INTRODUCTION

Various studies have shown that the carcinogenic effects of genes are mainly exerted by transcription and protein encoding of genes. 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. Noncoding RNA (ncRNA) can regulate gene expression at different levels such as epigenetic modification, transcription and posttranscription. NcRNAs can be divided into short ncRNAs, midsize ncRNAs and IncRNAs according to the length of their nucleotides. Their lengths are 50, 50-200, and more than 200 nucleotides, respectively. Long noncoding RNAs (IncRNAs) are longer than 200 nucleotides, which participate in the development of tumors in many ways. LncRNAs can directly or indirectly interact with target genes at the transcriptional level. At the same time, they can regulate histone modification and chromatin remodeling, as well as affect other RNA generations. Additionally, they can act as competitive endogenous RNAs (ceRNAs) or precursors to small RNA molecules. 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. Some scientists proposed that they might be regulated by host genes through cotranscription, but studies have also shown that the biological properties of host genes are independent of their snoRNA genes. In the human genome, there are 232 host genes, including 15 non-protein coding small nucleolar host genes, 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. Scientists have investigated many Inc-SNHGs in multiple cancers. For instance, Lan et al described that the inhibition of NUA1 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 NUA1 and promoted nasopharyngeal carcinoma distant metastasis. Wang et al also discovered that SNHG1 could inhibit MIR-302/372/373/520’s influence on TGFβ1/SMAD3 and RAB11A/Wnt signaling pathway to promote pituitary tumor cell growth, migration and metastasis. Researchers have also shown that most Inc-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. SNHG17 bound with EZH2 and inhibited the expression of CDKN2B and CDKN1C to promote gastric cancer cell cycle progression. 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. Subsequently, SNHG3, GAS5, SNHG5, SNHG6, SNHG7, SNHG8, SNHG9, SNHG12, DANC (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. 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. Moreover, the relationship with transcriptional activation also participates in the progression. 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).
3 Biological Functions and Mechanisms of SNHG5 in Digestive Cancers

3.1 SNHGs in colorectal cancer

Among the causes of death from malignant tumors, colon cancer ranks the fourth in China. 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 colon cancer tumors. The recurrence rate of colorectal cancer 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 colon cancer tumors.

SNHG1 expression indicated a poor prognosis in colon cancer. It is increasingly important to study the treatment of colon cancer tumors. SNHG1 expression indicated a poor prognosis in colon cancer.

SNHG5 and SNHG7 were the direct target gene of SNHG5. SNHG5 sponged MIR-132-3p and positively regulated CREB5 to inhibit colon cancer cell apoptosis but promoted cancer cell proliferation, migration, and invasion. The up-regulation 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. Li and Li et al verified that the expression of SNHG6 in colon cancer tissues was higher than that in normal tissues. SNHG6 could induce EZH2 to bind with the promoter of CDKN1A and inhibit the CDKN1A function, leading to the growth of cancer cells. In the cytoplasm, SNHG6 sponged MIR760 and upregulated its target gene FOXC1 to promote colon cancer cell proliferation, migration, and invasion. SNHG7 was located in the cell cytoplasm in colon cancer and was highly expressed in colon cancer tissues. Although several mRNAs, including B3GALT1, FUT2, MFG, MGAT4A, GALNT7, 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. SNHG7 also could sponged MIR216B, to increase GALNT1 and activate EMT to promote colorectal cancer cell migration and invasion. 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. Shorter overall survival rate and disease-free survival rate were correlated with higher DANCER expression. It was determined as an individual poor prognosis factor in colon cancer. DANCER could upregulate colon cancer cell proliferation and migration ability by sponging MIR577 and increase the expression of HSPB1. Huang et al and Zhang et al concluded that SNHG15 and SNHG16 were both highly expressed in colon cancer samples. SNHG15 could only increase the protein level of SNAI2 but not the mRNA level through preventing SNAI2’s ubiquitin. Wnt signaling pathway and ceRNA mechanism might participate in the progression of SNHG16. SNHG17 could bind with EZH2 and regulate CDKN1C to promote cell proliferation.
| SNHG member | Aliases | 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 | 11q12.3 | Cytoplasm | Colon cancer; gastric cancer; liver cancer; esophageal cancer; cholangiocarcinoma; pancreatic cancer | MIR497/MIR-195-5p, EZH2, KLF2, CDKN2B, HNRNPC, TP53, MYC, CTNNB1, MMP9, MIR140, ADAM10, DNMT1, TP53, BAX, FAS, CDKNIA, DNMT1, MIR195, MIR338, CST3, CASP8 | 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] |
| SNHG2 | GAS5 | 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 | Proliferation, cell cycle, apoptosis, migration | Oncogene | [47,91,92] |
| SNHG5 | C6orf160, LINC00044, NCRNA00044, U50HG | 6q14.3 | Cytoplasm | Colon cancer; gastric cancer; liver cancer; esophageal 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 | 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, ZEB1, CDH2, 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 | 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] |
| 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-I23; LINC00100; ASLINC0040; NCRNA00100 | SNORA44, SNORA61, SNORA16A, SNORD99 | 1p35.3                 | Cytoplasm                  | Colon cancer; gastric cancer; liver cancer | CDK4, CDK6, CCND1, CASP3, MIR-199a-5p, MIR20, MIR-199a-5p | NF-κB signaling pathway | —            | Proliferation, cell cycle, apoptosis | Oncogene | [54,73,74,95] |
| DANCR       | AGU2; ANCR; SNHG13; KIAA0174; IncRNA-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-ASI; UBE3A-ATS; UBE3ATS | SNORD115-(1 ~ 48), SNORD116-(1 ~ 30), SNORD (64,107,108) | 15q11.2                 | Cytoplasm                  | Gastric cancer               | MIR-145, SOX9 | PI3KCA/akt/MTOR signaling pathway | Migration, invasion, apoptosis | Oncogene | [77]       |
| SNHG15      | C7orf90, 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      | Nhsa10727, Nhsa12061, neRAN | 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, cell cycle, apoptosis | Antioncogene/ oncogene | [59,97,109,110] |
| SNHG17      | 9430008C03Rk | SNORA71A, SNORA71B, SNORA71C, SNORA71D | 20q11.23                | Nucleus                   | Colon cancer; gastric cancer | EZH2, CDKN1C, CDKN2B | —              | Proliferation, cell cycle | Oncogene | [26,60]     |
| SNHG18      | —         | SNORD123 | 5p15.3                | —                        | 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 | SNHG5s 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.66 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-mercaptopemethanlyase (METase). Increased METase promoted gastric cancer cell apoptosis by upregulating the expression of SNHG5. Uрегuplated SNHG5 reduced MIR20A and led to the overexpression of the apoptosis proteins BECN1, ATG5, ATG7 resulting in increased proportion of LC3-II/LC3-I.58 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.53 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 IncRNA. 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.33 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. 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 plasma 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. 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. SNHG1 promoted liver cancer cell cycle and inhibited apoptosis by suppressing the expression of TP53’s target genes, including BAX, FAS, and CDKNIA. 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. Other scientists researched the impact of SNHG1 on sorafenib resistance. Overexpression of SNHG1 could significantly enhance the sorafenib resistance of liver cancer. Moreover, SNHG1 sponged MIR195 to promote cancer cell proliferation and metastasis.

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. GAS5 could downregulate MIR21 to prevent cancer cell migration and invasion. Chang et al indicated that GAS5 repressed cell proliferation by means of reducing VIM, increasing CDH1 and influencing EMT pathway.

The overexpression of SNHG3 predicted high rates of larger tumor size, portal vein tumor thrombus, sorafenib resistance and relapse. It directly combined with MIR128 to upregulate the expression CD151, and activated EMT to promote cell invasion. 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. 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, 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. 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. 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. SNHG12 also sponged MIR-199a/b-5p, which directly targeted the key markers of the NF-kB signaling pathway. Similar to SNHG1, the high expression level of DANCRI might be a more advanced marker than AFP to identify hepatic cancer no matter in the sensitivity or specificity. DANCRI might promote cancer cell proliferation and invasion by inhibiting protein CTNNB1. 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. Liu J et al showed that SNHG20 played an oncogenic role in liver cancer, and promoted the EMT pathway in cancer progression.

3.4 | SNHGs in esophageal cancer

Esophageal cancer is a common digestive system tumor with the number of cases increasing annually; more than 300,000 people die from this cancer each year. 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, 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. 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 CASP8.5,6,102 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. However, Ke et al insisted that GAS5 was an anticancer gene in esophageal tumor. Overexpression of GAS5 significantly impeded tumorigenesis via EMT. Huang et al verified the influences of GAS5 on proliferation, invasion and migration, which was consistent with Ke K’s opinions. SNHG6 and SNHG7 were both expressed higher in esophageal cancer tissues than normal tissues, and promoted cancer cell proliferation and metastasis. Xu et al suggested that CDKN2B and CDKN2A were partially connected to SNHG7 in the proliferation and metastasis progression. Additionally, reduced SNHG16...
resulted in the downregulation of key markers of the Wnt signaling pathway, such as MYC, CTNNB1, and CCND1.\textsuperscript{109} Furthermore, SNHG16 showed a positive correlation with ZEB1 to promote esophageal cancer tumorigenesis by sponging MIR-140-5p.\textsuperscript{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 promotes 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.\textsuperscript{111} Cui et al. suggested that SNHG1 could upregulate the key markers of the NOTCH signaling pathway to affect pancreatic cancer proliferation and invasion.\textsuperscript{112} Additionally, SNHG1 also played a crucial role in pancreatic ductal adenocarcinoma. The PIK3CA/AKT signaling pathway was activated when SNHG1 was overexpressed.\textsuperscript{39} Gao et al. put forward that GAS5 reduced the drug resistance of cancer cells through regulating MIR-181c-5p and Hippo pathway.\textsuperscript{113} Moreover, GAS5 could downregulate MIR-32-5p and increase the PTEN protein level.\textsuperscript{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.\textsuperscript{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.\textsuperscript{116,117}

### 3.6 SNHGs in other digestive cancer types

Cholangiocellular carcinoma is a type of tumor with high invasive character.\textsuperscript{118} The survival time of most patients is only 2 years after the diagnosis.\textsuperscript{119} Yang et al.\textsuperscript{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,\textsuperscript{121,122} and the interaction between SNHG1 and EZH2 could target CDKN1A to promote the biological behavior of cholangiocarcinoma.\textsuperscript{120}

### 4 SMALL NUCLEOLAR HOST GENES AND SNORNAS

SnoRNAs could be regulated by their host genes, copy number variation, and DNA methylation.\textsuperscript{19} Some scientists pointed out that the host genes may affect the expression of snoRNAs by cotranscription\textsuperscript{10}; however, other scholars reported that the functions of some SNHG members were independent of their snoRNAs.\textsuperscript{21} Moreover, recent studies have shown that some snoRNAs are also related to cancer tumorigenesis.\textsuperscript{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.\textsuperscript{123} Some researchers call these products as sno-miRNAs.\textsuperscript{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.

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### 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.
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