AKT signaling pathway in pancreatic ductal adenocarcinoma. _J Cancer_. 2018;9(15):2713-2722.

40. Bai J, Xu J, Zhao J, Zhang R. lncRNA SNHG1 cooperated with miR-497/miR-195-5p to modify epithelial-mesenchymal transition underlying colorectal cancer exacerbation. _J Cell Physiol_. 2019.

41. Tian T, Qiu R, Qiu X. SNHG1 promotes cell proliferation by acting as a sponge of miR-145 in colorectal cancer. _Oncotarget_. 2018;9(2):2128-2139.

42. Xu MU, Chen X, Lin K, et al. The long noncoding RNA SNHG1 regulates colorectal cancer cell growth through interactions with EZH2 and miR-154-5p. _Mol Cancer_. 2018;17(1):141.

43. Cheng K, Zhao Z, Wang G, Wang J, Zhu W. lncRNA GAS5 inhibits colorectal cancer cell proliferation via the miR1825p/FOXO3a axis. _Oncol Rep_. 2018;40(4):2371-2380.

44. Liu L, Meng T, Yang XH, et al. Prognostic and predictive value of long non-coding RNA GAS5 and mircoRNA-221 in colorectal cancer and their effects on colorectal cancer cell proliferation, migration and invasion. _Cancer Biomark_. 2018;22(2):283-299.

45. Yang Y, Shen Z, Yan Y, et al. Long non-coding RNA GAS5 inhibits cell proliferation, induces G0/G1 arrest and apoptosis, and functions as a prognostic marker in colorectal cancer. _Oncol Lett_. 2017;13(5):3151-3158.

46. Yuan S, Wu Y, Wang Y, Chen J, Chu L. An oncolytic adenovirus expressing SNORD44 and GAS5 exhibits antitumor effect in colorectal cancer cells. _Hum Gene Ther_. 2017;28(8):690-700.

47. Huang W, Tian Y, Dong S, et al. The long non-coding RNA SNHG3 functions as a competing endogenous RNA to promote malignant development of colorectal cancer. _Oncol Rep_. 2017;38(3):1402-1410.

48. Zhang M, Li Y, Wang H, Yu W, Lin S, Guo J. LncRNA SNHG5 affects cell proliferation, metastasis and migration of colorectal cancer through regulating miR-132-3p/CREB5. _Cancer Biol Ther_. 2018;1-13.

49. Damas ND, Marcatti M, Côme C, et al. SNHG5 promotes colorectal cancer cell survival by counteracting STAU1-mediated mRNA destabilization. _Nat Commun_. 2016;7:13875.

50. Li M, Bian Z, Yao S, et al. Up-regulated expression of SNHG6 predicts poor prognosis in colorectal cancer. _Pathol Res Pract_. 2018;214(5):784-789.

51. Li Z, Qiu R, Qiu X, Tian T. SNHG6 promotes tumor growth via repression of P21 in colorectal cancer. _Cell Physiol Biochem_. 2018;49(2):463-478.

52. Zhu Y, Xing Y, Chi F, Sun W, Zhang Z, Piao D. Long noncoding RNA SNHG6 promotes the progression of colorectal cancer through sponging miR-760 and activation of FOXC1. _Onco Targets Ther_. 2018;11:5743-5752.

53. Li Y, Zeng C, Hu J, et al. Long non-coding RNA-SNHG7 acts as a target of miR-34a to increase GALNT7 level and regulate PI3K/Akt/mTOR pathway in colorectal cancer progression. _J Hematol Oncol_. 2018;11(1):89.

54. Wang JZ, Xu CL, Wu H, Shen SJ. LncRNA SNHG12 promotes cell growth and inhibits cell apoptosis in colorectal cancer cells. _Braz J Med Biol Res_. 2017;50(3):e6079.

55. Liu Y, Zhang M, Liang L, Li J, Chen YX. Over-expression of lncRNA DANCR is associated with advanced tumor progression and poor prognosis in patients with colorectal cancer. _Int J Clin Exp Pathol_. 2015;8(9):11480-11484.

56. Wang Y, Lu Z, Wang N, et al. Long noncoding RNA DANCR promotes colorectal cancer proliferation and metastasis via miR-577 sponging. _Exp Mol Med_. 2018;50(5):57.

57. Huang L, Lin H, Kang L, et al. Aberrant expression of long noncoding RNA SNHG15 correlates with liver metastasis and poor survival in colorectal cancer. _J Cell Physiol_. 2019;234(5):7032-7039.

58. Jiang H, Li T, Qu YI, et al. Long non-coding RNA SNHG15 interacts with and stabilizes transcription factor Slug and promotes colon cancer progression. _Cancer Lett_. 2018;425:78-87.

59. Christensen LL, True K, Hamilton MP, et al. SNHG16 is regulated by the Wnt pathway in colorectal cancer and affects genes involved in lipid metabolism. _Mol Oncol_. 2016;10(8):1266-1282.

60. Ma Z, Gu S, Song M, et al. Long non-coding RNA SNHG17 is an unfavourable prognostic factor and promotes cell proliferation by epigenetically silencing P57 in colorectal cancer. _Mol Biosyst_. 2017;13(11):2350-2361.

61. Li C, Zhou L, He J, Fang XQ, Zhu SW, Xiong MM. Increased long noncoding RNA SNHG20 predicts poor prognosis in colorectal cancer. _BMC Cancer_. 2016;16:655.

62. Yu B, Xie J. Identifying therapeutic targets in gastric cancer: the current status and future direction. _Acta Biochim Biophys Sin (Shanghai)_. 2016;48(1):90-96.

63. Barati T, Haddadi M, Sadeghi F, et al. AGS cell line xenograft tumor as a suitable gastric adenocarcinoma model: growth kinetic characterization and immunohistochemistry analysis. _Iran J Basic Med Sci_. 2018;21(7):678-681.

64. Guo W, Huang J, Lei P, Guo L, Li X. LncRNA SNHG1 promoted HGC-27 cell growth and migration via the miR-140/ADAM10 axis. _Int J Biol Macromol_. 2019;122:817-823.

65. Hu Y, Ma Z, He Y, Liu W, Su Y, Tang Z. LncRNA-SNHG1 contributes to gastric cancer cell proliferation by regulating DNMT1. _Biochem Biophys Res Commun_. 2017;491(4):926-931.

66. Sun M, Jin FY, Xia R, et al. Decreased expression of long noncoding RNA GAS5 indicates a poor prognosis and promotes cell proliferation in gastric cancer. _BMC Cancer_. 2014;14:319.

67. Liu X, Jiao T, Wang Y, Su W, Tang Z, Han C. Long non-coding RNA GAS5 acts as a molecular sponge to regulate miR-23a in gastric cancer. _Minerva Med_. 2016. PMID: 27827524. [Epub ahead of print]

68. Xin L, Zhou LQ, Liu L, Yuan YW, Zhang HT, Zeng F. METase promotes cell autophagy via promoting SNHG5 and suppressing miR-20a in gastric cancer. _Int J Biol Macromol_. 2019;122:1046-1052.

69. Zhao L, Guo H, Zhou B, et al. Long non-coding RNA SNHG5 suppresses gastric cancer progression by trapping MTA2 in the cytosol. _Oncogene_. 2016;35(44):5770-5780.

70. Yan K, Tian J, Shi W, Xia H, Zhu Y. LncRNA SNHG6 is associated with poor prognosis of gastric cancer and promotes cell proliferation and EMT through epigenetically silencing p27 and sponging miR-101-3p. _Cell Physiol Biochem_. 2017;42(3):999-1012.

71. Li Y, Li D, Zhao M, et al. Long noncoding RNA SNHG6 regulates p21 expression via activation of the JNK pathway and regulation of EZH2 in gastric cancer cells. _Life Sci_. 2018;208:295-304.

72. Wang MW, Liu J, Liu Q, et al. LncRNA SNHG7 promotes the proliferation and inhibits apoptosis of gastric cancer cells by repressing the P15 and P16 expression. _Eur Rev Med Pharmacol Sci_. 2017;21(20):4613-4622.

73. Yang BF, Cai W, Chen B. LncRNA SNHG12 regulated the proliferation of gastric carcinoma cell BGC-823 by targeting microRNA-199a/b-5p. _Eur Rev Med Pharmacol Sci_. 2018;22(5):1297-1306.

74. Zhang H, Lu W. LncRNA SNHG12 regulates gastric cancer progression by acting as a molecular sponge of miR320. _Mol Med Rep_. 2018;17(2):2743-2749.

75. Hao YP, Qiu JH, Zhang DB, Yu CG. Long non-coding RNA DANCR, a prognostic indicator, promotes cell growth and tumorigenicity in gastric cancer. _Tumour Biol_. 2017;39(6):1010428317699798.

76. Mao Z, Li H, Du B, et al. LncRNA DANCR promotes migration and invasion through suppression of lncRNA-LET in gastric cancer cells. _Biosci Rep_. 2017;37(6):BSR20171070.

77. Liu Z, Yan Y, Cao S, Chen Y. Long non-coding RNA SNHG14 contributes to gastric cancer development through targeting miR-145/SOX9 axis. _J Cell Biochem_. 2018;119(8):6905-6913.

78. Chen SX, Yin JF, Lin BC, et al. Upregulated expression of long noncoding RNA SNHG15 promotes cell proliferation and invasion through regulates MMP2/MMP9 in patients with GC. _Tumour Biol_. 2016;37(5):6801-6812.

79. Cui N, Liu J, Xia H, Xu D. LncRNA SNHG20 contributes to cell proliferation and invasion by upregulating ZFX expression sponging miR-495-3p in gastric cancer. _J Cell Biochem_. 2019;120(3):3114-3123.

80. Bishayee A. The role of inflammation and liver cancer. _Adv Exp Med Biol_. 2014;816:401-435.

81. Pan Y, Tong S, Cui R, et al. Long non-coding MALAT1 functions as a competing endogenous RNA to regulate vimentin expression by sponging miR-30a-5p in hepatocellular carcinoma. _Cell Physiol Biochem_. 2018;50(1):108-120.

82. Gao S, Xu X, Wang Y, Zhang W, Wang X. Diagnostic utility of plasma lncRNA small nucleolar RNA host gene 1 in patients with hepatocellular carcinoma. _Mol Med Rep_. 2018;18(3):3305-3313.

83. Zhang M, Wang W, Li T, et al. Long noncoding RNA SNHG1 predicts a poor prognosis and promotes hepatocellular carcinoma tumorigenesis. _Biomed Pharmacother_. 2016;80:73-79.

84. Li SJ, Wang L, Sun ZX, Sun SJ, Gao J, Ma RL. LncRNA SNHG1 promotes liver cancer development through inhibiting p53 expression via binding to DNMT1. _Eur Rev Med Pharmacol Sci_. 2019;23(7):2768-2776.

85. Li W, Dong X, He C, et al. LncRNA SNHG1 contributes to sorafenib resistance by activating the Akt pathway and is positively regulated by miR-21 in hepatocellular carcinoma cells. _J Exp Clin Cancer Res_. 2019;38(1):183.

86. Zhang H, Zhou D, Ying M, et al. Expression of long non-coding RNA (lncRNA) small nucleolar RNA host gene 1 (SNHG1) exacerbates hepatocellular carcinoma through suppressing miR-195. _Med Sci Monit_. 2016;22:4820-4829.

87. Wang Y, Jing W, Ma W, Liang C, Chai H, Tu J. Down-regulation of long non-coding RNA GAS5-AS1 and its prognostic and diagnostic significance in hepatocellular carcinoma. _Cancer Biomark_. 2018;22(2):227-236.

88. Tu ZQ, Li RJ, Mei JZ, Li XH. Down-regulation of long non-coding RNA GAS5 is associated with the prognosis of hepatocellular carcinoma. _Int J Clin Exp Pathol_. 2014;7(7):4303-4309.

89. Hu L, Ye H, Huang G, et al. Long noncoding RNA GAS5 suppresses the migration and invasion of hepatocellular carcinoma cells via miR-21. _Tumour Biol_. 2016;37(2):2691-2702.

90. Chang L, Li C, Lan T, et al. Decreased expression of long noncoding RNA GAS5 indicates a poor prognosis and promotes cell proliferation and invasion in hepatocellular carcinoma by regulating vimentin. _Mol Med Rep_. 2016;13(2):1541-1550.

91. Zhang PF, Wang F, Wu J, et al. LncRNA SNHG3 induces EMT and sorafenib resistance by modulating the miR-128/CD151 pathway in hepatocellular carcinoma. _J Cell Physiol_. 2019;234(3):2788-2794.

92. Zhang T, Cao C, Wu D, Liu L. SNHG3 correlates with malignant status and poor prognosis in hepatocellular carcinoma. _Tumour Biol_. 2016;37(2):2379-2385.

93. Cui H, Zhang Y, Zhang Q, Chen W, Zhao H, Liang J. A comprehensive genome-wide analysis of long noncoding RNA expression profile in hepatocellular carcinoma. _Cancer Med_. 2017;6(12):2932-2941.

94. Dong J, Teng F, Guo W, Yang J, Ding G, Fu Z. lncRNA SNHG8 promotes the tumorigenesis and metastasis by sponging miR-149-5p and predicts tumor recurrence in hepatocellular carcinoma. _Cell Physiol Biochem_. 2018;51(5):2262-2274.

95. Lan T, Ma W, Hong Z, Wu L, Chen X, Yuan Y. Long non-coding RNA small nucleolar RNA host gene 12 (SNHG12) promotes tumorigenesis and metastasis by targeting miR-199a/b-5p in hepatocellular carcinoma. _J Exp Clin Cancer Res_. 2017;36(1):11.

96. Ma X, Wang X, Yang C, et al. DANCR acts as a diagnostic biomarker and promotes tumor growth and metastasis in hepatocellular carcinoma. _Anticancer Res_. 2016;36(12):6389-6398.

97. Xu F, Zha G, Wu Y, Cai W, Ao J. Overexpressing lncRNA SNHG16 inhibited HCC proliferation and chemoresistance by functionally sponging hsa-miR-93. _Onco Targets Ther_. 2018;11:8855-8863.

98. Liu J, Lu C, Xiao M, Jiang F, Qu L, Ni R. Long non-coding RNA SNHG20 predicts a poor prognosis for HCC and promotes cell invasion by regulating the epithelial-to-mesenchymal transition. _Biomed Pharmacother_. 2017;89:857-863.

99. Low DE, Allum W, De Manzoni G, et al. Guidelines for perioperative care in esophagectomy: enhanced recovery after surgery (ERAS((R))) society recommendations. _World J Surg_. 2019;43:299-330.

100. Shi Y, Zhang B, Feng X, et al. Apoptosis and autophagy induced by DVDMs-PDT on human esophageal cancer Eca-109 cells. _Photodiagnosis Photodyn Ther_. 2018;24:198-205.

101. Short MW, Burgers KG, Fry VT. Esophageal cancer. _Am Fam Physician_. 2017;95(1):22-28.

102. Zhang Y, Jin X, Wang Z, Zhang X, Liu S, Liu G. Downregulation of SNHG1 suppresses cell proliferation and invasion by regulating Notch signaling pathway in esophageal squamous cell cancer. _Cancer Biomark_. 2017;21(1):89-96.

103. Li W, Zhao W, Lu Z, Zhang W, Yang X. Long noncoding RNA GAS5 promotes proliferation, migration, and invasion by regulation of miR-301a in esophageal cancer. _Oncol Res_. 2018;26(8):1285-1294.

104. Ke K, Sun Z, Wang Z. Downregulation of long non-coding RNA GAS5 promotes cell proliferation, migration and invasion in esophageal squamous cell carcinoma. *Oncol Lett*. 2018;16(2):1801-1808.

105. Huang J, Li Y, Lu Z, et al. Long non-coding RNA GAS5 is induced by interferons and plays an antitumor role in esophageal squamous cell carcinoma. *Cancer Med*. 2018. https://doi.org/10.1002/cam4.1524. [Epub ahead of print].

106. Xu LJ, Yu XJ, Wei B, et al. LncRNA SNHG7 promotes the proliferation of esophageal cancer cells and inhibits its apoptosis. *Eur Rev Med Pharmacol Sci*. 2018;22(9):2653-2661.

107. Fan RH, Guo JN, Yan W, et al. Small nucleolar host gene 6 promotes esophageal squamous cell carcinoma cell proliferation and inhibits cell apoptosis. *Oncol Lett*. 2018;15(5):6497-6502.

108. Zhang Y, Li R, Ding X, Zhang K, Qin W. Upregulation of long non-coding RNA SNHG6 promote esophageal squamous cell carcinoma cell malignancy and its diagnostic value. *Am J Transl Res*. 2019;11(2):1084-1091.

109. Han GH, Lu KJ, Wang P, Ye J, Ye YY, Huang JX. LncRNA SNHG16 predicts poor prognosis in ESCC and promotes cell proliferation and invasion by regulating Wnt/beta-catenin signaling pathway. *Eur Rev Med Pharmacol Sci*. 2018;22(12):3795-3803.

110. Zhang K, Chen J, Song H, Chen LB. SNHG16/miR-140-5p axis promotes esophagus cancer cell proliferation, migration and EMT formation through regulating ZEB1. *Oncotarget*. 2018;9(1):1028-1040.

111. Li D, Qian X, Xu P, et al. Identification of lncRNAs and their functional network associated with chemoresistance in SW1990/GZ pancreatic cancer cells by RNA sequencing. *DNA Cell Biol*. 2018;37(10):839-849.

112. Cui L, Dong Y, Wang X, et al. Downregulation of long noncoding RNA SNHG1 inhibits cell proliferation, metastasis, and invasion by suppressing the Notch-1 signaling pathway in pancreatic cancer. *J Cell Biochem*. 2019;120(4):6106-6112.

113. Gao ZQ, Wang JF, Chen DH, et al. Long non-coding RNA GAS5 antagonizes the chemoresistance of pancreatic cancer cells through down-regulation of miR-181c-5p. *Biomed Pharmacother*. 2018;97:809-817.

114. Gao ZQ, Wang JF, Chen DH, et al. Long non-coding RNA GAS5 suppresses pancreatic cancer metastasis through modulating miR-32-5p/PTEN axis. *Cell Biosci*. 2017;7:66.

115. Zhang B, Li C, Sun Z. Long non-coding RNA LINC00346, LINC00578, LINC00673, LINC00671, LINC00261, and SNHG9 are novel prognostic markers for pancreatic cancer. *Am J Transl Res*. 2018;10(8):2648-2658.

116. Ma Z, Huang H, Wang J, et al. Long non-coding RNA SNHG15 inhibits P15 and KLF2 expression to promote pancreatic cancer proliferation through EZH2-mediated H3K27me3. *Oncotarget*. 2017;8(48):84153-84167.

117. Guo XB, Yin HS, Wang JY. Evaluating the diagnostic and prognostic value of long non-coding RNA SNHG15 in pancreatic ductal adenocarcinoma. *Eur Rev Med Pharmacol Sci*. 2018;22(18):5892-5898.

118. Kizy S, Altman AM, Marmor S, et al. Surgical resection of lymph node positive intrahepatic cholangiocarcinoma may not improve survival. *HPB (Oxford)*. 2019;21:235-241.

119. Lee MY, Li YZ, Huang KJ, Huang HC, Lin CY, Lee YR. Indirubin-3'-oxime suppresses human cholangiocarcinoma through cell-cycle arrest and apoptosis. *Eur J Pharmacol*. 2018;839:57-65.

120. Yu Y, Zhang M, Wang N, et al. Epigenetic silencing of tumor suppressor gene CDKN1A by oncogenic long non-coding RNA SNHG1 in cholangiocarcinoma. *Cell Death Dis*. 2018;9(7):746.

121. Shen X, Liu Y, Hsu YJ, et al. EZH1 mediates methylation on histone H3 lysine 27 and complements EZH2 in maintaining stem cell identity and executing pluripotency. *Mol Cell*. 2008;32(4):491-502.

122. Yamaguchi H, Hung MC. Regulation and role of EZH2 in Cancer. *Cancer Res Treat*. 2014;46(3):209-222.

123. Ender C, Krek A, Friedlander MR, et al. A human snoRNA with microRNA-like functions. *Mol Cell*. 2008;32(4):519-528.

124. Brameier M, Herwig A, Reinhardt R, Walter L, Gruber J. Human box C/D snoRNAs with miRNA like functions: expanding the range of regulatory RNAs. *Nucleic Acids Res*. 2011;39(2):675-686.