Hepatocellular carcinoma (HCC) is among the utmost deadly human malignancies. This type of cancer has been associated with several environmental, viral, and lifestyle risk factors. Among the epigenetic factors which contribute in the pathogenesis of HCC is dysregulation of long non-coding RNAs (lncRNAs). These transcripts modulate expression of several tumor suppressor genes and oncogenes and alter the activity of cancer-related signaling axes. Several lncRNAs such as NEAT1, MALAT1, ANRIL, and SNHG1 have been up-regulated in HCC samples. On the other hand, a number of so-called tumor suppressor lncRNAs namely CASS2 and MEG3 are down-regulated in HCC. The interaction between lncRNAs and miRNAs regulate expression of a number of mRNA coding genes which are involved in the pathogenesis of HCC. Some genetic polymorphisms within non-coding regions of the genome have been associated with risk of HCC in certain populations. In the current paper, we describe the recent finding about the impact of lncRNAs in HCC.

Keywords: lncRNA, biomarker, hepatocellular carcinoma, expression, polymorphism

INTRODUCTION

Liver cancer is among the most lethal malignancies among both sexes. More than 8% of cancer-related mortalities are due to this type of cancer (1). Hepatocellular carcinoma (HCC) includes more than 75% of the primary liver neoplasms (1). Several factors have been related with elevated risk of HCC among them are chronic infection with hepatitis B virus (HBV) B or hepatitis C virus (HCV), dietary exposure with aflatoxin, excessive alcohol use, obesity, and smoking (2). The cirrhosis-induced carcinogenic alterations have been detected in 90% of HCC patients (3). High throughput sequencing methods have shown the occurrence of several genetic changes in the HCC samples (4) among the early events are inactivating mutations in insulin-like growth factor 2 receptor (5). Catenin Beta 1 (CTNNB1) and Tumor Protein P53 (TP53) are the utmost recurrently mutated oncogene and tumor suppressor gene in HCC, respectively (4). In addition to these somatic
mutations, several epigenetic factors partake in the evolution of HCC. Such involvement is further highlighted by the fact that liver is an organ that is continuously adapting to extremely various environmental factors (6). Non-coding RNAs are among epigenetic elements that contribute in the pathogenesis of HCC. Long non-coding RNAs (lncRNAs) can affect expression of genes via diverse mechanisms including recruitment of regulatory protein complexes, acting as a decoy, changing genome organization and modulating the distribution of posttranslational modifications (7). These transcripts have sizes longer than 200 nucleotides and are comparable with mRNAs in the terms of chromatin state of genome loci, their transcription by RNA polymerase II, polyadenylation, 5' capping and being spliced, yet they do not produce large-sized polypeptides (8). However, there are several reports demonstrating the presence of stable, functional micropeptides being translated from lncRNAs (9). Several lines of evidence indicates that these transcripts contribute in the pathophysiology of HCC (10). In the present manuscript, we review the current knowledge about the partake of lncRNAs in the pathogenesis of HCC.

UP-REGULATED LNCRNAS IN HCC

The LINC01138 is located in a frequently amplified region in HCC. This lncRNA transcript is stabilized by IGF2BP1/IGF2BP3. Over-expression of LINC01138 in HCC confers malignant characteristics and is associated with poor survival of patients. Mechanistically, this lncRNA interacts with arginine methyltransferase 5 and increases the stability of this protein through inhibiting ubiquitin-mediated degradation in proteasomes (11). Over-expression of the lnc-Epidermal Growth Factor Receptor (EGFR) regulatory T cells (Tregs) has been related with tumor size and levels of EGFR/Foxp3. Its over-expression has also been negatively correlated with the levels of interferon (IFN)-γ in HCC patients and animal models. This lncRNA promotes Treg differentiation, inhibits function of cytotoxic T cells and increases HCC growth. These effects are exerted through binding of lnc-EGFR with EGFR, increasing its stability and activation of the AP-1/NF-AT1 axis (12). The oncogenic lncRNA HULC has been shown to exert its effects via modulation of phosphorylation pattern of YB-1. Notably, up-regulation of this lncRNA in HCC has been correlated with pathological grade and patients’ outcome. HULC can also increase cell proliferation, migration, and invasion and suppress cisplatin-associated cell apoptosis (13). LncRNA-MUF is another over-expressed lncRNA in HCC tissues whose up-regulation has been correlated with poor clinical outcome. This lncRNA has an indispensable impact in epithelial-mesenchymal transition (EMT). Such effects have been exerted through binding with Annexin A2 and induction of the Wnt/β-catenin signaling. Mechanistically, LncRNA-MUF serves as a competing endogenous RNA (ceRNA) for miR-34a, resulting in up-regulation of Snail1 induction of EMT process (14). GHET1 over-expression in HCC sections has been associated with vascular invasion, cirrhosis, size of tumor, histological grade, and poor clinical outcome. GHET1 silencing has suppressed cell proliferation and prompted both cell cycle arrest and cell apoptosis. GHET1 can suppress expression of KLF2 in HCC cells through recruitment of PRC2 into its promoter (15). MALAT1 is another up-regulated lncRNA in HCC, which affect neoplastic transformation through several mechanisms among them is its role as a ceRNA. Figure 1 depicts this mechanism in HCC.

Down-Regulated lncRNAs in HCC

Through a high throughput approach, Ni et al. have identified uc.134 as a novel lncRNA which is under-expressed in a highly aggressive HCC cell line. They further verified its down-regulation in clinical HCC samples compared with paired nearby tissues. Notably, down-regulation of uc.134 has been related with poor prognosis of HCC patients. Functionally, this lncRNA suppresses cell proliferation, invasion, and metastasis through binding with CUL4A suppressing its nuclear export. Besides, uc.134 suppresses the CUL4A-associated ubiquitination of LAT51 and enhances YAP1/27 phosphorylation which results in down-regulation of YAP target genes of YAP (223). LncRNA-PRAL has been shown to suppress HCC growth and stimulate apoptosis via a p53-dependent route. Certain motifs at the 5' end of this lncRNA have been identified that participate in competitive inhibition of MDM2-dependent p53 ubiquitination (224). Expression of the lncRNA-LET has been decreased in HCC. Further experiments have shown the role of hypoxia-induced histone deacetylase 3 in down-regulation of this lncRNA. Notably, repression of lncRNA-LET has been identified as an important step in the stabilization of nuclear factor 90 protein and subsequent hypoxia-associated tumor cell invasion. The association between down-regulation of lncRNA-LET and metastatic potential of HCC has also been verified in clinical samples (225). TSLNc8 is also down-regulated in HCC samples. Down-regulation of this lncRNA in HCC has been shown to confer malignant phenotype. TSLNc8 competitively interacts with transketolase and STAT3 and alters the phosphorylation patterns and transcriptional activity of STAT3 leading to suppression of the IL-6-STAT3 signaling (226). CASC2 is another down-regulated lncRNAs in HCC samples, particularly in the samples obtained patients with aggressive and recurrent forms of HCC. CASC2 suppresses migration and invasive properties of HCC cells and inhibits EMT program in these cells. Mechanistically, it serves as a competing endogenous RNA for miR-367 to increase expression of its target gene FBXW7. Notably, CASC2 down-regulation and miR-367 up-regulation have been associated with the metastasis-associated characteristics in the clinical samples (227). Table 2 displays the impact of down-regulated lncRNAs in HCC.

DIAGNOSTIC AND PROGNOSTIC IMPACT OF LNCRNAS IN HCC

Expression patterns of several lncRNAs have been related with overall survival or disease-free survival of patients with liver
neoplasm. Oncogenic lncRNAs which decrease survival of HCC patients include NEAT1, PTTG3P, UBE2CP3, LINC00461, MALAT1, MNX1-AS1, MCM3AP-AS1, ANRIL, AWPPH, PVT1, SNHG1, ENST00000429227.1, LINC00665, CRNDE, FOXD2-AS1, HULC and some other lncRNAs. Instead, low expressions of several tumor suppressor lncRNAs namely PSTAR, CASC2, Inc-FTX, LINC00472, TSLNcb8, miR503HG, MEG3, LIN00607, AOC4P, uc.134, GASB-AS1, LINC00657, MAGI2-AS3, LINC01093, GASS, SchLAH, and NKILA predict patients’ outcome. Univariate/multivariate cox regression analyses have confirmed the role of these lncRNAs in the determination of HCC prognosis. Table 3 lists the results of studies which evaluated the prognostic roles of lncRNAs in patients with HCC.

**GENOMIC VARIANTS WITHIN LNCRNAS AND RISK OF HCC**

Genetic polymorphisms include at least four type of variations namely, single nucleotide polymorphisms, small insertion/deletion polymorphisms, polymorphic repetitive elements and microsatellites. The importance of somatic copy number variations (SCNVs) loci in non-coding regions in the development of HCC has been assessed by...
TABLE 1 | Function of over-activated lncRNAs in HCC (ANT, adjacent non-cancerous tissue; HBS Ag, hepatitis B surface antigen).

| IncRNA   | Sample Description                                      | Cell line          | Interacting partners | Signaling pathway | Association with clinical features | Function                                                                 | Reference |
|----------|---------------------------------------------------------|--------------------|----------------------|-------------------|-------------------------------------|----------------------------------------------------------------------------|-----------|
| NEAT1    | 40 HCC tissues and paired ANTs, Male BALB/c nude mice  | L02, 293 T, HepG2, Huh-7, SK-Hep-1, HCCLM3 | mIR-124-3p, ATGL    | –                  | Patient survival                    | Promotes HCC cell growth through miR-124-3p-mediated downregulation of ATGL   | (24)      |
| NEAT1    | 30 HCC tissues and paired ANTs, BALB/c athymic nude mice | HepG2, L02, Huh-7, HepG2, Bel-7402, SK-Hep1, LO2, HEK-293T | mIR-129-5p, VCP, IκB, STAT3 | –                  | –                                   | Enhances proliferation of HCC cells via affecting miR-129-5p-VCP-IκB          | (25)      |
| NEAT1    | –                                                       | Huh7, Hep3B, HepG2, Bel-7404, SK-Hep1, LO2, HEK-293T | mIR-485, STAT3     | –                  | –                                   | Contributes to evolution of HCC through sequestering miR-485 and upregulation of STAT3 | (26)      |
| NEAT1    | 86 HCC tissues and paired ANTs                          | Huh7, Hep3B, THLE-2 | –                    | –                  | Patient survival, liver cirrhosis, microvascular invasion, TNM stage | Promotes proliferation HCC cells                                             | (27)      |
| NEAT1    | 62 HCC tissues and paired ANTs                          | MHC97H, MHCC97L, SMCC7721, Huh-7, LO2 | mIR-613             | –                  | Patient survival, tumor size, vascular invasion | Stimulates proliferation and invasion via regulating mIR-613 | (28)      |
| NEAT1    | 12 female BALB/c, nude mice                             | Hep3B, LM3, MHCC97L, SK-hep1, HepG2, LO2, HEK-293T | hsa-miR-139-5p, TGF-β1 | –                  | –                                   | Promotes HCC progression via sequestering hsa-miR-139-5p and upregulation of TGF-β1 | (29)      |
| NEAT1_2  | 21 HCC tissues and paired ANTs                          | L02, Huh7, SMCC-7721, PLC5, Bel-7402 | mIR-101-3p, WEE1    | –                  | –                                   | Reduces radiosensitivity through mIR-101-3p-WEE1 axis                         | (30)      |
| PTTG3P   | 46 HCC tissues and paired ANTs, 90 paraffin-embedded tissues and ANTs, male BALB/c nude mice | HepG2, Hep3B, PTTG1 | PI3K/AKT signaling pathway | –                  | Patient survival, tumor size, TNM stage | Stimulates proliferation, migration and invasion and blocks apoptosis via upregulating PTTG1 | (31)      |
| PTTG3P   | 50 HCC tissues and paired ANTs, female nude mice        | HepG2, Hep3B, Huh-7, HLF, SK-Hep-1, SNJ-449, LO2 | COND1, PARP2, mIR-383 | –                  | Tumor size, tumor stage, metastasis | Promotes proliferation, migration, and invasion and inhibits apoptosis in HCC cells | (32)      |
| UBE2CP3  | 46 HCC tissues and ANTs, male BALB/c nude mice          | HepG2, SMCC-7721, HUVEC | –                    | –                  | Patient survival, tumor invasion, tumor number | Promotes migration, invasion, and angiogenesis through activating ERK/HIF-1/VEGF-A signaling | (33)      |
| LIN00461 | 87 HCC tissues and paired ANTs, mice                    | Huh7, SMCC-7721, MHCC97H, Hep3B, HepG2, LO2 | mIR-149-5p, LRG2    | –                  | Advanced stage, metastasis          | Promotes proliferation, migration, and invasiveness via mIR-149-5p-LRG2 axis | (34)      |
| MALAT1   | 20 HCC tissues and paired ANTs, female Nude mice        | LC2 cells, HepG2 cells, Huh-7 cells, THP-1, HUVEC | mIR-140, VEGF-A    | –                  | –                                   | Promotes angiogenesis of HCC cells through targeting mIR-140 and upregulating VEGF-A | (16)      |
| MALAT1   | 20 HCC tissues and paired ANTs                          | LO2, Bel7404, Huh-7, HepG2 | mIR-204, SIRT1      | –                  | –                                   | Promotes migration and invasion of HCC cells through sponging mIR-204 and upregulating VEGF-A | (17)      |
| MALAT1   | 56 HCC tissues and paired ANTs                          | Huh-6, HepG2, SMCC-7721, Bel-7402, LO2 | mIR-143-3p, ZEB1    | –                  | Patient survival, TNM stage, distant metastasis | Promotes HCC development via sequestering mIR-143-3p and regulation of ZEB1 | (35)      |
| MALAT1   | 30 HCC tissues and paired ANTs, male BALB/c nude mice   | HepG2, Huh-7, HEK-293T | mIR-30a-5p, Vimentin | –                  | –                                   | Promotes migration and invasion in HCC cells via affecting mIR-30a-5p-Vimentin axis | (19)      |
| MALAT1   | –                                                       | Huh7, SNJ-423, PLC, Hep3B | mIR-200a            | –                  | –                                   | Regulates proliferation, migration, and invasion under                       | (36)      |

(Continued)
| IncRNA     | Sample                                                                 | Cell line                          | Interacting partners | Signaling pathway       | Association with clinical features                                                                 | Function                                                                                                                                   | Reference |
|------------|------------------------------------------------------------------------|------------------------------------|----------------------|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| MALAT1     | 15 HCC tissues and paired ANTs, male BALB/c nude mice                  | HepG2, HuH7, HEK293T               | miR-124-3p, Slug      | Patient survival, tumor size, MVI, differentiation status | hypoxic condition through sponging miR-200a.                                                                                                             | Promotes migration and invasion of HCC cells through influencing miR-124-3p/Slug axis                                                 | (21)      |
| MALAT1     | –                                                                     | L-02, QSG-7701, HepG2, MHCC97      | miR-195, EGFR         | –                       | Promotes growth and motility of HCC cells through regulation of miR-195/EGFR axis                                                                          |                                                                                                                                               | (22)      |
| MALAT1     | 30 HCC tissues and paired ANTs, female BALB/c nude mice                | HepG2, Hep3B, HuH7, PLC/PRF5       | miR-22, SNAI1         | –                       | Contributes to HCC progression through sponging miR-22 and upregulation of SNAI1 expression                                                                 | Enhances proliferation and invasion of HCC cells through targeting miR-218-5p and inhibition of COMMD8                                    | (23)      |
| MNX1-AS1   | 81 HCC tissues and paired ANTs, mice                                  | Huh7, SMMC-7721, MHCC97H, Hep3B, HepG2, and LO2 | miR-218-5p, COMMD8   | Patient survival, TNM stage, metastasis | Promotes proliferation, colony formation, and cell cycle transition and decreases apoptosis in HCC cells                                                                 |                                                                                                                                               | (37)      |
| MCM3AP-AS1 | 80 HCC tissues and paired ANTs, male BALB/c nude mice                 | HepG2, Hep3B, HuH7, SMMC-7721      | miR-194-5p, FOXA1     | Poor prognosis, tumor size, tumor grade, advanced tumor stage | Promotes HCC metastasis through interacting with and regulation of EGFR axis                                                                                       | Promotes HCC metastasis through interacting with and regulation of EGFR expression                                                                 | (38)      |
| MCM3AP-AS1 | 25 HCC tissues and paired ANTs                                        | HepG2, HuH-7, 293T                 | miR-455               | Patient survival        | Promotes HCC cells proliferation through epigenetically repression of KLF2                                                                                   |                                                                                                                                               | (39)      |
| TUG1       | 77 HCC tissues and paired ANTs, male BALB/c nude mice                 | HepG2, MHCC-97H, Hep3B, L02        | KLF2                 | tumor size, BCLC stage  | Affects cell growth, metastasis, and glycolysis via miR-455-3p/AMPKβ2 axis                                                                                   |                                                                                                                                               | (40)      |
| TUG1       | HCC tissues and paired ANTs                                            | –                                  | miR-455-3p, AMPKβ2    | Patient survival        | Enhances proliferation and migration, and tumorgenesis via interacting with miR-144                                                                            |                                                                                                                                               | (41)      |
| TUG1       | 92 HCC tissues and paired ANTs, female BALB/c athymic nude mice        | HepG2, Hep3B, SMMC-7721, HCCLM5, Bel, 7402 | miR-142-3p, ZEB1      | –                       | Enhances mitochondrial function in HCC cells by amplifying PTEN/AKT signaling                                                                                   | Enhances mitochondrial function in HCC cells by amplifying PTEN/AKT signaling                                                                 | (42)      |
| TUG1       | 41 HCC tissues and paired ANTs, female BALB/C athymic nude mice        | Hep3B, HuH7, Bel7402, HepG2, SMMC-7721, HCCLM5, Bel, 7402 | miR-144              | JAK2/STAT3 signaling pathway |                                                                                                                                                                  |                                                                                                                                               | (43)      |
| THOR       | 80 HCC tissues and paired ANTs, nude mice                             | HCCLM5, SMMC7721                  | –                    | Patient survival        | Promotes proliferation and migration, and tumorgenesis via interacting with miR-144                                                                            |                                                                                                                                               | (44)      |
| ANRIL      | FFPE specimens of 43 pairs of HCC tissues and ANTs, male athymic BALB/c nude mice | HuH7, SMMC7721, HepG2, Hep3B, LO2 | miR-199a-5p, ARL2     | –                       | Enhances mitochondrial function in HCC cells through regulation of miR-199a-5p/ARL2 axis                                                                 | Enhances mitochondrial function in HCC cells through regulation of miR-199a-5p/ARL2 axis                                                                 | (45)      |
| ANRIL      | –                                                                     | HepG2                             | miR-191              | –                       | Enhances mitochondrial function in HCC cells through regulation of miR-199a-5p/ARL2 axis                                                                 | Enhances mitochondrial function in HCC cells through regulation of miR-199a-5p/ARL2 axis                                                                 | (46)      |
| ANRIL      | 77 HCC tissues and paired ANTs, male BALB/c nude mice                 | HepG2, Hep3B, MHCC-97H             | KLF2                 | tumor size, BCLC stage  | Enhances mitochondrial function in HCC cells through regulation of miR-199a-5p/ARL2 axis                                                                 | Enhances mitochondrial function in HCC cells through regulation of miR-199a-5p/ARL2 axis                                                                 | (47)      |

(Continued)
| IncRNA | Sample | Cell line | Interacting partners | Signaling pathway | Association with clinical features | Function | Reference |
|--------|--------|-----------|----------------------|-------------------|----------------------------------|----------|-----------|
| ANRIL  | 31 HCC tissues and paired ANTs, female BALB/C athymic nude mice | SMCC772, HUH7, Hep3B, HepG2 | miR-122-5p | – | – | Promotes proliferation, metastasis and invasion of HCC cells via affecting miR-122-5p expression | (48) |
| ANRIL  | 130 tissues and paired ANTs | HepG2 | – | – | Patient survival, histologic grade, TNM stage | Promotes proliferation, migration, and invasion of HCC cell. | (49) |
| ANRIL  | – | MHC097, Li-7, THLE-3 | miR-144, Pbx3 | PI3K/AKT and JAK/STAT signaling pathways | – | Surges proliferation, migration, and invasion of HCC cells through sponging miR-144 and upregulation of Pbx3 | (50) |
| AWPPH  | 88 HCC tissues and paired ANT, male athymic BALB/c nude mice | QS7-7701, SMCC-7721, HCCLM3, Hu7, HepG2 | YBX1, SNAIL1, PI3KCA | PI3K/AKT signaling pathway | Patient survival, encapsulation, incomplete, microvascular invasion, TNM stage, BCLC stage | Promotes proliferation and migration of HCC cells through YBX1-mediated activation of SNAIL1 translation and PI3KCA transcription | (51) |
| PVT1   | 47 HCC tissues and paired ANTs, nude BALB/c male mice | L-02, SK-HEP-1, Hep G2, SMMC-7721, BEL-7402, Hep3B2-1-7, QGY-7703X4 | miR-150, HIG2 | – | – | Promotes proliferation, migration and invasion, and induced cell apoptosis in HCC cells through regulation of miR-150/HIG2 axis | (52) |
| PVT1   | 48 HCC tissues and paired ANTs | HepG2, Hep3B, Hu7, HCCLM3, SK-Hep1, SMCC-7721 | miR-186-5p, YAP1 | Patient survival, vascular invasion, liver cirrhosis, TNM stage | Promotes proliferation, migration, and invasion through targeting miR-186-5p and enhancement of YAP1 | (53) |
| PVT1   | 80 HCC tissues and paired ANTs | Bel-7402, Hu7, Hep3B, HepG2 | miR-365, ATG3 | TNM stage, tumor size | Promotes autophagy in HCC cells via sponging miR-365 and upregulation of ATG3 | (54) |
| SNHG1  | Male BALB/c nude mice | HL-7702, S Li-7, Hu7, HHCC, H-97, Hep3b, SMCC-7721 | miR-195-5p, PDCD4 | – | – | Promotes proliferation and migration of HCC cells through targeting miR-195-5p and upregulation of PDCD4 | (55) |
| SNHG1  | 82 HCC tissues and paired ANTs | SMCC-7721, MHC097H, HCCLM3, HepG2, QS7-7701, L02 | p53 | Patient survival, tumor size, tumor differentiation, BCLC stage | Stimulates proliferation, cell cycle progression, and blocks apoptosis in HCC cells via inhibiting p53 | (56) |
| SNHG1  | 122 HCC tissues and paired ANTs | HepG2 | miR-195 | – | – | Stimulates proliferation, migration, and invasiveness of HCC cells through inhibiting miR-195 is associated with poor prognosis in HCC | (57) |
| ENST000000429227.1 | 161 HCC tissues and paired ANTs | U937 | – | – | Patient survival, surgical margin, AFP, BCLC stage | – | (58) |
| H19    | 42 HCC tissues and paired ANTs | Huh 7 | – | MAPK/ERK signaling pathway | – | Its downregulation induces oxidative stress and reduces chemotherapy resistance of HCC cells. | (59) |
| H19    | 46 HCC tissues and paired ANTs | LI-85/hepG2, SMCC-7721, Bel-7402, Huh-7 | miR-15b, CDC42 | CDC42/PAK1 pathway | – | Promotes proliferation, migration, and invasion and reduces apoptosis in HCC cells through regulating miR-15b/CDC42 axis. | (60) |
| H19    | – | HepG2, MHC097L, SK-hep1, Hu7, SMCC-7721, L02, HEK-293T | miR-326, TWIST1 | – | – | Promotes proliferation, migration, and invasion of HCC cells through regulating miR-326/TWIST1 axis. | (61) |

(Continued)
| IncRNA | Sample | Cell line | Interacting partners | Signaling pathway | Association with clinical features | Function | Reference |
|--------|--------|-----------|----------------------|------------------|-----------------------------------|----------|-----------|
| HCG11  | 20 HCC tissues and paired ANTs | L-02, Huh7, HepG2, SMMC-7721, SK-Hep-1 | IGF2BP1 | MAPK signaling pathway | – | Promotes proliferation, migration, and invasion in HCC cells | (62) |
| LINC00665 | 76 HCC tissues and paired ANTs, 24 female BALB/c nude mice | Huh-7, HepG2, HCCLM6, MHCC-97L, Hep3B, HL-7702 | miR-186-5p, MAP4K3 | – | Patient survival, tumor size, Edmondson grade | Enhances cell viability and decreases apoptosis and autophagy through regulation of miR-186-5p/MAP4K3 axis | (63) |
| CRNDE | 46 HCC tissues and paired ANTs | HepG2, Huh-7, HCCLM3, SNU449, SNU475, HepaRG, HL-7702 | miR-217, MAPK1 | – | AJCC stage, vascular invasion, distant metastasis | Promotes proliferation, migration and invasion in HCC cells via affecting miR-217/MAPK1 axis | (64) |
| CRNDE | 23 HCC tissues and paired ANTs, BALB/c (nu/nu) mice | QSG-7701, HepG2, Hep3B, Huh7 | – | PI3K/Akt and Wnt/β-catenin signaling pathways | – | Patient survival | Promotes proliferation of HCC cells through regulation of mentioned signaling pathways | (65) |
| CRNDE | 12 HCC tissues and paired ANTs, male BALB/c nude mice | SMMC7721, SK-hep1, Huh7, HepG2 | miR-136-5P, IRX5 | – | – | Affects proliferation, migration, and invasiveness of HCC cells via targeting miR-136-5P and regulation of IRX5 | (66) |
| CRNDE | 25 HCC tissues and paired ANTs, 10 female athymic BALB/c nude mice | HepG2, Huh7, L-02 | miR-203, BCAT1 | – | – | Affects proliferation, migration, and invasiveness of HCC cells by regulating miR-203/BCAT1 axis | (67) |
| CRNDE | 60 HCC tissues and paired ANTs, male athymic BALB/c nude mice | HL7702, MHCC97L, HCCLM6, SNU-398, Huh7 | miR-337-3p, SIX1 | – | – | Affects proliferation, migration, and invasiveness of HCC cells by regulating miR-337-3p/SIX1 axis | (68) |
| FOXD2-AS1 | 18 HCC tissues and paired ANTs | L-02, HepG2, Huh-7, SMMC-7721, Bel-7402, Hep3B | miR-185, AKT | – | – | Supports proliferation and metastasis of HCC cells through regulation of miR-185/AKT axis | (69) |
| FOXD2-AS1 | 88 HCC tissues and paired ANTs | L-02, HepG2, Hep3B, SMMC-7721, LM3 | DKK1 | Wnt/β-catenin signaling pathway | Patient survival | Affects proliferation and angiogenesis of HCC cells through miR-330-3p-mediated upregulation of DKK1 | (70) |
| LINC00488 | 46 HCC tissues and paired ANTs, 30 nude mice | L02, Huh-7, Hep3B, HCCLM3, MHCC97 | miR-330-5p, TLN1 | – | – | Promotes progression of HCC through sponging miR-330-5p and upregulation of TLN1 | (71) |
| AY927503 | 57 HCC tissues and paired ANTs, female BALB/c nude mice | Hep3B, HepG2, SK-Hep1, LM3, BEL-7404, SMMC-7721, LO2, HUVEC, HEK-293T | ITGAV | – | Patient survival | Enhances cell migration, drug resistance, and metastasis in HCC cells through activation of ITGAV transcription | (72) |
| IncRNA-PE | 24 HCC tissues and paired ANTs | BEL-7402, SK-Hep-1, LO2 | miR-200a/b, ZEB1 | – | – | Enhances migration, invasion and EMT process in HCC cells through miR-200a/b/ZEB1 axis | (73) |
| HULC | 30 HCC tissues and paired ANTs | HepG2, SMMC7721, LO2 | miR-372-3p, Rab11a | – | TNM stage | Promotes proliferation and invasion and suppresses apoptosis through sponging miR-372-3p and upregulation of Rab11a | (74) |
| HULC | male athymic Balb/C mice | Hep3B | miR-15a, P62, PTEN | AKT-PI3K-mTOR | – | Affects proliferation and angiogenesis of HCC cells through miR-330-3p-mediated upregulation of DKK1 | (75) |
| lncRNA     | Sample                                      | Cell line                          | Interacting partners | Signaling pathway                      | Association with clinical features                          | Function                                                                 | Reference |
|------------|---------------------------------------------|-------------------------------------|----------------------|----------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------|-----------|
| HULC       | 41 HCC tissues and paired ANTs              | HepG2, SMMC-7721                    | YB-1                 | signaling pathway                      | Patient survival, differentiation                            | regulation of miR-15a, P62 and PTEN                                    | (76)      |
| SBF2-AS1   | 18 male Balb/c nude mice                    | HepG2, Hep3B, SUN475, BEL-7405, BEL-7404, BEL-7402, THLE-3 | miR-140-5p, TGFBR1    | –                                      | Patient survival, lymph node metastasis, histologic grade, TNM stage invasion, TNM stage | Promotes proliferation, migration and invasion and suppresses cisplatin-induced apoptosis in HCC cells | (77)      |
| SBF2-AS1   | 134 HCC tissues and paired ANTs             | HCCLM3, Huh7, SK-HeP1, HepG2, L02  | –                    | –                                      | vein invasion, TNM stage                                    | Affects proliferation, migration and invasion of HCC cells             | (78)      |
| UC001kfo   | 82 HCC tissues and 20 ANTs, SPF BALB/c nude mice | GSG701, Hep3B, HepG2, Huh7, SMMC 7721, HCC LM3, L02 | α-SMA                 | –                                      | Patient survival, macro-vascular invasion, TNM stage       | Affects proliferation, migration and invasion of HCC cells             | (79)      |
| HOTTIP     | 20 HCC tissues and 20 ANTs, male BALB/C nude mice | BEL7402, MHCC97H                   | miR-125b, HOXA        | –                                      | –                                                           | Promotes proliferation, migration, and tumorigenesis of HCC cells.     | (80)      |
| FOXO2-AS1  | 140 HCC tissues and paired ANTs, 12 female BALB/C nude mice | Hep3B, MHCC97-L, MHCC97-H, SK-HEP1, HCCLM3, HL7702 | miR–206, ANXA2       | –                                      | Patient survival                                           | Increases cell viability and metastasis of HCC cells through miR–206/ANXA2 axis | (81)      |
| LUCAT1     | 90 HCC tissues and paired ANTs, male BALB/C nude mice | HepG2, SMMC-7721, SNU-423, Hep3B, Huh7, MHCC-97H, L02 | –                    | –                                      | Patient survival, tumor size, metastasis, TNM stage         | Affects proliferation and metastasis of HCC cells through inhibition of phosphorylation of ANXA2 | (82)      |
| AK001796   | 73 HCC tissues and paired ANTs              | LO2, g SMMC-7721, Huh7, MHCC-97H, MHCC-97L | –                    | –                                      | Patient survival, tumor size, TNM stage                    | Affects proliferation and invasion of HCC cells                        | (83)      |
| FEZF1-AS1  | 139 HCC tissues and paired ANTs, male BALB/C nude mice | HepG2, SK-hep1, Huh7, HCCLM3, L02  | –                    | JAK2/STAT3 signaling pathway          | Patient survival, tumor size, TNM stage, venous invasion   | Promotes proliferation, migration and invasion of HCC cells           | (84)      |
| MINCR      | 161 HCC tissues and paired ANTs             | –                                  | –                    | –                                      | Patient survival, TNM stage, histological grade             | Contributes to progressive clinicopathological features and poor survival | (85)      |
| MINCR      | 70 primary HCC tissues and paired ANTs      | SMMC-7721, Huh7, HCC-LM3, HepG2, MHCC-97H, HL-7702 | –                    | –                                      | –                                                           | Promotes proliferation, migration, and invasion.                      | (86)      |
| LINC01152  | 30 pairs of HBV-HCC related tissues and HCC tissues, nude mice | Huh7, HepG2, Hep3B                 | IL-23                | –                                      | –                                                           | Enhances proliferation, survival and tumor formation ability through IL-23 | (87)      |
| XIST       | 88 HCC tissues and paired ANTs, male BALB/c-nu/nu mice | LM9, Hh7, Hep3B, HepG2, L02        | miR-139-5p, PDK1      | AKT signaling pathway                  | Patient survival, tumor size                                | Promotes cell proliferation and reduces apoptosis through regulation of miR-139-5p/PDK1/AKT axis | (88)      |
| XIST       | 52 HCC tissues and paired ANTs              | MHCC97L, MHCC97H, HepG2, SMMC7221, Huh7, Bel-7402, HL-7702 | miR-194-5p, MAPK1    | –                                      | Patient survival, tumor size, vascular invasion            | Promotes proliferation, migration and invasion of HCC cells through sponging miR-194-5p and regulation of MAPK1 expression | (89)      |
| TRPM2-AS   | 108 HCC tissues and paired ANTs             | HCCLM3, Huh7, SMMC-7721, SKHeP1, HepG2, QSG7701 | –                    | –                                      | Patient survival, tumor size, AJCC stage, tumor differentiation | Promotes proliferation and reduces apoptosis in HCC cells               | (90)      |

(Continued)
| IncRNA         | Sample and paired ANTs, blood samples from 80 HCC patients and 44 healthy controls | Cell line          | Interacting partners | Signaling pathway | Function                                                                 | Reference |
|---------------|----------------------------------------------------------------------------------|--------------------|----------------------|-------------------|--------------------------------------------------------------------------|-----------|
| LINC-ITGB1    | 56 HCC tissues and paired ANTs, blood samples from 80 HCC patients and 44 healthy controls | C3A, HEP G2, m, THLE-3 | ROCK1              | –                  | Promotes proliferation, migration and invasion of HCC cells through upregulation of ROCK1 | (91)      |
| LSNVCT5       | 126 HCC tissues and paired ANTs, female nude mice                                | 97L, HepG2, HepSB, 7721, and Huh7, 293T, L02 | miR-4516, HMGA2   | –                  | Patient survival, TNM stage, tumor size, metastasis                       | (92)      |
| XLOC          | 68 HCC tissues and paired ANTs                                                   | HepG2, Hep3B, SMCC-7721, Bel-7402 | –                   | –                  | Patient survival, vascular invasion, tumor size, Edmondson grade         | (93)      |
| HNF1A-AS1     | –                                                                                | SMCC-7721, Huh7, MHC97L, HepG2, L02 | NKD1, p21        | –                  | Promotes proliferation of HCC cells through inhibition of NKD1 and p21 via interacting with EZH2 | (94)      |
| HNF1A-AS1     | 40 HCC tissues and paired ANTs                                                   | HepG2, SMCC-7721, PLCC-PRF5, Huh7, HL7702 | hasa-miR-30b-5p, ATG5 | –                  | Promotes HCC progression through regulation of hasa-miR-30b-5p             | (95)      |
| U2RHC         | 52 HCC tissues and paired ANTs                                                   | HepG2, SMCC7721, Huh7, HL-7702 | ZAK                | ERK/MAPK signaling pathway | Patient survival, tumor size, tumor number                               | (96)      |
| UCA1          | 60 HCC tissues and paired ANTs, male BALB/C nude mice                            | LO2, MHC97L, Huh7, MHC97H, HEP-hep1 | miR-203, Snail2    | –                  | tumor size, vascular invasion, AJCC stage                                 | (97)      |
| AK021443      | 20 HCC tissues and paired ANTs, male BALB/c-nu/nu mice                           | Bel-7402, Sk-Hep1, HepG2, Huh7, Bel-7404, L02 | –                   | –                  | Promotes proliferation, migration, invasion and colony formation in HCC cells | (98)      |
| RUSC1-AS-N    | 66 HCC tissues and paired ANTs                                                   | QSG-7701, SMCC-7721, HCCLM9, Huh7 | –                   | –                  | Promotes cell viability and reduces apoptosis and cell cycle arrest        | (99)      |
| CCA1          | 40 HCC tissues and paired ANTs                                                   | MHC97H, MHC97L, Hep3B, SMCC-7721, L02 | miR-490-3p, CDK1 | –                  | Promotes proliferation and invasion of HCC cells through targeting miR-490-3p and regulation of CDK1 | (100)     |
| CCA1          | 66 HCC tissues and paired ANTs                                                   | LO2 and QSG-7701, SMCC-7721, Hep3B, Huh7, HepG2 | let-7, HMGA2, c-Myc | –                  | Patient survival, tumor size, microvascular invasion, AFP                | (101)     |
| CCA1          | 39 HCC tissues and paired ANTs                                                   | HCCLM9, Huh7, Hep3B, HepG2, L02 | miR-181a-5p, ATG7 | –                  | –                                                                         | (102)     |
| CCA1          | 65 HCC tissues and 35 normal liver samples                                       | Hep3B               | miR-30c-2-3p, CCNE1 | –                  | Promotes HCC cells proliferation by sequestering miR-30c-2-3p and upregulation of CCNE1 | (103)     |
| CCA1          | 20 HCC tissues and paired ANTs, male BALB/c-nude mice                            | SMCC7721, SK-hep1, HepG2, Huh7, L02 | NDRG1             | –                  | Promotes proliferation and metastasis of HCC cells through upregulation of NDRG1 | (104)     |
| SNHG16        | 71 HCC tissues and paired ANTs                                                   | HL-7702, SK-Hep1, Huh7, Hep3B, HepG2 | –                   | –                  | Patient survival, tumor size, AFP level, PVTT, metastasis                | (105)     |
TABLE 1 | Continued

| IncRNA   | Sample                                      | Cell line           | Interacting partners | Signaling pathway | Association with clinical features | Function                                                                 | Reference |
|----------|---------------------------------------------|---------------------|----------------------|-------------------|------------------------------------|--------------------------------------------------------------------------|-----------|
| SNHG16   | 40 HCC tissues and paired ANTs, BALB/c nude mice | HepG2, SMCC7721, Hep3B, Bel7402, Huh7, LO2 | miR-195              | –                  | TNM stage, metastasis              | Enhances proliferation, invasion and tumorigenesis of HCC cells through targeting miR-195 | (106)     |
| SNHG10   | 64 HCC tissues and paired ANTs              | SNU-182, Huh-7, Hep3B, SK-Hep1, and SNU-387, HEK293T, HCCLM3 | miR-150-5p           | –                  | Patient survival                   | Contributes to HCC progression and metastasis through modulating SCARNA13 | (107)     |
| SNHG12   | 48 HCC tissues and paired ANTs              | SK-Hep1             | miR-199a/b-5p, MLK3  | NF-κB signaling pathway | –                                  | Enhances tumorigenesis and metastasis of HCC cells via targeting miR-199a/b-5p and regulation of NF-κB expression | (108)     |
| SNHG20   | 96 HCC tissues and paired ANTs              | LO2, MHCC97L, SMCC7721, MHCC97H, Huh-7 | miR-26a/b-5p         | Wnt/β-catenin signaling pathway | –                                  | Promotes proliferation and invasion of HCC cells through binding to EZH2 and regulation of E-cadherin expression | (109)     |
| SNHG5    | 48 HCC tissues and paired ANTs              | Hep3B, HepG2, SMCC7721, MHCC97L, MHCC97H, Huh7, LO2 | miR-26a/b-5p         | Wnt/β-catenin signaling pathway | –                                  | Promotes HCC progression and metastasis through targeting miR-26a/b-5p and regulation of GSK3β | (110)     |
| SNHG6    | Expression data of HCC obtained from TCGA and GEO | MHCC97H, HCC-LM3     | let-7c-5p, c-Myc     | –                  | Patient survival                   | Enhances proliferation of HCC cells through sponging let-7c-5p and upregulation of c-Myc | (111)     |
| SNHG6    | 12 HCC tissues and paired ANTs, female BALB/c mice | Huh-7, HepG2, Hep3b, HLE, Huh7 | miR-139-5p           | –                  | –                                  | Promotes HCC progression via targeting miR-139-5p and regulation of SERPINH1 | (112)     |
| SNHG6-003| 52 HCC tissues and paired ANTs, FFPE tissues from 160 patients | BEL-7402, SMCC7721, MHCC97H, SK-Hep-1, Huh7, HCC-LM3 | miR-26a/b, TAK1     | –                                  | Patient survival, portal vein tumor thrombus, Barcelona Clinic Liver Cancer stage, distant metastasis | Promotes HCC cells proliferation and drug resistance by sponging miR-26a/b and upregulation of TAK1 | (113)     |
| SNHG7    | 40 HCC tissues and paired ANTs, male BALB/c nude mice | HepG2, HCC-LM3      | miR-425              | Wnt/β-catenin/ EMT signaling pathway | –                                  | Enhances proliferation, migration and invasiveness via sponging miR-425 and regulation of Wnt/β-catenin/ EMT signaling pathway | (114)     |
| SNHG7    | 80 HCC tissues and paired ANTs, BALB/c nude mice | LO2, Huh7, Hep3B, HCCLM3, MHCC97H | miR-122-5p, RPL4    | –                  | Patient survival, tumor stages, tumor grades, vascular invasion | Promotes proliferation, migration and invasiveness via affecting miR-122-5p and RPL4 | (115)     |
| SNHG8    | 23 HCC tissues and paired ANTs, female immune-deficient nude mice | LO2, Huh6, Huh7, SK-hep1, HepG2, PLC5 | miR-149              | –                  | Recurrence                         | Promotes Tumorigenesis and metastasis through sponging miR-149 | (116)     |
| SNHG15   | 101 HCC tissues and paired ANTs             | Huh-1, Huh-7, LO2   | miR-490-3p           | –                  | Tumor size, Edmondson-Steiner grading, TNM stage | Promotes proliferation, migration and invasion via regulating miR-490-3p/ HDAC2 axis | (117)     |
| CCAL     | 37 HCC tissues and ANTs, 60 male nude mice  | Huh7, HCCLM3, LO2   | AP-2α                | Wnt/β-catenin signaling pathway | –                                  | Tumor metastasis, TNM stage                                             | Promotes proliferation and invasion of HCC cells through upregulation of AP-2α | (118)     |
| Sox2ot   | 84 HCC tissues and ANTs                    | HepG2, SMCC7721     | –                    | Patient survival, histological grade, TNM stage, vein invasion | –                                  | Promotes HCC cells metastasis                                           | (119)     |

(Continued)
### TABLE 1 | Continued

| IncRNA          | Sample                          | Cell line                      | Interacting partners | Signaling pathway | Association with clinical features | Function                                                                 | Reference |
|-----------------|---------------------------------|--------------------------------|----------------------|-------------------|------------------------------------|---------------------------------------------------------------------------|-----------|
| SPRY4-IT1       | male nude mice                  | MHCC97H, MHCC97L, Shk1-1, LO2   | E-cadherin           | –                 | –                                  | Stimulates proliferation and invasion of HCC cells via interaction with EZH2 and repression of E-cadherin levels | (120)     |
|                 |                                  |                                |                      |                   |                                    |                                                                           |           |
|                  | 82 HCC tissues and paired ANTs  | HL7702, MHCC97L, MHCC97H, HepG2, SMMC7721 | ERα                  | –                 | Patient survival, TNM stage, metastasis | Promotes proliferation, migration and invasion and decreases apoptosis via suppressing ERα expression | (121)     |
| PANDAR          | 482 HCC tissues and paired ANTs | HCCLM3, HepG3B, Hep2, Huh-7, MHCC97L, PLC, SMMC7402, SMMC7721 | –                    | –                 | Patient survival, liver cirrhosis, HBsAg, AFP, tumor nodule, vascular invasion, TNM stage | Promotes HCC tumorigenesis and is associated with poor prognosis | (122)     |
| long-ROR        | female BALB/c nude mice         | HepG2, SMMC7721                | miR-145, RAD18       | –                 | –                                  | Promotes metastasis, EMT process and radioresistant in HCC cells through targeting miR-145 and regulation of RAD18 expression | (123)     |
| CARG-5          | 97 HCC tissues and paired ANTs  | HepG2, Hep3B, SK-Hep1, SMMC7721, MHCC97-L, MHCC97-H, PLC, PRF/5, HCCLM3 | –                    | –                 | Patient survival, liver cirrhosis, tumor number, vascular invasion, capsular formation, Edmondson-Steiner grade | Promotes proliferation, migration and invasion of HCC cells | (124)     |
| AB019562        | 50 HCC tissues and paired ANTs  | SMMC7721, PLC/PRF/5, C3AHCC, THLE-3, HepG2 | –                    | –                 | –                                  | Promotes proliferation, migration and invasive features and reduces apoptosis in HCC cells | (125)     |
| PcnRNA-1        | 84 HCC tissues and paired ANTs, male BALB/c nu/nu mice | HCCLM3, Huh7, SK-Hep1, HepG2, LO2 | –                    | –                 | Patient survival, tumor size, vascular invasion, TNM stage | Promotes metastasis and EMT process in HCC cells and is correlated with poor prognosis | (126)     |
| IncRNA-TPE2P1   | 72 HCC tissues and 66 normal tissues, | HepG2, Huh7, MHCC97L, Bel7402, SMMC7721, HCCLM3 | –                    | –                 | tumor size, distant metastasis, differentiation degree, TNM stage | Promotes proliferation, migration and EMT process of HCC cells | (127)     |
| PCAT-1          | 82 HCC tissues and paired ANTs  | HepG2, Bel-7402                | –                    | –                 | –                                  | Increases proliferation and migration and inhibits apoptosis in HCC cells | (128)     |
| PCAT-14         | 39 HCC tissues and paired ANTs  | Huh7, HCCLM3, HepG2, SMMC7721, PLC5, QGY7701, HOLO2 | miR-372              | –                 | Patient survival, TNM stage, tumor metastasis, tumor size | Promotes proliferation and invasion of HCC cells through inducing methylation of miR-372 | (129)     |
| BLACAT1         | 37 HCC tissues and paired ANTs, male athymic nude (nu/nu) mice | HepG2, MHCC97L, Huh7, Hep3B, SK-Hep-1, SNU-449, SNU-182, SNU-429, bel-7402, THLE2, THLE3 | has-miR-485-5p       | –                 | –                                  | Promotes proliferation and invasion in HCC cells via upregulation of has-miR-485-5p. | (130)     |
| DLX6-AS1        | 60 HCC tissues and paired ANTs, 20 male BALB/c nude mice | MHCC97L, HCCLM3, HepG2, Hep3B, Huh7, LO2 | miR-203a, MMP-2     | –                 | tumor size, Edmondson grading, TNM stage | Contributes to HCC progression via regulating miR-203a/MMP-2 axis | (131)     |
| RAB5F           | –                               | HepG2, Huh3B, Huh7, MF-7, AS49, HeLa | LGR5                 | –                 | –                                  | Promotes HCC progression via LGR5 mediated elevation of β-catenin and c-Myc | (132)     |

(Continued)
| IncRNA   | Sample                                                                 | Cell line                                                                 | Interacting partners | Signaling pathway | Association with clinical features | Function                                                                 | Reference |
|----------|------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------|------------------|-----------------------------------|--------------------------------------------------------------------------|-----------|
| LOC90784 | 64 HCC tissues and paired ANTs                                         | L02, HepG2, SMCC7721, Bel-7404, PLC/PRF/5                                 | –                    | –                | Patient survival, tumor differentiation, TNM stage, venous invasion, HBV status, serum AFP | Promotes cell proliferation, migration and invasion and reduces apoptosis | (133)    |
| HOTAIR  | 53 HCC tissues and paired ANTs                                         | HepG2, Bel-7402                                                           | RBM38                | –                | –                                 | Enhances migration and invasion of HCC cells via regulating RBM38         | (134)    |
| HOTAIR  | 30 HCC tissues and paired ANTs, female BALB/c nude mice                | HepG2, Huh7, Hep3B, SMCC7721, MHC97H, LHL-3                               | miR-122              | –                | –                                 | Promotes cell proliferation and reduces cell cycle arrest through upregulation of miR-122 | (135)    |
| B2RAP1-AS1 | 49 HCC tissues and paired ANTs, 90 specific pathogen-free female nude mice | L-02, Huh-7, HCCLM3, L7, BEL-7405, SK-Hep-1, BGLC-9                     | THBS1                | –                | tumor size, microvascular invasion, TNM stage | Promotes proliferation, migration and angiogenesis                        | (136)    |
| SNAI3-AS1 | 46 HCC tissues and paired ANTs                                         | MHC97L, HepG2, Hep3B, Hep7, L02                                         | UPF1, Smad7          | TGF-β/Smad signaling pathway | Patient survival, tumor size, tumor nodule number, TNM stage | Promotes proliferation, metastasis and EMT process via regulation of UPF1 | (137)    |
| TP73-AS1 | 84 HCC tissues and paired ANTs                                         | HCCLM3, MHC97L, SMCC7722, Hep3B, HepG2, HL-7702, human HCC cell line HepG2, Hep3B, Hep7, L02 | miR-200a, HMGB1, RAGE | –                | Patient survival, tumor size, tumor nodule number, TNM stage | Promotes proliferation of HCC cells through regulation of miR-200a/HMGB1/RAGE axis | (138)    |
| TP73-AS1 | 72 HCC tissues and paired ANTs, male BALB/c nude mice                  | HepG2, Hep3B, Hep7, LO-2                                                  | PTEN/Akt signaling pathway | –                | –                                 | Promotes cell proliferation and reduces apoptosis and radiosensitivity of HCC cells | (139)    |
| HANR     | 35 HCC tissues and paired ANTs, male nude mice                         | HepG2, Huh7, SK-Hep-1, HLE, L02                                         | GSK1, GSK3β          | –                | TNM stage, distant metastasis    | Promotes cell growth, inhibits apoptosis and induces chemoresistance HCC   | (140)    |
| MIAT     | 45 HCC tissues and paired ANTs, BALB/c nude mice                       | HepG2, Huh7, SK-Hep-1, HLE, L02                                         | miR-214              | –                | –                                 | Promotes proliferation and invasion of HCC cells through sequestering miR-214 | (141)    |
| MIAT     | 20 HCC tissues and paired ANTs                                         | HepG2, SMCC7721, PLC/PRF/5, Hep7, SK-hep-1, 293T                         | miR-22-3p, sirt1      | –                | –                                 | Its knockdown promotes cellular senescence and represses HCC tumorigenesis by regulating miR-22-3p/sirt1 axis | (142)    |
| IncRNA FAL1 | 30 HCC tissues and paired ANts                                       | L02, SMCC7721, HepG2, Hep3B, Hep7, Hep2.2.15                            | miR-1236             | –                | Patient survival                  | Promotes HCC progression and is associated with poor prognosis            | (143)    |
| CDKN2B-AS1 | 100 HCC tissues and paired ANTs, 24 BALB/c male nude mice             | HepG2, Huh7, SMCC7721, Huh7, Hep7, Hep2.2.15                            | let-7c-5p, NAP1L1    | PI3K/AKT/mTOR signaling pathway | Patient survival                  | Promotes HCC cells proliferation and metastasis in HCC cells through targeting miR-1236 | (144)    |
| CDKN2B-AS1 | 48 HCC tissues and paired ANts                                       | QGY-7703, PLC/PRF/5, HEB111, MHC97                                      | –                    | –                | Patient survival, tumor size, TNM stage | Promotes HCC progression through interaction with poor prognosis           | (145)    |
| CDKN2BAS  | 86 HCC tissues and paired ANTs, nude mice                             | HCCLM3, SK-Hep-1, Huh7, MHC97H, L02                                     | mir-153-5p, ARH-GAP18 | MEK-ERK1/2 signaling pathway | –                                 | Enhances proliferation and metastasis of HCC cells through sponging miR-153-5p and upregulation of ARH-GAP18 | (146)    |
| IncRNA-PDCK2P | 60 HCC tissues and paired ANts, nude mice                           | MHC97L, SMCC7721, BEL-7404, HCCLM3, MHC97H, BEL-7404, HCCLM3, SMCC7721 | PDK1                 | PDK1/ AKT/caspase 3              | Patient survival, tumor embolus, tumor differentiation                  | Promotes HCC progression through interaction with poor prognosis           | (147)    |

(Continued)
| lncRNA | Sample | Cell line | Interacting partners | Signaling pathway | Association with clinical features | Function | Reference |
|--------|--------|-----------|----------------------|-------------------|-----------------------------------|----------|-----------|
| Ftx    | 73 HCC tissues and paired ANTs | LO2, Huh7, SMMC-7721, Bel-7402 | – | – | – | Promotes proliferation, migration and invasion in HCC cells through PPARγ pathway | (148) |
| MIR4435-2HG | 64 HCC tissues and paired ANTs | SNU-398, SNU-182 | miRNA-487a | – | tumor size | Promotes proliferation of HCC cells through upregulation of miRNA-487 | (149) |
| SOX9-AS1 | 67 HCC tissues and paired ANTs, male BALB/C nude mice | Huh7, HepG2, HCCLM3, Hep3B, Lo2 | miR-5590-3p, SOX9 | Wnt/β-catenin | Patient survival | Contributes to tumor growth and metastasis through sponging miR-5590-3p and upregulation of SOX9 | (150) |
| SOX21-AS1 | 68 HCC tissues and paired ANTs | Hep3B, LM3, MHHCC97H, HepG2, Huh7, Lo2 | p21 | – | Patient survival, tumor size, Edmonson Grade, vascular invasion, cirrhosis | Contributes to HCC progression through epigenetically silencing p21 by recruiting EZH2 to the promoter of p21 | (151) |
| HOXA11-AS | 66 HCC tissues and paired ANTs | HL-7702, HepG2, Hep3B, MHC-97H, BEL7402 | miR-124 | – | Patient survival, tumor size, differentiation, TNM stage, lymph node metastasis, recurrence | Enhances migration and invasion of HCC cells through suppression of miR-124 by binding to EZH2 | (152) |
| HOXA-AS2 | 58 HCC tissues and paired ANTs, female BALB/c nude mice | MHHCC97L, Huh7, HepG2, HCCLM3, SMMC-7721, MHHCC97H, HL-7702 | miR-520c-3p, GPC3 | – | – | Promotes migration and invasion of HCC cells through sponging miR-520c-3p and upregulation of GPC3 | (153) |
| HOXB-AS3 | 36 HCC tissues and paired ANTs | HepG, PLC, Hep3B, LM3 | p53 | – | – | Its downregulation inhibits proliferation and induced apoptosis and cell cycle arrest in HCC cells through regulation of p53 | (154) |
| LINC00978 | 33 HCC tissues and paired ANTs, sera of 58 HCC patients, 49 liver benign disease patients and 45 healthy controls, 10 BALB/c nude mice | 7721, 7402, HepG2, LM3 | EZH2, p21, E-cadherin | – | – | Promotes proliferation, migration, and invasion through epigenetically silencing p21 and E-cadherin | (155) |
| IncRNA-ATB | 72 HCC tissues and paired ANTs | SMMC-7721, HepG2 | YAP, ATG5 | – | Patient survival, tumor size, TNM stage | Promotes proliferation and clonogenicity and also promotes autophagy by activating YAP and increasing ATG5 expression | (156) |
| NR2F1-AS1 | 47 HCC tissues from oxaliplatin-resistant and oxaliplatin-sensitive, male nude mice | Huh7, HepG2, Lo2 | miR-363, ABCC1 | – | – | Its knockdown suppresses migration, invasion and drug-resistant of HCC cells via regulating miR-363/ABCC1 axis | (157) |
| DANCR | Male athymic BALB/C nude mice | LO2, MHHCC-97H, Huh7, HCC-LM3, HepG2, MHHCC-97L, Hep3B, SMMC-7721 | miR-27a-3p, ROCK1/LIMK1/Cofilin1 pathway | – | Patient survival, metastasis | Enhances proliferation and metastasis and regulates EMT process through targeting miR-27a-3p | (158) |
| DAAVCR | BALB/c mice | Hep3B, HepG2, Huh7, SNU449, SK-hep-1, LO2 | miR-216a-5p, KLF12 | – | – | Promotes HCC malignancy and progression through sponging miR-216a-5p and regulation of KLF12 expression | (159) |

(Continued)
| IncRNA      | Sample                                      | Cell line                  | Interacting partners | Signaling pathway | Association with clinical features                                      | Function                                                                 | Reference |
|------------|---------------------------------------------|----------------------------|----------------------|-------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------|-----------|
| LINC00205  | 80 HCC tissues and paired ANTs              | LO2, Hep3B, Huh7, HEK293T  | miR-122-5p           | –                 | Tumor size, venous infiltration, TNM stage                                | Enhances proliferation, migration and invasion in HCC cells via miR-122-5p | (160)     |
| OSER1-AS1  | 34 HCC tissues and paired ANTs              | HepG2, Hep3b               | miR-372-3p, Rab23    | –                 | Patient survival, tumor size, tumor stages                                | Its knockdown suppresses cell proliferation, invasion and migration and induces apoptosis via miR-372-3p-mediated upregulation of Rab23 | (161)     |
| DLEU2      | 50 HCC tissues and paired ANTs              | SMMC721, LO2, Huh7, HCCLM3 | EZH2                 | –                 | vascular invasion, tumor stage                                           | Its knockdown represses proliferation, migration and invasion of HCC cells | (162)     |
| DBH-AS1    | 45 HCC tissues and paired ANTs, male BALB/c nude mice | HepG2, SMMC-7721, Hep3B, MHC97H, SK- Hep1, LO2, QSO7701 | – | MAPK signaling pathway | HBsAg, tumor size                                                         | Promotes proliferation and survival of HCC cells by activating MAPK signaling pathway | (163)     |
| DBH-AS1    | 46 HCC tissues and paired ANTs              | Huh7, PLC, HepG2, Hep3B, LO2 | miR-138, AK/Src/ERK signaling pathway | – | tumor size, TNM stage, lymph node metastasis                              | Promotes tumorigenesis of HCC through targeting miR-138 by AK/Src/ERK signaling pathway | (164)     |
| LINC00152  | BALB/c mic                                  | HCCLM3, HepG2, MHC97H, SNU449, THLE-3, LO2 | miR-215, CDK13 | – | –                                                                         | Its knockdown inhibits proliferation, migration and invasion and induces apoptosis in HCC cells through regulation of miR-215/CDK13 axis | (165)     |
| LINC00152  | 70 HCC tissues and paired ANTs, male BALB/c mice | Hep3B, HCCLM3, MHC97H, HepG2 | miR-139, P3K/Akt/mTOR signaling pathway | – | –                                                                         | Supports cell cycle transition through sponging miR-139 and upregulation of P3K/Akt/mTOR signaling pathway | (166)     |
| LINC00152  | 80 HCC tissues and paired ANTs, male athymic BALB/c nude mice | Huh7, HCCLM3, Hep3B | miR-193a/b-3p, CCND1 | P3K/Akt/mTOR signaling pathway | –                                                                         | Supports cell cycle transition through sponging miR-193a/b-3p and upregulation of CCND1 | (167)     |
| AFAP1-AS1  | 156 HCC tissues and paired ANTs, nude mice  | LO2, SMMC-7721, Bel-7402, MHC97 L, MHC97H | – | – | Patient survival, tumor size, TNM stage, vascular invasion tumor size, BCLC stage, vascular invasion | Its silencing attenuates proliferation, migration and invasion and induces apoptosis in HCC cells through regulation of CCND1 | (168)     |
| LINC473    | 70 HCC tissues and paired ANTs              | Hep3B, Huh-1, SMMC-7721, PLC/PRF/5, SK-Hep-1 | survivin | – | –                                                                         | Promotes proliferation, invasion and EMT process and suppresses apoptosis in HCC cells via stabilizing survivin | (169)     |
| CHRF       | 48 HCC tissues and paired ANts              | HepG2, Huh-7               | miR-21               | P3K/Akt and Wnt/β-catenin pathways | TNM stage, differentiation, tumors size                                  | Promotes proliferation, cell viability and EMT process in HCC cells through targeting miR-21 | (170)     |
| NORAD      | 29 HCC tissues and paired ANTs              | SMMC-7721, Huh7, PLC/PRF/5, Hep3B | miR-202-5p | TGF-β pathway | Patient survival, HbsAg, tumor size                                       | Stimulates proliferation, migration and invasion of HCC cells via targeting miR-202-5p | (171)     |
| IncPARP1   | 70 HCC tissues and paired ANTs, male BALB/c nude mice | SMMC-7721, HepG2, Huh7, SK-Hep-1, Bel-7402 | PPAR1 | – | Patient survival, elderly age, serum level of α-fetoprotein (AFP), tumor size, recurrence | Its knockdown suppresses proliferation, migration, and invasion, while induced apoptosis in HCC cells via regulating PPAR1 | (172)     |
| IncARSR    | 92 HCC tissues and paired ANTs, male athymic BALB/c nude mice | SMMC-7721, HepG2 | PTEN | P3K/Akt signaling pathway | Patient survival, tumor size, BCLC stage                                  | Promotes doxorubicin resistance of HCC cells through downregulating PTEN | (173)     |

(Continued)
| IncRNA   | Sample                                                                 | Cell line                                                                 | Interacting partners | Signaling pathway | Association with clinical features | Function                                                                 | Reference |
|---------|------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------|-------------------|-----------------------------------|---------------------------------------------------------------------------|-----------|
| LASP1-AS| 423 HCC tissues and paired ANTs, athymic male BALB/c nude mice          | HCCLM, MHCC97H, d PLC/PRF5, Hep3B, Hep2, SMMC-7721, Bel-7402, Heuh7         | LASP1               | –                 | Patient survival, tumor size, tumor encapsulation, TNM stage             | PTEN and activation of PI3K/Akt signaling pathway Supports proliferation, migration and invasion of HCC cells via upregulation of LASP1 | (174)    |
| CCH1    | 112 HCC tissues and paired ANTs                                       | MHC97H, Hep2, Hep3B, Heuh7, HCCLM3, LO2                                  | –                    | ERK/MAPK signaling pathway | Patient survival, tumor number, tumor size, TNM stage                   | Its knockdown induces growth arrest and apoptosis in HCC cells             | (175)    |
| TUC338  | 12 HCC tissues and paired ANTs, male nude mice                         | Hep2, SMMC-7721, BEK-7402, Hep3B, Heuh7                                  | RASAL1              | –                 | –                                 | Its down-regulation constrains cell proliferation and invasion and sensitizes HCC cells to sorafenib by activation of RASAL1. | (176)    |
| G1HCG   | 70 HCC tissues and paired ANTs, male athymic BALB/c nude mice          | L02, QSG7701, SMMC7721, Hep3B, Heuh7, HCCLM3                            | miR-200b/a429       | –                 | Patient survival, tumor size, microvascular invasion, BCLC stage        | Stimulates proliferation, migration and invasion of HCC cells via epigenetically silencing miR-200b/a429 | (177)    |
| IncAKHE | 60 HCC tissues and paired ANTs, 10 male BALB/c nude mice               | LO2, Hep3B, 7402, Heuh7, Hep2                                            | YEATS4              | NOTCH2 signaling pathway | Patient survival                                                        | Stimulates proliferation and migration of HCC cells via cooperating with YEATS4 and activation of NOTCH2 signaling | (178)    |
| DUXAP10 | 32 HCC tissues and paired ANTs                                        | Hep2, SMMC7721, LO2                                                      | –                    | PI3K/Akt and Wnt/β-catenin signaling pathway                            | –                                 | Its knockdown suppresses proliferation, migration and invasion and induces apoptosis in HCC cells | (179)    |
| ZEB1-AS1| 102 HCC tissues and 21 healthy liver samples, athymic BALB/c mice      | Huh7, Hep2, Hep3B, SMMC7721, LM3, LO2                                   | –                    | –                 | Patient survival, microvascular invasion, recurrence                    | Influences tumor growth and metastasis in HCC cells                      | (180)    |
| MYCNOS  | 30 HCC tissues and paired ANTs, female BALB/c mice                     | HL-7702, Huh-7, Hep3B, JHH-7, SNU598                                     | miR-340, PREX2      | –                 | Patient survival                                                         | Influences proliferation and invasion of HCC cells through sponging miR-340 and upregulation of PREX2 | (181)    |
| AGAP2-AS1| 137 HCC tissues and paired ANTs                                        | LO2, Hep3B, HCCLM3, Heuh7, MHCC97H, SMMC-7721                          | miR-16-5p, ANXA11   | AKT signaling pathway        | Patient survival, TNM stage, venous invasion, Edmondson, tumor size     | Promotes proliferation, migration, invasion and EMT process and suppresses apoptosis in HCC cells through sponging miR-16-5p and upregulation of ANXA11 | (182)    |
| Linc00176| –                                                                       | Hep2, Huh7, Hep3B, HLE, HLF, HeLa, HEK29                                | miR-9, miR-185      | –                 | Patient survival                                                         | Its knockdown disrupts the cell cycle and activates necroptosis in HCC cells through releasing miR-9 and miR-185 | (183)    |
| AK002107| 134 HCC tissues and paired ANTs, BALB/c nu/nu mice                    | Hep2, MHC97H, MHCC7721, Hep3B, BEL-7402, LO2                             | miR-140-5p, TGFBR1  | –                 | Patient survival, Child-Pugh stage, AFP, macrovascular invasion, microvascular invasion, tumor size                      | Induces HCC progression and EMT process through regulating miR-140-5p/TGFBR1 axis | (184)    |
| DDX11-AS1| 40 HCC tissues and paired ANTs, 6 immune-deficient nude mice           | Hep2, SMMC-7721, SK-hep1, Huh7, HCCLM3, LO2                             | LATS2               | –                 | Patient survival, serum AFP, TNM stage                                  | Promotes HCC progression and metastasis by repressing LATS2 expression    | (185)    |
| IncRNA          | Sample                                                                 | Cell line                                      | Interacting partners | Signaling pathway                                                                 | Association with clinical features                                      | Function                                                                 | Reference |
|-----------------|------------------------------------------------------------------------|-----------------------------------------------|----------------------|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------|-----------|
| GATA3-AS1       | 80 HCC tissues and paired ANTs                                         | Hep3B, HCCLM3                                 | PTEN, CDKN1A, TPS3   | –                                                                                 | Patient survival, tumor size, TNM stage, lymph node metastasis          | Promotes proliferation and metastatic ability of HCC cells through repressing PTEN, CDKN1A and TPS3 | (186)    |
| DLEU1           | 56 HCC tissues and paired ANTs, male BALB/c nude mice                  | SMCC-7721, Hep3B, HepG2, HepG2, SNJ423,      | miR-133a, IGF-1R     | PI3K/AKT signaling pathway                                                        | Patient survival, TNM stage, vascular metastasis                        | Endorses HCC progression through sponging miR-133a and regulation of IGF-1R | (187)    |
| Lnc-Myd88       | 110 HCC tissues and paired ANTs, BAB/c nude mice                       | HepG2, Huh7, 97H, 97 L, HeLa, L02             | Myd88, H3K27Ac       | –                                                                                 | Tumor size, metastasis, Edmondson grade                                 | Endorses proliferation and metastasis of HCC cells through increasing Myd88 expression and by H3K27 modification | (188)    |
| K7N1-AS1        | 80 HCC tissues and paired ANTs, mice                                   | Huh7, SMMC-7721, Bel-7402, L02               | miR-23c, ERBB2IP     | –                                                                                 | Patient survival, tumor size, tumor grade TNM stage                      | Promotes proliferation and tumor growth of HCC by regulating miR-23c/ERBB2IP axis | (189)    |
| Lnc-GALH        | 108 HCC tissues and paired ANTs, 12 normal liver tissues              | Huh7, SNL-423, MHCC-97H, MHCC-97L, SMMC-7721 | Gankyrin             | –                                                                                 | Patient survival, vascular invasion, intrahepatic metastasis, distant metastasis, | Promotes migration and invasion HCC cells via epigenetically regulating Gankyrin | (190)    |
| MITA1           | SCID mice                                                              | HepG2, A549, U87, PC3, Huh7, HCCLM3, SK-Hep1, SMMC-7721, LO2, HGC27, U251 | Slug                 | –                                                                                 | –                                                                       | Its knockdown suppresses migration and invasion of HCC cells            | (191)    |
| Inc-UQID        | 139 HCC tissues and paired ANTs female NSG mice                       | HeK293T, L02, HepG2, QGY-7703                 | CDK6                 | –                                                                                 | Patient survival                                                        | Promotes cell cycle progression and HCC growth through suppressing DHX9-Mediated CDK6 Down-regulation | (192)    |
| Eif3J-AS1       | 80 HCC tissues and paired ANTs                                         | HepG2, SMMC-7721, MHCC-97H, LO2              | miR-122-5p, CTNN2     | tumor size, vascular invasion, tumor stage                                        | –                                                                       | Its knockdown suppresses proliferation, migration and invasion of HCC cells through regulation of miR-122-5p/CTNN2 axis | (193)    |
| IncRNA n335586  | 3 HBV positive HCC tissues and 3 HBV negative HCC tissues, female athymic BALB/c nude mice | Huh7, HepG2                                    | miR-924, CKMT1A      | –                                                                                 | –                                                                       | Promotes migration, invasion and EMT process through sponging miR-924 and upregulation of CKMT1A | (194)    |
| FGFR3-AS1       | 49 HCC tissues and 15 paired peritumor tissues, male BALB/c nude mice | SMCC-7721, Bel-7404 (7404), Huh7, Hep3B, HepG2, Huh7-7470 | –                    | PI3K/AKT signaling pathway                                                        | –                                                                       | Its knockdown suppresses proliferation, migration and invasion and induces apoptosis in HCC cells | (195)    |
| LINC00473       | Male nude mice                                                         | SMCC-7721, HepG2, Huh7, HCCLM3, QGY-7703     | miR-195, HMG2       | –                                                                                 | –                                                                       | Contributes to HCC progression through sponging miR-195 and upregulation of HMG2 | (196)    |
| LINC01551       | 60 HCC tissues and paired ANTs                                         | L-02, MHCC97-H, HepG2, SMCC7721               | miR-122-5p, ADAM10   | –                                                                                 | –                                                                       | Enhances proliferation, migration and invasion of HCC cells via sponging miR-122-5p and upregulation of ADAM10 | (197)    |
| IncRNA-6195     | 47 HBV-related HCC tissues and ANT                                      | Huh7, HepG2, 293T, L02                         | ENO1                 | –                                                                                 | Patient survival, Edmondson-Steiner grade                              | Suppresses proliferation of HCC cells through repressing enzymatic activity of ENO1 and inhibiting the energy metabolism | (198)    |

(Continued)
| lncRNA | Sample                                                                 | Cell line                                                                 | Interacting partners | Signaling pathway | Association with clinical features                                                                 | Function                                                                 | Reference |
|--------|------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------|-----------------|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|-----------|
| LINC00511 | 127 HCC tissues and paired ANTs                                     | LO2, Hep3B, HepG2, SMCC-7721, MHCC97H, Huh7, HCCLM3                       | miR-424              | –               | Patient survival, nodal metastasis, vascular invasion, clinical stage                               | Promotes proliferation and metastasis of HCC cells through modulating miR-424 | (199)     |
| LINC00511 | Expression data of HCC patients obtained from GEO and TCGA         | SMCC7721, HepG2, Hep3B, L-02                                             | miR-195, EYA1        | –               | Patient survival, tumor stage                                                                        | Promotes HCC progression through sponging miR-195 and upregulation of EYA1 | (200)     |
| lnc00462 | 49 HCC tissues and paired ANTs                                     | HCC-LM3, Huh7, SK-hep-1, QSG-7701                                         | –                    | PI3K/AKT signaling pathway                          | portal vein tumor thrombus tumor size, tumor number, BCLC stage          | Its down-regulation decreases proliferation, migration and invasion of HCC cells. | (201)     |
| NR027113 | 134 HCC tissues and paired ANTs                                     | Bel-7402, SK-HEP-1, PLC/PRF/5, MHCC97H, SMCC-7721                         | –                    | PI3K/Akt signaling pathway                          | Patient survival, TNM stage, tumor size                                  | Its down-regulation decreases proliferation, metastasis and EMT process in HCC cells | (202)     |
| ASLNC02525 | 5 HCC tissues and paired ANTs                                      | .HepG2, QGY-7701, SMCC-7721, L-02                                       | hsa-miR-489-3p, twist1 | –               | –                                                                                                   | Its silencing suppresses proliferation and invasion of HCC cells through regulating hsa-miR-489-3p/twist1 axis | (203)     |
| LncDQ    | 84 HCC tissues and paired ANTs, 50 serum samples from HCC patients and 30 serum samples from healthy controls, male BALB/c athymic nude mice | Huh-7, HepG2, HepG3B, SMCC7721, L-02                                      | –                    | –               | Patient survival, tumor stage, lymph node metastasis, tumor number                                 | Its down-regulation decreases proliferation, migration and invasion of HCC cells | (204)     |
| LINC00963 | 48 HCC tissues and paired ANTs                                      | L-02, HepG2, HB611, HHCC                                                 | –                    | PI3K/AKT signaling pathway                          | Patient survival, tumor size, TNM stage                                  | Promotes proliferation of HCC cells through activating PI3K/AKT signaling pathway | (205)     |
| DCST1-AS1 | 60 HCC tissues and paired ANTs, immunodeficient mice                  | L02, HepG2, SMCC-7721, Bel-7404, SK-hep-1                                | miR-1254, FAIM2      | –               | Patient survival, tumor size                                                                        | Its knockout suppresses proliferation and induces apoptosis and cell cycle arrest through regulating miR-1254/FAIM2 axis | (206)     |
| IncRNA00673 | 55 HCC tissues and paired ANTs, male BALB/c mice                    | HepG2, HepG3B, MHCC-97H, L-02                                           | –                    | Notch signaling pathway                             | –                                                                 | Its knockdown suppresses proliferation and induces cell cycle arrest and apoptosis in HCC cells | (207)     |
| TGFB2-AS1 | –                                                                    | HepG2                                                                    | –                    | –               | Tumor stage                                                                                         | Its down-regulation decreases proliferation, migration and invasion and induces apoptosis in HCC cells | (208)     |
| FLVCR1-AS1 | 60 HCC tissues and paired ANTs, BALB/c nude mice                    | LO2, Hep3B, HepG2, Huh7, PLC/PRF-5                                       | miR-513c, MET       | –               | TNM stage, tumor size                                                                              | Promotes HCC development and progression through sponging miR-513c and upregulation of MET | (209)     |
| LINC00707 | 12 BALB/c mice                                                       | SMCC7721, HepG2, Hep3B, SNU-449, Huh7, L-02                              | miR-206, CDK14      | –               | –                                                                                                   | Promotes HCC progression via sponging miR-206 and upregulation of CDK14 | (210)     |
| IncZic2  | 12 advanced HCC tissues, 7 early HCC tissues and 19 peritumor specimens, BALB/c nude mice | –                                                                       | MARCKS, MARCKSL1    | –               | –                                                                                                   | Regulates self-renewal of liver tumor-initiating cells by increasing MARCKS and MARCKSL1 expression through interacting with BRG1 | (211)     |
| GHET1   | 68 HCC tissues and paired ANTs                                      | HepG2, Hep3B, Bel-7402, SMCC-7721, L-02                                 | KLF2                | –               | Patient survival, vascular invasion, cirrhosis, tumor                                              | Promotes proliferation of HCC cells through epigenetically silencing KLF2 | (15)      |

(Continued)
Zhou et al. Such investigation has led to identification of recurrent deletion of lncRNA-PRAL in HCC samples in association with poor clinical outcome (224). The lncRNA TSLNC8 on 8p12 is another tumor suppressor lncRNA which is commonly deleted in HCC tissues (226). Table 5 shows the summarized results of studies which assessed association between lncRNAs insertion/deletion or tetranucleotide repeat polymorphisms and HCC.

### DISCUSSION

LncRNAs contribute in the pathogenesis of HCC through diverse mechanisms including modulation of oncogenes and tumor suppressor genes as well as modification of tumor microenvironment. The latter route of action has been best exemplified by the lnc-EGFR which enhances differentiation of...
| IncRNA     | Sample                                                                 | Assessed cell line          | Gene interaction | Signaling pathway | Association with clinical features                                                                 | Function                                                                 | Reference |
|------------|------------------------------------------------------------------------|-----------------------------|------------------|------------------|------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------|
| PSTAR      | 127 HCC tissues and ANTs                                               | PHH, HUVEPM, HepG2, MHCC-97H, HCCLM3, Hep3B, HuH7, HEC290T, OHT116 | p53, hnRNPK      | p53 signaling pathway                                | Patient survival, tumor size, tumor stage                                                                 | Suppresses proliferation and tumorigenicity of HCC cells by promoting p53 signaling and cell cycle arrest | (228)      |
| TPTEP1     | 32 primary HCC tissues and paired ANTs, 18 male BALB/c nude mice       | HepG2, SMMC-7721, QGY-7703, Huh-7, MHCC97h, SNU-449, Sk-hep1, and L02 | STAT3            | –                | –                                                                                                    | Represses proliferation, invasion and tumorigenicity of HCC cells through inhibiting STAT3 phosphorylation | (229)      |
| CASC2      | 75 HCC tissues and ANTs, nude mice                                     | MHCC-97L, Hep-3B, HepG2, HuH7, SMMC-7721, MHCC-97H, LO2   | miR-367, FBXW7   | –                | Patient survival, venous infiltration, high Edmondson-Stainer grading, TNM tumor stage             | Inhibit migration, invasion and EMT process by sponging miR-367 and upregulation of FBXW7 | (227)      |
| CASC2      | 30 HCC tissues and paired ANTs                                         | LO2, HepG2, Hep3B, QSG-7701, SMMC-7721, Huh-7               | miR-183          | Wnt/b-catenin signaling pathway                       | –                                                                                                    | Represses cell viability, colony formation, migration, and invasion through targeting miR-183 | (230)      |
| CASC2      | 50 HCC tissues and paired ANTs                                         | HepG2, HuH7, Hep3B, SMMC7221, Bel7402, LO2                  | –                | MAPK signaling pathway                                | –                                                                                                    | Its overexpression suppresses proliferation, migration and invasion and induces apoptosis in HCC cells | (231)      |
| CASC2      | 80 HCC tissues and paired ANTs                                         | HepG2, SMMC-7721, Hep3B, Huh-7, SMMC-7721, LO2             | miR-362-5p       | NF-κB signaling pathway                               | tumor size, differentiation statuses                                                                    | Its overexpression suppresses migration and invasiveness of HCC cells through affecting miR-362-5p. | (232)      |
| CASC2      | 20 HCC tissues and paired ANTs, BALB/c nude mice                       | HepG2, HuH7                                                      | miR-24-3p        | –                | –                                                                                                    | Suppresses cell viability and induces apoptosis in HCC cells via regulating miR-24-3p. | (233)      |
| EPB41L4A-AS2| 10 HCC tissues and 10 normal tissues, Neonatal B6C3F1 mice             | SMMC-7721, QGY-7703, QSG-7701                                  | miR-301a-5p, FOXL1| –                | –                                                                                                    | Its upregulation inhibits proliferation, migration and invasion by sponging miR-301a-5p and upregulation of FOXL1. | (234)      |
| LINC00467  | 65 HCC tissues and paired ANTs                                         | SMMC-7721, HepG2                                                 | miR-9-5a, PPARA  | –                | metastasis                                                                                           | Its ectopic expression reduces proliferation, migration and invasive features of HCC cells through sponging miR-9-5a and increasing PPARA. | (235)      |
| Inc-DILC   | 196 HCC tissues and paired ANTs, NODSCID mice                        | HuH7, HepG2, CSQ7-2                                            | IL-6             | JAK2/STAT3 activation                                 | Patient survival                                                                                     | Suppresses liver cancer stem cell expansion through inhibition of autocrine IL-6/STAT3 signaling. | (236)      |
| Inc-FTX    | 129 HCC tissues and paired ANTs,                                       | SMMC-7721, HCCLM3, Hep3B, HepG2, HuH7, 97H, GSG7701          | miR-374a, MCM2   | Wnt/b-catenin signaling pathway                       | Patient survival                                                                                     | Suppresses proliferation, invasion and EMT process in HCC cells through physically binding miR-374a and MCM2. | (237)      |
| LINC00472  | 109 HCC tissues and 35 ANTs                                           | LO2, HepG2, BEL7404, Hep3B, SMMC-7721, Huh-7                  | miR-93-5p, PDCD4 | –                | Patient survival                                                                                     | Its forced expression suppressed cell proliferation, migration and invasion and promotes apoptosis through miR-93-5p/PDCD4 axis. | (238)      |
| FENDRR     | 30 HCC tissues and paired ANTs, BALB/c male nude mice                 | HepG2, Hep3B, LO2                                              | GPC3             | –                | –                                                                                                    | Suppresses proliferation, migration and invasion and induces apoptosis in HCC cells through epigenetically silencing GPC3. | (239)      |
| TSLNC8     | 120 HCC tissues and paired ANTs, nude mice                            | Huh-7, SNU-449, SMMC-7721                                      | STAT3            | –                | Patient survival                                                                                     | Suppresses cell proliferation and metastasis of HCC cells               | (226)      |
| mir603HG   | 93 HCC tissues and paired ANTs                                        | SMMC-7721, HuH7, LO2                                           | HNRNPA2B1       | NF-κB signaling pathway                               | Patient survival, tumor recurrence                                                                  | Represses HCC cells invasion and metastasis through stimulation of HNRNPA2B1 degradation | (151)      |
TABLE 2 | Continued

| IncRNA       | Sample                                                                 | Assessed cell line | Gene interaction | Signaling pathway | Association with clinical features                                                                 | Function                                                                 | Reference |
|--------------|------------------------------------------------------------------------|--------------------|------------------|-------------------|------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|-----------|
| MEG3         | 54 HCC tissues and paired ANTs, serum samples from 54 HCC patients and 54 healthy controls | HepG2, SNU-398, CSA, AML12, | TGF-β1 | –                  | Patient survival, distant tumor metastasis                                                          | Its silencing promotes proliferation, migration and invasion in HCC cells through upregulation of TGF-β1 | (240)     |
| MEG3         | 30 HCC tissues and paired ANTs                                          | 293T, SK-HEP-1, Huh7 | miR-9-5p, SOX11 | –                  | TNM stage, metastasis                                                                                | Its overexpression represses cell growth and promotes apoptosis in HCC cells by sponging miR-9-5p and upregulation of SOX11 | (241)     |
| TSLD8        | 108 HCC tissues and paired ANTs                                         | SMMC-7721, Huh7, HepG2, Hep3B, L02, HEK293T | WWOX | –                  | TNM stages, tumor dimension, metastatic ability, occurrence of cancer embolus                      | Inhibits migration and cell viability of HCC cells through stabilizing WWOX | (241)     |
| Lnc00312     | 23 HCC tissues and paired ANTs, female SCID mice                       | HepG2, MKN-74      | –                | –                  | –                                                                                                     | –                                                                         | (242)     |
| IncNRON      | 215 HCC tissues and paired ANTs, 5 male nude mice                      | QGY-7703, HepG2, BEL-7404, Hep3B, SMMC-7721, MHC97, L02 | NFAT | –                  | Patient survival, tumor size, tumor differentiation, Vascular tumor thrombus                          | Suppresses proliferation, migration and invasion of HCC cells            | (243)     |
| PTEKP1       | –                                                                      | Mahlavu            | miR-17, miR-19b, miR-20a, PTEN, PHLPP | P38/KAK signaling pathway | –                                                                                                     | Its overexpression suppresses proliferation, migration and invasion and supports autophagy and apoptosis in HCC cells | (244)     |
| LNM00607     | 159 HCC tissues and paired ANTs, nude mice                            | MHC97H, HCCLM3, PLC, Hep3B, HepG2, 7721 | p65, p53 | –                  | Patient survival                                                                                     | Its overexpression reduces cell proliferation and induces apoptosis in HCC cells through suppression of p65 transcription | (245)     |
| AOC4P        | 108 HCC tissues and paired ANTs, male BALB/C nude mice                 | J7, SK-Hep1        | Vimentin         | –                  | Patient survival, clinical stage, capsule invasion, vessel invasion                                  | Constrains proliferation and metastasis of HCC cells by increasing Vimentin degradation and inhibition of EMT process | (246)     |
| AK058003     | 50 HCC tissues and paired ANTs, male athymic BALB/c nude mice          | HepG2, SK-Hep1, HEK 293T | HuR, γ-synuclein | –                  | –                                                                                                     | Suppresses proliferation and metastasis of HCC cells by interacting with HuR and inhibiting γ-synuclein expression | (247)     |
| Linc-USP16   | 70 HCC tissues and paired ANTs, 4 Female athymic BALB/c nude mice       | MHC97H, MHC97L, HepG2, SMMC-7721, L02, BEL7402, 293T | miR-21, miR-590-5p, PTEN | AKT signaling pathway | tumor size, clinical stage, metastasis                                                            | Suppresses proliferation and migration of HCC cells through regulation of miR-21/miR-590-5p/PTEN route | (247)     |
| FER1L4       | 35 HCC tissues and paired ANTs, 14 Female athymic BALB/c nude mice      | LO2, Hep3B Huh7, 293T | PTEN | –                  | –                                                                                                     | Suppresses proliferation of HCC cells via regulating PTEN               | (248)     |
| FER1L4       | 36 HCC tissues and paired ANTs, Female nude (BALB/c-nu) mice           | HepG2, Huh7, Hep3B, HCCM3, L02 | miR-106a-5p | –                  | –                                                                                                     | Constrains proliferation, invasion and tumorigenicity of HCC cells via targeting miR-106a-5p | (249)     |
| FER1L4       | 31 HCC tissues and paired ANTs                                         | HepG-2, Hep3b, SMMC-7721, L-02 | – | P38/KAK signaling pathway | –                                                                                                     | Its overexpression reduces cell proliferation, migration and invasion and induces apoptosis | (250)     |
| PANDA        | 48 HCC tissues and paired ANTs, immunodeficient mice                   | HCC LM3, Huh7      | –                | –                  | –                                                                                                     | Its overexpression enhances proliferation of HCC cells by repressing senescence associated inflammatory factor ILB | (251)     |
| HHIP-AS1     | 60 HCC tissues and paired ANTs                                         | Hep3B, PLC/PREF/5, Huh7, HepG2, MHC97 h | HHIP | –                  | tumor size, metastasis, TNM stage                                                                   | Constrains proliferation, migration and invasion and induces             | (252)     |
| IncRNA         | Sample                                                                 | Assessed cell line | Gene interaction | Signaling pathway | Association with clinical features                                                                 | Function                                                                 | Reference |
|---------------|------------------------------------------------------------------------|--------------------|------------------|-------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|-----------|
| XIST          | 40 HCC tissues and paired ANTs                                         | HepG2             | miR-155-5p       | –                 | –                                                                                                  | apoptosis in HCC cells via stabilizing HHIP                              | (253)     |
| JPX           | 40 HCC tissues and paired ANTs                                         | HepG2             | XIST             | –                 | –                                                                                                  | Its overexpression inhibits HCC cell growth by targeting miR-155-5p      | (253)     |
| uc.134        | 170 paraffin-embedded samples of HCC tissues and ANTs, male BALB/c nude mice | MHCC97,           | LATS1, CUL4A     | –                 | Patient survival, TNM stage, lymph node metastasis, tumor number, Serum AFP,                         | Its overexpression HCC cell growth through upregulation of v         | (223)     |
|               |                                                                        | HCCM3, MHCC97L, Huh7, L02, HepG2, Bel-7402 |                  |                  |                                                                                                   | Constrains proliferation, invasion and metastasis of HCC cells through suppressing CUL4A-mediated ubiquitination of LATS1 | (223)     |
| C10T1NFI-AS1  | 11 HCC tissues and paired ANTs, 12 male BALB/c nude mice              | HepG2, Huh7       | miR-221-3p, SOCS3 | JAK/STAT signaling pathway | –                                                                                                  | Its overexpression inhibits proliferation, migration and invasion of HCC cells through targeting miR-221-3p and upregulation of SOCS3 | (254)     |
| GAS5-AS1      | 82 HCC tissues and paired ANTs, male BALB/c nude mice                 | HepG2, SMMC7721   | GAS8             | –                 | Patient survival                                                                                   | Suppresses proliferation, migration and invasion and induces apoptosis by epigenetically activating GAS8 | (255)     |
| LINC00657     | 49 HCC tissues and paired ANTs, female nude (BALB/c-rcnu) mice        | HepG2, Huh7,      | miR-106a-5p, PTEN | –                 | Patient survival, tumor size, vascular invasion, TNM stage                                        | Suppresses proliferation, migration and invasion through sponging miR-106a-5p and regulation of PTEN expression | (256)     |
| LINC-ncdh4-2  | –                                                                     | SK-Hep-1, Huh7    | R-cadherin       | –                 | –                                                                                                  | Represses migration and invasion of HCC cells through regulation of R-cadherin | (257)     |
|               | (TCONS_00027978)                                                     |                    |                  |                   |                                                                                                   |                                                                           |           |
| MAG2-AS3      | 88 HCC tissues and paired ANTs, 12 male BALB/c nude mice              | L02, HepG2, Hep3B, MHCC-97H | miR-374b-5p, SMG1 | –                 | Patient survival, tumor size, lymph node metastasis, TNM stage                                      | Suppresses proliferation and migration of HCC cells via sponging miR-374b-5p and increasing SMG1 | (258)     |
| LINC01093     | 70 HCC tissues and paired ANTs, BALB/c-rcnu mice                      | Huh7, BEL-7402    | IGF2BP1, GLI1    | –                 | Patient survival, cancer embolus, TNM stage                                                         | Suppresses proliferation and metastasis of HCC cells via interaction with IGF2BP1 and facilitation of GLI1 degradation | (259)     |
| GAS5          | 50 HCC tissues and paired ANTs                                         | Huh7, Hep3B, HepG2, QGY-7701, MHCC97L, HCCLM9h, L02 | vimentin          | –                 | Patient survival, PVTT, histologic grade                                                            | Inhibits proliferation and invasion of HCC cells through regulating Vimentin | (260)     |
| GAS5          | 32 HCC tissues and paired ANTs                                         | Bel-7402, SMMC-7721, HCCLM3, L-02 | miR-21           | –                 | Patient survival, TNM stage, tumor size                                                           | Its overexpression suppresses migration and invasion of HCC cells through targeting miR-21 | (261)     |
| GAS5          | 32 HCC tissues and paired ANTs                                         | HepG2, Hep3B, LO2 | miR-21, PTEN     | –                 | Patient survival                                                                                            | Its downregulation promotes proliferation and drug resistance HCC cells through reducing PTEN | (262)     |
| GAS5          | 38 HCC tissues and paired ANTs                                         | Lo-2, HepG2, Huh7 | miR-222          | VEGF signaling pathway | Patient survival                                                                                   | Enhances sensitivity of HCC cells to cisplatin through sponging miR-222 | (263)     |
| SchLAH        | 132 HCC tissues and paired ANTs, BALB/c nude mice                     | HepG2, Hep3B, SMMC7721 | FUS             | –                 | Patient survival                                                                                   | Represses migration and lung metastasis of HCC cells via interacting with FUS | (264)     |
| NKILA         | 54 HCC tissues and paired ANTs                                         | QSG-7701, SMMC-7721, Hep3B, HCCLM3, HepG2 | – | NF-κB signaling | Patient survival                                                                                   | Its overexpression enhances baicalein effect on inhibition of proliferation and migration and induction of apoptosis | (265)     |
| LINC00261     | 66 HCC tissues and paired ANTs                                         | SMMC-7721, MHCC97L, MHCC97H, LO2 | – | Notch signaling pathway | Patient survival, tumor size, TNM stage                                                             | Inhibits proliferation, colony formation, invasion and EMT process | (266)     |

(Continued)
TABLE 2 | Continued

| IncRNA     | Sample                        | Assessed cell line       | Gene interaction | Signaling pathway | Association with clinical features | Function                                                                 | Reference |
|------------|-------------------------------|--------------------------|------------------|------------------|-----------------------------------|---------------------------------------------------------------------------|-----------|
| MIR31HG3   | 42 HCC tissues and paired ANTs, BALB/c nude mice | SMMC7721, HepG2, Hep3B, SK-hep1, L02 | miR-575, ST7L    | –                | Patient survival, Tumor, size, tumor nodule number, vascular invasion | Suppresses proliferation, migration and invasion of HCC cells             | (266)    |
| LINC01554  | 167 HCC tissues and paired ANTs | BEL7402, OGY7701, OGY7703, SMMC7721, PLC8024, HepG2, Huh7, Hep3B | miR-365a, PKM2   | Akt/mTOR signaling pathway | Patient survival, tumor invasion, tumor size, tumor stage                | Inhibits cell growth, colony formation in soft agar, foci formation, and tumor formation through downregulation of PKM2 | (267)    |
| FAM99B     | 80 HCC tissues and paired ANTs | MHC97L, MHC97H, HCOCLM, Huh-7, HepG2, Hep3B | –                | –                | Patient survival, vascular invasion, histologic grade, T stage          | Its overexpression suppresses proliferation and invasion of HCC cells      | (268)    |
| RGMB-AS1   | 108 HCC tissues and 25 ANTs    | OGY7703, Huh7, BEL7402, HepG2 | RGMB             | –                | Patient survival, clinical stage, tumor size, metastasis               | Its overexpression represses proliferation, migration and invasion of HCC cells | (269)    |
| LINC00052  | 12 HCC tissues and paired ANTs | SMMC7721, HepG2, SK-hep1, Huh7, L02, 293T | miR-101-3p, SOX9 | –                | –                                                                              | Constrains proliferation and metastasis via affecting miR-101-3p and suppressing SOX9 | (270)    |
| DGCR5      | –                             | HepG2, Hep3B, MHC97L, M-HC97H, SNU-449, M-HC97H, SMMC7721, THLE-5 | miR-346, KLF14   | –                | –                                                                              | Its overexpression attenuates proliferation, migration and invasion of HCC cells through sponging miR-346 and modulating KLF14 expression | (271)    |
| ID2-AS1    | 144 HCC tissues and paired ANTs, NOG-SCID mice | MHC97L, MHC97H, HCOCLM, Huh-7, HepG2-C3A, SK-hep1, HEK-293T | ID2              | –                | Patient survival                                                               | Represses migration, invasion and metastasis of HCC cells via binding to HDAC8 and regulation of ID2 expression | (272)    |
| F11-AS1    | –                             | HepG2, Hep3B, Huh6, SMMC7721, LO2 | miR-3146, PTEN   | –                | –                                                                              | Represses HCC progression via acting as ceRNA for miR-3146 and affecting PTEN level | (273)    |

Tregs therefore increasing immune evasion (12). Moreover, certain lncRNAs such as MUF and SNHG7 facilitate EMT process through modulation of Wnt/β-catenin signaling pathway (14, 114). Other lncRNAs can modulate EMT through sponging a number of miRNAs. MAPK, PI3K/AKT and JAK/STAT signaling pathways are other cancer-related pathways that are modulated by several lncRNAs in HCC. The interactions between lncRNAs, miRNAs and mRNAs have functional importance in the pathogenesis of HCC. Examples of such trios include H19/miR-15b/CDC42, H19/miR-326/TWIST1, NEAT1/miR-485/STAT3, MALAT1/miR-124-3p/Slug, MALAT1/miR-195/EGFR, MALAT1/miR-22/SNA11 and ANRIL/miR-144/PBX3.

Functional roles of lncRNAs in HCC have been appraised in animal models. These models have facilitated identification of lncRNAs targets and related pathways (304), which can be used as therapeutic candidates in HCC. HCC-associated lncRNAs can affect gene expression via recruiting epigenetic factors (305), regulation of transcription factors (306), modulation of protein degradation (307) and alteration of phosphorylation of proteins (308).

Genomic alterations and polymorphisms within lncRNA-coding regions have been shown to confer risk of HCC. Such variations might also predict survival of these patients. However, the observed association between these variants and HCC should be verified in independent samples from different ethnic groups. Integration of the results of genome-wide association studies with high throughput sequencing data obtained from microarray and RNA seq experiments would help in discovery of HCC-related single nucleotide polymorphisms within lncRNAs.

The biomarker role of lncRNAs in HCC has been verified by several studies indicating their importance both in the diagnosis and in the prognosis of this cancer. Expression levels of lncRNAs can differentiate HCC patients from inactive HBs Ag carriers, patients with chronic hepatitis and those with liver cirrhosis. In addition, the high diagnostic power values of peripheral levels of a number of lncRNAs such as UCA1 and NEAT1 have potentiated them as methods for non-invasive diagnosis of HCC. Moreover, lncRNAs can be regarded as therapeutic targets in HCC. The importance of lncRNAs as therapeutic targets in HCC has been noted by several experiments in animal models of HCC. Yet, such experiments wait approval in clinical settings. In vivo delivery of a number of lncRNAs such as lncRNA-PRAN, uc.134 and TSLNC8 has been shown to attenuate tumor growth and enhance lifespan of xenograft models of HCC (223, 224, 226). Moreover, a number of
| IncRNA       | Sample number                      | Kaplan-Meier analysis                                                                 | Univariate cox regression | Multivariate cox regression | Reference |
|--------------|------------------------------------|--------------------------------------------------------------------------------------|---------------------------|-----------------------------|-----------|
| NEAT1        | 40 HCC specimens and paired ANTs   | Its elevated level is related with short OS.                                         | –                         | –                           | (24)      |
| NEAT1        | 86 HCC specimens and paired ANTs   | Its elevated level is related with poor OS.                                          | correlated with OS        | an independent prognostic factor for OS | (27)      |
| PTTG3P       | 90 paraffin-embedded HCC specimens and ANTs | Its elevated level is related with low OS.                                          | –                         | an independent prognostic factor for OS | (31)      |
| UBE2CP3      | 46 HCC specimens and ANTs         | Its elevated level is related with poor OS.                                          | –                         | –                           | (33)      |
| lncRNA0461   | 87 HCC specimens and paired ANTs   | Its elevated level is related with decreased OS.                                     | –                         | –                           | (34)      |
| MALAT1       | 56 HCC specimens and paired ANTs   | Its elevated level is related with decreased OS.                                     | –                         | –                           | (35)      |
| MNX1-AS1     | 81 HCC specimens and paired ANTs   | Its elevated level is related with poor OS.                                          | –                         | –                           | (37)      |
| MCM3AP-AS1   | 80 HCC specimens and paired ANTs   | Its elevated level is related with shorter OS.                                       | –                         | –                           | (38)      |
| ANRIL        | 130 tissues and paired ANTs        | Its elevated level is related with low OS.                                          | correlated with OS        | an independent prognostic marker for OS | (49)      |
| AWPPH        | 88 HCC specimens and paired ANT    | Its elevated level is related with poor DFS and OS.                                  | –                         | an independent prognostic factor for RFS and OS | (51)      |
| PVT1         | 48 HCC specimens and paired ANTs   | Its elevated level is related with poor OS.                                          | –                         | –                           | (53)      |
| SNHG1        | 82 HCC specimens and paired ANTs   | Its elevated level is related with poor PFS and OS.                                  | –                         | –                           | (56)      |
| ENST00000429227.1 | 161 HCC specimens and paired ANTs | Its elevated level is related with poor OS.                                          | correlated with OS        | an independent prognostic marker for OS | (58)      |
| lncRNA0665   | 76 HCC specimens and paired ANTs   | Its elevated level is related with shorter OS.                                       | –                         | –                           | (63)      |
| CRNDE        | 23 HCC specimens and paired ANTs   | Its elevated level is related with shorter DFS and OS.                               | –                         | –                           | (65)      |
| FOXD2-AS1    | 88 HCC specimens and paired ANTs   | Its elevated level is related with poor OS.                                          | –                         | –                           | (73)      |
| HULC         | 41 HCC specimens and paired ANTs   | Its elevated level is related with shorter OS.                                       | correlated with OS        | an independent prognostic marker for PFS and OS. | (76)      |
| SBF2-AS1     | 134 HCC specimens and paired ANTs  | Its elevated level is related with shorter OS.                                       | correlated with OS        | an independent prognostic marker for PFS and OS. | (78)      |
| UC0011kb     | 82 HCC tissues and 20 ANTs         | Its elevated level is related with poor progression-free survival (PFS) and OS.      | correlated with OS        | an independent prognostic marker for PFS and OS | (79)      |
| LUCAT1       | 90 HCC tissues and paired ANTs      | Its elevated level is related with poor OS.                                          | correlated with PFS and OS, OS, correlated with OS | an independent prognostic marker for OS | (82)      |
| AK001796     | 73 HCC tissues and paired ANTs     | Its elevated level is related with poor OS.                                          | correlated with OS        | an independent prognostic marker for OS | (83)      |
| FEZF1-AS1    | 139 HCC tissues and paired ANTs    | Its elevated level is related with poor OS.                                          | –                         | –                           | (84)      |
| MINCR        | 161 HCC tissues and paired ANTs    | Its elevated level is related with poor OS.                                          | correlated with OS        | an independent prognostic marker for OS | (85)      |
| XIST         | 88 HCC tissues and paired ANTs     | Its elevated level is related with short DFS.                                        | –                         | –                           | (88)      |
| XIST         | 52 HCC tissues and paired ANTs     | Its elevated level is related with poor survival of HCC patients.                    | –                         | –                           | (89)      |
| TRPM2-AS     | 108 HCC tissues and paired ANTs    | Its elevated level is related with poor OS.                                          | –                         | –                           | (90)      |
| LSINCT5      | 126 HCC tissues and paired ANTs    | Its elevated level is related with poor OS.                                          | –                         | –                           | (92)      |
| XLOC         | 68 HCC tissues and paired ANTs     | Its elevated level is related with poor OS.                                          | –                         | an independent prognostic marker for OS | (93)      |

(Continued)
| IncRNA | Sample number | Kaplan-Meier analysis | Univariate cox regression | Multivariate cox regression | Reference |
|--------|---------------|-----------------------|---------------------------|-----------------------------|-----------|
| URHC   | 52 HCC tissues and paired ANTs | Its elevated level is related with short OS after surgery. | – | – | (96) |
| RUSC1-AS-N | 66 HCC tissues and paired ANTs | Its elevated level is related with short RFS and OS. | – | – | (99) |
| CCAT1  | 66 HCC tissues and paired ANTs | Its elevated level is related with low RFS and OS. | – | – | (101) |
| SNHG16 | 71 HCC tissues and paired ANTs | Its elevated level is related with poor DFS and OS. | correlated with OS | an independent prognostic marker for OS | (105) |
| SNHG12 | 48 HCC tissues and paired ANTs | Its elevated level is related with poor DFS and OS. | – | – | (108) |
| SNHG20 | 96 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | – | – | (109) |
| SNHG5  | 48 HCC tissues and paired ANTs | Its elevated level is related with poor RFS and OS. | correlated with RFS and OS | an independent prognostic marker for RFS and OS | (110) |
| SNHG6-003 | 52 HCC tissues and paired ANTs, FFPE tissues from 160 patients | Its elevated level is related with poor DFS and OS. | correlated with OS | an independent prognostic marker for OS | (113) |
| SNHG7  | 40 HCC tissues and paired ANTs | Its elevated level is related with low OS. | – | – | (114) |
| SNHG7  | 80 HCC tissues and paired ANTs | Its elevated level is related with short OS. | – | – | (115) |
| Sox2ot  | 84 HCC tissues and ANTs | Its elevated level is related with poor OS. | correlated with OS | an independent prognostic marker for OS | (119) |
| SPRY4-IT1 | 82 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | – | – | (121) |
| PANDAR | 482 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | correlated with OS | an independent prognostic marker for OS | (122) |
| CARLo-5 | 97 HCC tissues and paired ANTs | Its elevated level is related with shorter DFS and OS. | correlated with DFS and OS | an independent prognostic factor for DFS and OS | (124) |
| PlncRNA-1 | 84 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | correlated with OS | an independent prognostic factor for OS | (126) |
| PCAT-14 | 39 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | – | – | (129) |
| DLX6-AS1 | 60 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | – | – | (131) |
| TP73-AS1 | 84 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | correlated with OS | an independent prognostic factor for OS | (138) |
| HANR  | 35 HCC tissues and paired ANTs, | Its elevated level is related with poor OS. | – | – | (140) |
| IncRNA FAL1 | 30 HCC tissues and paired ANTs | Its elevated level is related with poor OS. | – | – | (143) |
| CDKN2B-AS1 | 100 HCC tissues and paired ANTs, | Its elevated level is related with poor OS. | – | – | (144) |
| IncRNA-PDPIK2P | 60 HCC tissues and paired ANTs, | Its elevated level is related with poor OS. | correlated with OS | an independent prognostic factor for OS | (147) |
| SOX9-AS1 | 67 HCC tissues and paired ANTs | Its elevated level is related with low OS. | – | – | (150) |
| SOX21-AS1 | 68 HCC tissues and paired ANTs | Its elevated level is related with shorter OS. | – | – | (151) |
| HOX11-AS | 66 HCC tissues and paired ANTs | Its elevated level is related with shorter OS. | – | – | (152) |
| IncRNA-ATB | 72 HCC tissues and paired ANTs | Its elevated level is related with shorter OS. | – | – | (156) |
| OSER1-AS1 | 34 HCC tissues and paired ANTs | Its elevated level is related with shorter DFS and OS. | – | – | (161) |
| AFAP1-AS1 | 156 HCC tissues and paired ANTs | Its elevated level is related with shorter DFS and OS. | – | – | (168) |
| LNC473 | 70 HCC tissues and paired ANTs | Its elevated level is related with low OS. | – | – | (169) |

(Continued)
| IncRNA     | Sample number                      | Kaplan-Meier analysis                                                                 | Univariate cox regression | Multivariate cox regression | Reference |
|------------|-----------------------------------|--------------------------------------------------------------------------------------|---------------------------|-----------------------------|-----------|
| NORAD      | 29 HCC tissues and paired ANTs    | Its elevated level is related with shorter DFS and OS.                               | correlated with OS        | an independent prognostic factor for OS | (171)    |
| IncPARP1   | 70 HCC tissues and paired ANTs    | Its elevated level is related with shorter DFS and OS.                               | correlated with OS        | an independent prognostic factor for OS | (172)    |
| IncARSR    | 92 HCC tissues and paired ANTs    | Its elevated level is related with shorter RFS and OS.                               | correlated with OS        | an independent prognostic factor for OS | (173)    |
| LASP1-AS   | 423 HCC tissues and paired ANTs   | Its elevated level is related with poor RFS and OS.                                  | correlated with OS        | an independent prognostic factor for RFS and OS | (174)    |
| CCHE1      | 112 HCC tissues and paired ANTs   | Its elevated level is related with low OS.                                            | an independent prognostic factor for OS | (175)    |
| G1HCG      | 70 HCC tissues and paired ANTs    | Its elevated level is related with low RFS and OS.                                   | correlated with OS        | an independent prognostic factor for DFS and OS | (177)    |
| IncAKHE    | 60 HCC tissues and paired ANTs    | Its elevated level is related with low DFS and OS.                                   | –                         | –                           | (178)    |
| ZEB1-AS1   | 102 HCC tissues and 21 healthy liver samples | Its elevated level is related with low RFS and OS.                                 | –                         | –                           | (180)    |
| MYCNOS     | 30 HCC tissues and paired ANTs    | Its elevated level is related with poor OS.                                          | –                         | –                           | (181)    |
| AGAP2-AS1  | 137 HCC tissues and paired ANTs   | Its elevated level is related with poor DFS and OS.                                  | –                         | –                           | (182)    |
| AK002107   | 134 HCC tissues and paired ANTs   | Its elevated level is related with poor DFS and OS.                                  | –                         | –                           | (183)    |
| DDX11-AS1  | 40 HCC tissues and paired ANTs    | Its elevated level is related with low OS.                                            | –                         | –                           | (185)    |
| GATA3-AS1  | 80 HCC tissues and paired ANTs    | Its elevated level is related with low OS.                                            | –                         | –                           | (186)    |
| DLEU1      | 56 HCC tissues and paired ANTs    | Its elevated level is related with low OS.                                            | –                         | –                           | (187)    |
| KT1-AS1    | 80 HCC tissues and paired ANTs    | Its elevated level is related with low OS.                                            | –                         | –                           | (189)    |
| Linc-QALH  | 108 HCC tissues and paired ANTs, 12 normal liver tissues | Its elevated level is related with poor RFS and OS.                              | –                         | –                           | (190)    |
| LNCO0511   | 127 HCC tissues and paired ANTs   | Its elevated level is related with low OS.                                            | correlated with OS        | an independent prognostic factor for OS | (199)    |
| NR027113   | 134 HCC tissues and paired ANTs   | Its elevated level is related with low OS.                                            | correlated with OS        | an independent prognostic factor for survival | (202)    |
| LncDQ      | 84 HCC tissues and paired ANTs, 50 serum samples from HCC patients and 30 serum samples from healthy controls | Its elevated level is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (204)    |
| GHET1      | 68 HCC tissues and paired ANTs    | Its elevated level is related with low OS.                                            | –                         | –                           | (19)     |
| OR3A4      | 78 HCC tissues and paired ANTs    | Its elevated level is related with low OS.                                            | –                         | –                           | (213)    |
| PitPNA-AS1 | 60 HCC tissues and paired ANTs    | Its elevated level is related with low OS.                                            | –                         | –                           | (216)    |
| AK021443   | 193 HCC tissues and paired ANTs   | Its elevated level is related with low OS.                                            | correlated with OS        | an independent prognostic factor for OS | (274)    |
| UCA1       | Serum samples from 105 HCC patients, 105 persons with benign liver diseases and 105 healthy controls | Its elevated level is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (275)    |
| SNHG15     | 105 HCC tissues and paired ANTs   | Its elevated level is related with low OS.                                            | correlated with OS        | an independent prognostic factor for OS | (276)    |
| PSTAR      | 127 HCC tissues and ANTs          | Its low expression is related with poor OS and RFS.                                  | –                         | –                           | (228)    |
| CASC2      | 75 HCC tissues and ANTs           | Its low expression is related with poor OS and DFS.                                  | –                         | –                           | (227)    |
| Inc-FTX    | 129 HCC tissues and paired ANTs   | Its low expression is related with poor OS and DFS.                                  | –                         | –                           | (237)    |
| LINC00472  | 109 HCC tissues and 35 ANTs       | Its expression is correlated with short OS.                                          | –                         | –                           | (238)    |
Expression levels of lncRNAs can differentiate HCC tissues from non-tumoral tissues indicating the role of these transcripts as diagnostic biomarkers for HCC. The best diagnostic power values have been reported for NEAT1, PANDAR, CCHE1 and SNHG1. Most notably, serum or plasma levels of a number of lncRNAs such as LINC-ITGB1, LINC00978, LncDQ, PAPAS, MEG3, UCA1 and NEAT1 could be used as diagnostic markers for this kind of cancer (Table 4).

### Table 3

| IncRNA     | Sample number                                           | Kaplan-Meier analysis                                                                 | Univariate Cox regression | Multivariate Cox regression | Reference |
|------------|---------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------|-----------------------------|-----------|
| TSLNC8     | 120 HCC tissues and paired ANTs                         | Its low expression is related with low OS.                                          |                           |                             | (226)     |
| miR603HG   | 93 HCC tissues and paired ANTs                          | Its expression level is related with TTR and OS.                                    | correlated with TTR and OS| an independent prognostic factor for TTR and OS | (151)     |
| MEG3       | serum samples from 54 HCC patients and 54 healthy controls | Its low expression is related with shorter survival time.                         |                           |                             | (240)     |
| LIN00807   | 159 HCC tissues and paired ANTs                         | Its low expression is related with low OS.                                          |                           |                             | (245)     |
| AOC4P      | 108 HCC tissues and paired ANTs                         | Its low expression is related with low DFS and OS.                                 |                           | an independent prognostic factor for DFS and OS | (246)     |
| uc.134     | 170 paraffin-embedded samples of HCC tissues and ANTs   | Its low expression is related with low OS.                                          |                           |                             | (223)     |
| GAS8-AS1   | 82 HCC tissues and paired ANTs                          | Its low expression is related with low OS.                                          |                           |                             | (255)     |
| LINC00657  | 49 HCC tissues and paired ANTs                          | Its low expression is related with low OS.                                          |                           |                             | (256)     |
| MAGI2-AS3  | 88 HCC tissues and paired ANTs                          | Its low expression is related with low OS.                                          |                           |                             | (258)     |
| LINC01093  | 70 HCC tissues and paired ANTs                          | Its low expression is related with short OS.                                        | correlated with OS        | an independent prognostic factor for OS | (259)     |
| GAS5       | 50 HCC tissues and paired ANTs                          | Its low expression is related with short OS.                                        | correlated with OS        | an independent prognostic factor for OS | (260)     |
| GAS5       | 71 HCC tissues and paired ANTs                          | Its low expression is related with short OS.                                        | correlated with OS        | an independent prognostic factor for OS | (277)     |
| GAS5       | 38 HCC tissues and paired ANTs                          | Its low expression is related with short OS.                                        |                           |                             | (262)     |
| SchLAH     | 132 HCC tissues and paired ANTs                         | Its low expression is related with low OS.                                          |                           |                             | (263)     |
| NKILA      | 54 HCC tissues and paired ANTs                          | Its low expression is related with low OS.                                          |                           |                             | (264)     |
| LINC00261  | 66 HCC tissues and paired ANTs                          | Its low expression is related with low OS.                                          |                           |                             | (265)     |
| MIR31HG    | 42 HCC tissues and paired ANTs                          | Its low expression is related with low OS.                                          |                           |                             | (266)     |
| LINC01554  | 167 HCC tissues and paired ANTs                         | Its low expression is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (267)     |
| RGMB-AS1   | 108 HCC tissues and 25 ANTs                             | Its low expression is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (269)     |
| ID2-AS1    | 144 HCC tissues and paired ANTs                         | Its low expression is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (272)     |
| CCAT2      | 122 HCC tissues and paired ANTs                         | Its elevated level is related with low OS.                                          |                           | an independent prognostic factor for OS | (278)     |
| GAS5-AS1   | 83 HCC tissues and paired ANTs                          | Its low expression is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (279)     |
| JPX        | 68 HCC tissues and paired ANTs, plasma samples from 42 patients and 68 healthy controls | Its low expression is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (280)     |
| XIST       | 68 HCC tissues and paired ANTs, plasma samples from 42 patients and 68 healthy controls | Its low expression is related with low OS.                                          | correlated with OS        | an independent prognostic factor for OS | (281)     |
| GMDS-DT    | 198 HCC tissues and paired ANTs                         | Its low expression is related with low DFS and OS.                                 |                           | an independent prognostic factor for DFS and OS | (282)     |
| X91348     | 107 HCC tissues and paired ANTs, serum samples from 107 HCC patients and 92 healthy controls | Its low expression is related with low OS.                                          |                           | an independent prognostic factor for OS | (283)     |
| TCONS_00027978 | 241 HCC tissues and paired ANTs                         | Its low expression is related with low DFS and OS.                                 |                           | an independent prognostic factor for DFS and OS | (283)     |
### TABLE 4 | Diagnostic role of lncRNAs in HCC.

| lncRNA      | Expression pattern | Sample          | Type of biomarker                                                                 | ROC curve analysis | Reference |
|-------------|--------------------|-----------------|----------------------------------------------------------------------------------|-------------------|-----------|
|             |                    |                 |                                                                                | Sensitivity | Specificity | Area under ROC curves (AUC) |
| MALAT1      | Upregulated        | Tissue samples  | Diagnostic biomarker                                                             | –          | –          | 0.76 (21) |
| LINC-ITGB1  | Upregulated        | Serum samples   | Diagnostic biomarker (diagnosis of HCC from controls)                           | –          | –          | 0.8520 (91) |
| PANDAR      | Upregulated        | Tissue samples  | Diagnostic biomarker (diagnosis of HCC)                                          | –          | –          | 0.9564 (122) |
| LINC00978   | Upregulated        | Serum samples   | Diagnostic biomarker (diagnosis of HCC)                                          | 76%        | 96%        | 0.910 (155) |
| CCHE1       | Upregulated        | Tissue sample   | Diagnostic biomarker (diagnosis of HCC)                                          | –          | –          | 0.9262 (175) |
| LncDQ       | Upregulated        | Serum samples   | Diagnostic biomarker (diagnosis of HCC)                                          | 72%        | 80%        | 0.804 (204) |
| LINC00963   | Upregulated        | Tissue samples  | Diagnostic biomarker (diagnosis of HCC)                                          | –          | –          | 0.763 (205) |
| PAPAS       | Upregulated        | Plasma samples  | Diagnostic biomarker (diagnosis of Stage I HCC patients from healthy controls)  | –          | –          | 0.88 (214) |
| MEG3        | Downregulated      | Serum samples   | Diagnostic biomarker (diagnosis of HCC)                                          | 70.0%      | 63.7%      | 0.8866 (240) |
| FAM898      | Downregulated      | Tissue samples  | Diagnostic biomarker (diagnosis HCC from controls)                              | 76%        | 96%        | 0.910 (268) |
| UCA1        | Upregulated        | Serum samples   | Diagnostic biomarker (discriminating HCC patients from healthy controls)        | 73.3%      | 99.0%      | 0.902 (275) |
| JPX         | Downregulated      | Plasma samples  | Diagnostic biomarker (diagnosis of HCC)                                          | 71.4%      | 94.3%      | 0.848 (280) |
| X91348      | Downregulated      | Serum samples   | Diagnostic biomarker (diagnosis of HCC)                                          | 100%       | 52.4%      | 0.814 (281) |
| MOC-AS1     | Upregulated        | Tissue samples  | Diagnostic biomarker (diagnosis of HCC)                                          | 82%        | 75.4%      | 0.807 (282) |
| POLR2J4     | Upregulated        | Blood samples   | Diagnostic biomarker (tumor vs. non-tumor)                                       | –          | –          | 0.832 (284) |
| EIF3J-AS1   | Upregulated        | Blood samples   | Diagnostic biomarker (detection of HCC/HCV from HCV and healthy control group)   | 93.3%      | 100%       | –          |
| SERHL       | Upregulated        | Blood samples   | Diagnostic biomarker (detection of HCC/HCV from HCV and healthy control group)   | 96.6%      | 72.5%      | –          |
| RMS1        | Upregulated        | Blood samples   | Diagnostic biomarker (detection of HCC/HCV from HCV and healthy control group)   | 67%        | 78%        | –          |
| PVT1        | Upregulated        | Blood samples   | Diagnostic biomarker (detection of HCC/HCV from HCV and healthy control group)   | 93.3%      | 100%       | –          |
| CASC2       | Downregulated      | Blood samples   | Diagnostic biomarker (detection of HCC/HCV from HCV and healthy control group)   | 96.6%      | 72.5%      | –          |
| TUG1        | Upregulated        | Blood samples   | Diagnostic biomarker (detection of HCC/HCV from HCV and healthy control group)   | 67%        | 78%        | –          |
| TUG1        | Upregulated        | Blood samples   | Diagnostic biomarker (detection of HCC/HCV from HCV and healthy control group)   | 93.3%      | 100%       | –          |
| AC015908.3  | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.769 (285) |
| AC091057.3  | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.769 (286) |
| TMCC1-AS1   | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.769 (287) |
| DCST1-AS1   | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.769 (288) |
| FOXD2-AS1   | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.769 (289) |
| NEAT1       | Upregulated        | Serum samples   | Diagnostic biomarker (diagnosis HCC from controls)                               | 100%       | 88.9%      | 0.981 (287) |
| NEAT1       | Upregulated        | Tissue samples  | Diagnostic biomarker (diagnosis HCC from controls)                               | –          | –          | 0.984 (288) |
| GASS-AS1    | Downregulated      | Tissue samples  | Diagnostic biomarker (diagnosis HCC from controls)                               | –          | –          | 0.984 (289) |
| RP11-160H22.5| Upregulated       | Plasma samples  | Diagnostic biomarker (distinguishing HCC from the cirrhosis)                      | –          | –          | 0.984 (290) |
| XLOC_014172 | Upregulated        | Tissue samples  | Diagnostic biomarker (for OS)                                                     | –          | –          | 0.703 (279) |
| LOC149086   | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.824 (280) |
| Risk score: | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.896 (281) |
| MIR100HG    | –                  | Tissue samples  | Diagnostic biomarker (for OS)                                                     | –          | –          | 0.934 (282) |
| SERHL       | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.73 (283)  |
| CTD-257422.4| –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.73 (284)  |
| SNAHG20     | –                  | Tissue samples  | Prognostic biomarker (for OS)                                                     | –          | –          | 0.73 (285)  |

(Continued)
| IncRNA | Expression pattern | Sample | Type of biomarker | ROC curve analysis | Reference |
|-------|--------------------|--------|-------------------|--------------------|-----------|
|       |                    |        |                   | Sensitivity | Specificity | Area under ROC curves (AUC) |
| ENSG00000258332.1 | Upregulated | Serum exosomes | Diagnostic biomarker (discrimination of HCC from chronic hepatitis B) | – | – | 0.719 (291) |
| LINC00635 | Upregulated | Serum exosomes | Diagnostic biomarker (discrimination of HCC from chronic hepatitis B) | – | – | 0.750 |
| ENSG00000258332.1 | Upregulated | Serum exosomes | Diagnostic biomarker (discrimination of HCC from chronic hepatitis B) | – | – | 0.894 |
|        | Upregulated | Serum exosomes | Diagnostic biomarker (discrimination of HCC from chronic hepatitis B) | – | – | 0.894 |
| IncRNA-D16368 | Downregulated | Serum samples | Diagnostic biomarker (diagnosis of HCC) | 65.5% | 84.6% | 0.752 (292) |
| IncRNA-752X | Upregulated | Serum samples | Diagnostic biomarker (diagnosis of HCC) | 87.7% | 72.7% | 0.866 (293) |
| CAS9 | Upregulated | Serum samples | Diagnostic biomarker (diagnosis of HCC) | – | – | 0.933 (294) |
| ZFAS1 | Upregulated | Serum samples | Diagnostic biomarker (diagnosis of HCC) | – | – | 0.801 (295) |
| IncRNA-p34822 | Upregulated | Plasma samples | Diagnostic biomarker (diagnosis of HCC) | 80.9% | 75.8% | 0.845 (296) |
| Lnc-PCDH9-13:1 | Upregulated | Salivary samples | Diagnostic biomarker (diagnosis of HCC from healthy controls) | 85% | 98% | 0.898 (297) |
|        |                  |        | Diagnostic biomarker (diagnosis of HCC from inactive HBsAg carriers) | 87% | 98% | 0.897 |
|        |                  |        | Diagnostic biomarker (diagnosis of HCC from chronic hepatitis B patients) | 87% | 98% | 0.896 |
|        |                  |        | Diagnostic biomarker (diagnosis of HCC from liver cirrhosis patients) | 87% | 92% | 0.881 |
| SNHG18 | Downregulated | Plasma samples | Diagnostic biomarker (diagnosis of HCC from healthy controls with α-fetoprotein levels below 200 ng/ml) | 75.61% | 73.49% | – (298) |
| SNHG1 | Upregulated | Plasma samples | Diagnostic biomarker (diagnosis of HCC from healthy controls) | – | – | 0.92 (299) |
| CTC-297N7.9 | Downregulated | Tissue samples | Diagnostic biomarker (diagnosis of HCC) | – | – | 0.73 (300) |
| LncRNA-AT085935 | Upregulated | Serum samples | Diagnostic biomarker (diagnosis of HCC) | – | – | 0.988 (301) |
|        |                  |        | Diagnostic biomarker (discrimination of HBV-positive HCC from healthy controls) | – | – | 0.664 |
|        |                  |        | Diagnostic biomarker (discrimination of HBV-positive HCC from HBV patients) | – | – | 0.955 |
| IncRNA-uc003wbd | Upregulated | Serum samples | Diagnostic biomarker (discrimination of HBV-positive HCC from healthy controls) | – | – | 0.994 |
|        |                  |        | Diagnostic biomarker (discrimination of HBV-positive HCC from HBV patients) | – | – | 0.982 |
|        |                  |        | Diagnostic biomarker (discrimination of HBV-positive HCC from HBV patients) | – | – | 0.810 |

| TABLE 4 | Association between lncRNAs polymorphisms and HCC. |
|-----------------|-----------------|---------------|-----------------|
| IncRNA | Polymorphism type | Identifier | Samples | Association with HCC | Association with patient outcome | Functional experiments | Reference |
|-------|-----------------|-----------|---------|---------------------|--------------------------|------------------------|-----------|
| GASS | Indel polymorphism | rs145204276 | 1034 HCC patients and 1054 controls | Deletion allele is associated with increased risk of HCC. | Deletion allele is correlated with higher expression of GASS in HCC tissues. | – | (302) |
| KCNQ1OT1 | Tetranucleotide repeat polymorphism (STR) | rs35622507 | 510 HCC patients and 1014 age and sex matched healthy controls | Heterozygote subjects with one allele 10 and those without allele 10 compared with subjects with homozygote 10-10 genotype have decreased risk of HCC. | – | Genotypes of this polymorphism are associated with methylation status of GASS promoter region. | Cell lines without allele 10 have higher expression of KCNQ1OT1. | (303) |
lncRNAs such as HULC confer resistance to chemotherapeutic agents (13), indicating the potential of targeted therapies against these transcripts in enhancement of response of HCC patients to conventional therapeutic options. Antisense oligonucleotides and small interfering RNAs are putative methods for suppression of expression of lncRNAs (309, 310) whose efficacies have been verified in animal models and cell line experiments. Yet, this knowledge has not been translated into clinical practice.

Taken together, lncRNAs as important class of regulatory transcripts can influence pathogenesis of HCC from different aspects and can be used as suitable markers for differentiation of HCC from related pathogenic conditions.

AUTHOR CONTRIBUTIONS

SG-F and MT wrote the draft and revised it. BH and MG designed the tables and figures. All authors contributed to the article and approved the submitted version.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: Cancer J Clin (2018) 68 (6):394–424. doi: 10.3322/caac.21492
2. London WT, McGlynn K, Schottenfeld D, Fraumeni J. Cancer epidemiology and prevention. Cancer Epidemiology and Prevention. 3rd edition. In: Schottenfeld D, Fraumeni JR, editors. New York, NY: Oxford University Press (2006) p. 763–86.
3. Zhang DY, Friedman SL. Fibrosis-dependent mechanisms of hepatocarcinogenesis. Hepatology (2012) 56(2):769–75. doi: 10.1002/hep.25670
4. Ghouri YA, Mian I, Rowe JH. Review of hepatocellular carcinoma: Epidemiology, etiology, and carcinogenesis. J Carcinog (2017) 16:1–.
5. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology (2007) 132(7):2557–76. doi: 10.1053/j.gastro.2007.04.061
6. Toh TB, Lim JJ, Chow EK-H. Epigenetics of hepatocellular carcinoma. Clin Trans Med (2019) 8(1):13–. doi: 10.1186/s40169-019-0230-0
7. Long Y, Wang X, Youmans DT, Cech TR. How do lncRNAs regulate transcription? Sci Adv (2017) 3(9):eaao2110–eaao. doi: 10.1126/sciadv.aao2110
8. Guttman M, Amit I, Garber M, French C, Lin MF, Feldser D, et al. Chromatin signature reveals over a thousand highly conserved large non-coding RNAs in mammals. Nature (2009) 458(7235):223–7. doi: 10.1038/nature07672
9. Choi S-W, Kim H-W, Nam J-W. The small peptide world in long noncoding RNAs. Brief Bioinform (2019) 20(5):1853–64. doi: 10.1093/bib/bby055
10. Miyake N, Ghanem A, Zhou L, Zhang YJ, Chen Y, et al. Molecular regulation of lncRNAs in hepatocellular carcinoma. J Exp Clin Cancer Res (2019) 38 (1):198–.
11. Li Z, Zhang J, Liu X, Li S, Wang Q, Di C, et al. The LINCO1138 drives malignancies via activating arginine methyltransferase 5 in hepatocellular carcinoma. Nat Commun (2018) 9(1):1572. doi: 10.1038/s41467-018-04006-8
12. Jiang R, Tang J, Chen Y, Deng L, Ji J, Xie Y, et al. The long noncoding RNA Inc-EGFR stimulates T-regulatory cells differentiation thus promoting hepatocellular carcinoma immune evasion. Nat Commun (2017) 8:15129. doi: 10.1038/ncomms15129
13. Li D, Liu X, Zhou J, Ji J, Zang D, Liu J, et al. Long noncoding RNA HULC modulates the phosphorylation of YB-1 through serving as a scaffold of extracellular signal-regulated kinase and YB-1 to enhance hepatocarcinogenesis. Hepatology (2017) 65(5):1612–27. doi: 10.1002/hep.29010
14. Yan X, Zhang D, Wu W, Wu S, Qian J, Hao Y, et al. Mesenchymal Stem Cells Promote Hepatocarcinogenesis via IncRNA-MUP Interaction with ANXA2 and miR-34a. Cancer Res (2017) 77(23):6704–16. doi: 10.1158/0008-5472.CAN-17-1915
15. Jin J, He Y, Tang S, Huang S. IncRNA GHET1 predicts poor prognosis in hepatocellular carcinoma and promotes cell proliferation by silencing KLF2. J Cell Physiol (2018) 233(6):4726–34. doi: 10.1002/jcp.26257
16. Hou Z-H, Xu X-W, Fu X-Y, Zhou L-D, Liu S-P, Tan D-M. Long non-coding RNA MALAT1 promotes angiogenesis and immunosuppressive properties of HCC cells by sponging miR-140. Am J Physiology-Cell Physiol (2020) 318 (3):C649–C63. doi: 10.1152/ajpcell.00510.2018
17. Hou Z, Xu X, Zhou L, Fu X, Tao S, Zhou J, et al. The long non-coding RNA MALAT1 promotes the migration and invasion of hepatocellular carcinoma by sponging miR-204 and releasing SIRT1. Tumor Biol (2017) 39(7):1014028317718135. doi: 10.1177/1014028317718135
18. Peng J, Wu H, Zhang H, Fang S, Zeng R, et al. miR-143-3p inhibits proliferation and invasion of hepatocellular carcinoma cells by regulating its target gene FGFR1. Clin Trans Oncol (2021) 23:468–480. doi: 10.1007/s12994-020-02440-5
19. Pan Y, Tong S, Cui R, Fan J, Liu C, Lin Y, 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):108–20. doi: 10.1159/000499396
20. Yao W-F, Liu J-W, Huang D-S. MiR-200a inhibits cell proliferation and EMT by down-regulating the ASPH expression levels and affecting ERK and PI3K/Akt pathways in human hepatoma cells. Am J Trans Res (2018) 10 (4):1117.
21. Cui RJ, Fan JL, Lin YC, Pan YJ, Liu C, Wan JH, et al. miR-124-3p availability is antagonized by LncRNA-MALAT1 for Slug-induced tumor metastasis in hepatocellular carcinoma. Cancer Med (2019) 8(4):6358–69. doi: 10.1002/cam4.2482
22. Liu D, Zhu Y, Peng J, Weng X, Feng X, Guo Y. Knockdown of long non-coding RNA MALAT1 inhibits growth and motility of human hepatoma cells via modulation of miR-195. J Cell Biochem (2018) 119(2):1368–80. doi: 10.1002/jcb.26297
23. Chen S, Wang G, Tao K, Cai K, Wu K, Ye L, et al. Long noncoding RNA metastasis-associated lung adenocarcinoma transcript 1 cooperates with enhancer of zeste homolog 2 to promote hepatocellular carcinoma development by modulating the microRNA-22/Snail family transcriptional repressor 1 axis. Cancer Sci (2020) 111(5):1582. doi: 10.1111/cas.14372
24. Liu X, Liang Y, Song R, Yang G, Han J, Lan Y, et al. Long non-coding RNA NEAT1-modulated abnormal lipolysis via ATGL drives hepatocellular carcinoma proliferation. Mol Cancer (2018) 17(1):1–18. doi: 10.1186/s12943-018-0835-8
25. Fang L, Sun J, Pan Z, Song Y, Zhong L, Zhang Y, et al. Long non-coding RNA NEAT1 promotes hepatocellular carcinoma cell proliferation through the regulation of miR-129-5p-VCP-XBP. Am J Physiology-Gastrointestinal Liver Physiol (2017) 313(2):G150–G6. doi: 10.1152/ajpgi.00426.2016
26. Zhang XN, Zhou J, Xu X, Hong Y, et al. The long noncoding RNA NEAT1 contributes to hepatocellular carcinoma development by sponging miR-485 and enhancing the expression of the STAT3. J Cell Physiol (2018) 233(9):6733–41. doi: 10.1002/jcp.26371
27. Liu Z, Chang Q, Yang F, Liu B, Yao H-W, Bai Z-G, et al. Long non-coding RNA NEAT1 overexpression is associated with unfavorable prognosis in patients with hepatocellular carcinoma after hepatectomy: A Chinese population-based study. Eur J Surg Oncol (2017) 43(9):1697–703. doi: 10.1016/j.ejso.2017.06.013
28. Wang Z, Zou Q, Song M, Chen J. NEAT1 promotes cell proliferation and invasion in hepatocellular carcinoma by negative regulating miR-613
expression. *Biomed Pharmacother* (2017) 94:612–8. doi: 10.1016/j.bip.2017.07.111

29. Yu J, Zhao Z, Xu M, Lu X, Chang L, Ji L. NEAT1 upregulates TGF-B1 to induce hepatocellular carcinoma progression by spilling hsa-mir-139-5p. *J Cell Physiol* (2018) 233(11):8578–87. doi: 10.1002/jcp.26524

30. Chen X, Zhang N. Downregulation of IncRNA NEAT1_2 radiosensitizes hepatocellular carcinoma cells through regulation of mir-101-3p/WEE1 axis. *Cell Biol Int* (2019) 43(1):44–55. doi: 10.1016/j.cellbi.2011.07.077

31. Huang J-L, Cao S-W, Ou Q-S, Yang B, Zheng S-H, Tang J, et al. The long non-coding RNA PTTG3P promotes cell growth and metastasis via up-regulating PTG1 and activating PI3K/AKT signaling in hepatocellular carcinoma. *Mol Cancer* (2018) 17(1):1–16. doi: 10.1186/s12943-018-0841-x

32. Zhou Q, Zhang W, Wang Z, Liu S. Long non-coding RNA PTTG2P functions as an oncogene by splicing miR-383 and up-regulating CCND1 and PARP2 in hepatocellular carcinoma. *BMC Cancer* (2019) 19(1):731. doi: 10.1186/s12885-018-5936-2

33. Lin J, Cao S, Wang Y, Hu Y, Liu H, Li J, et al. Long non-coding RNA UBE2CP3 enhances HCC cell secretion of VEGFA and promotes angiogenesis by activating ERK1/2/HIF-1α/VEGFA signalling in hepatocellular carcinoma. *J Exp Clin Res* (2018) 37(1):1–13. doi: 10.15340/jecr-08-0177-1

34. Ji D, Wang Y, Sun B, Luo X. Long non-coding RNA LINCO00461/miR-149-5p/LRG62 axis regulates hepatocellular carcinoma progression. *Biochem Biophys Res Commun* (2019) 513(2):176–81. doi: 10.1016/j.bbrc.2019.03.049

35. Chen L, Yao H, Wang K, Liu X. Long non-coding RNA MALAT1 regulates ZEB1 expression by splicing miR-143-3p and promotes hepatocellular carcinoma progression. *J Cell Biochem* (2017) 118(12):4836–43. doi: 10.1002/jcb.26158

36. Zhao Z-B, Chen F, Bai X-F. Long non-coding RNA TUG1 is up-regulated in hepatocellular carcinoma and sponging miR-195-5p in hepatocellular carcinoma. *Int J Oncol* (2018) 43(1):57. doi: 10.3892/ijo.2017.4179

37. Ji D, Wang Y, Sun B, Luo X. Long non-coding RNA TUG1 and activating PI3K/AKT signaling in hepatocellular carcinoma. *Mol Cancer* (2018) 17(1):1–16. doi: 10.1186/s12943-018-0841-x

38. Huang D, Wei Y, Zhu J, Wang F. Long non-coding RNA SNHG1 functions as a competitive endogenous RNA to regulate PDCD4 expression by epigenetic silencing of KLF2. *Anti-Cancer Drugs* (2019) 30(10):1013–21. doi: 10.1097/CAD.0000000000001807

39. Zhao X, Liu Y, Yu S. Long non-coding RNA AWPPH promotes hepatocellular carcinoma progression through YBX1 and serves as a prognostic biomarker. *Biochim Biophys Acta (BBA)-Molecular Basis Dis* (2017) 1863(7):1805–16. doi: 10.1016/j.bbadis.2017.04.014

40. Xu Y, Luo X, He W, Chen G, Li Y, Li W, et al. Long non-coding RNA PVT1/miR-150/HIG2 axis regulates the proliferation, invasion and the balance of iron metabolism of hepatocellular carcinoma. *Cell Physiol Biochem* (2018) 49(4):1403–19. doi: 10.1159/000493445

41. Lan T, Yan X, Li Z, Xu X, Mao Q, Ma W, et al. Long non-coding RNA PVT1 serves as a competing endogenous RNA for miR-186-5p to promote the tumorigenesis and metastasis of hepatocellular carcinoma. *Tumor Biol* (2017) 39(6):1010428317705338. doi: 10.1177/1010428317705338

42. Yang L, Peng X, Jin H, Liu J. Long non-coding RNA PVT1 promotes autophagy as ceRNA to target ATG3 by splicing microRNA-365 in hepatocellular carcinoma. *Gene* (2019) 697:94–102. doi: 10.1016/j.gene.2019.01.118

43. Huang D, Wei Y, Zhu J, Wang F. Long non-coding RNA SNHG1 functions as a competitive endogenous RNA to regulate PDCD4 expression by epigenetic silencing of KLF2. *Anti-Cancer Drugs* (2019) 30(10):1013–21. doi: 10.1097/CAD.0000000000001807

44. Zhao X, Liu Y, Yu S. Long non-coding RNA AWPPH promotes hepatocellular carcinoma progression through YBX1 and serves as a prognostic biomarker. *Biochim Biophys Acta (BBA)-Molecular Basis Dis* (2017) 1863(7):1805–16. doi: 10.1016/j.bbadis.2017.04.014

45. Xu Y, Luo X, He W, Chen G, Li Y, Li W, et al. Long non-coding RNA PVT1/miR-150/HIG2 axis regulates the proliferation, invasion and the balance of iron metabolism of hepatocellular carcinoma. *Cell Physiol Biochem* (2018) 49(4):1403–19. doi: 10.1159/000493445

46. Lan T, Yan X, Li Z, Xu X, Mao Q, Ma W, et al. Long non-coding RNA PVT1 serves as a competing endogenous RNA for miR-186-5p to promote the tumorigenesis and metastasis of hepatocellular carcinoma. *Tumor Biol* (2017) 39(6):1010428317705338. doi: 10.1177/1010428317705338

47. Yang L, Peng X, Jin H, Liu J. Long non-coding RNA PVT1 promotes autophagy as ceRNA to target ATG3 by splicing microRNA-365 in hepatocellular carcinoma. *Gene* (2019) 697:94–102. doi: 10.1016/j.gene.2019.01.118

48. Ma J, Li T, Han X, Yuan H. Knockdown of LncRNA ANRIL suppresses cell proliferation, metastasis, and invasion via regulating miR-122-5p expression in hepatocellular carcinoma. *J Cancer Res Clin Oncol* (2018) 144(2):205–14. doi: 10.1007/s00432-017-2543-y

49. Hua L, Wang C-Y, Yao K-H, Chen J-T, Zhang J-M, Ma W-L. High expression of long non-coding RNA ANRIL is associated with poor prognosis in hepatocellular carcinoma. *Int J Clin Exp Pathol* (2015) 8(3):3076.

50. Ma Y, Zhang H, Li G, Hu J, Liu X, Lin L. LncRNA ANRIL promotes cell growth, migration and invasion of hepatocellular carcinoma cells via sponging miR-144. *Anti-Cancer Drugs* (2019) 30(10):1013–21. doi: 10.1097/CAD.0000000000001807

51. Zhao X, Liu Y, Yu S. Long non-coding RNA AWPPH promotes hepatocellular carcinoma progression through YBX1 and serves as a prognostic biomarker. *Biochim Biophys Acta (BBA)-Molecular Basis Dis* (2017) 1863(7):1805–16. doi: 10.1016/j.bbadis.2017.04.014

52. Xu Y, Luo X, He W, Chen G, Li Y, Li W, et al. Long non-coding RNA PVT1/miR-150/HIG2 axis regulates the proliferation, invasion and the balance of iron metabolism of hepatocellular carcinoma. *Cell Physiol Biochem* (2018) 49(4):1403–19. doi: 10.1159/000493445

53. Lan T, Yan X, Li Z, Xu X, Mao Q, Ma W, et al. Long non-coding RNA PVT1 serves as a competing endogenous RNA for miR-186-5p to promote the tumorigenesis and metastasis of hepatocellular carcinoma. *Tumor Biol* (2017) 39(6):1010428317705338. doi: 10.1177/1010428317705338

54. Yang L, Peng X, Jin H, Liu J. Long non-coding RNA PVT1 promotes autophagy as ceRNA to target ATG3 by splicing microRNA-365 in hepatocellular carcinoma. *Gene* (2019) 697:94–102. doi: 10.1016/j.gene.2019.02.036

55. Huang D, Wei Y, Zhu J, Wang F. Long non-coding RNA SNHG1 functions as a competitive endogenous RNA to regulate PDCD4 expression by epigenetic silencing of KLF2. *Anti-Cancer Drugs* (2019) 30(10):1013–21. doi: 10.1097/CAD.0000000000001807
hepatocellular carcinoma. *Yonsei Med J* (2019) 60(9):842–53. doi: 10.3349/yymj.2019.60.9.842

61. Wang H, Ke J, Guo Q, Barnabzo Nampoukime KP, Yang P, Ma K. Long non-coding RNA CRNDE promotes the proliferation, migration and invasion of hepatocellular carcinoma cells through miR-217/MAPK 1 axis. *J Cell Mol Med* (2018) 22(12):5862–76. doi: 10.1111/jcmm.13856

62. Tang Q, Zheng X, Zhang J. Long non-coding RNA CRNDE promotes hepatocellular carcinoma cell proliferation by regulating PI3K/Akt/β-catenin signaling. *Biomed Pharmacother* (2018) 103:1187–93. doi: 10.1016/j.biopha.2018.04.128

63. Zhu L, Liu Y, Chen Q, Yu G, Chen J, Chen K, et al. miR-941 as a promising biomarker for the early diagnosis of hepatocellular carcinoma. *Cell Physiol Biochem* (2020) 56:2299–48. doi: 10.1007/s10029-020-4390-z

64. Li D, Jiang C, Zhang L, Liang N, Jiang T, Yang B, et al. LncRNA CRNDE promotes hepatocellular carcinoma cell proliferation, invasion, and migration through regulating miR-203/BCAT1 axis. *J Cell Physiol* (2019) 234(5):6548–60. doi: 10.1002/jcp.27396

65. Tang D, Zhao L, Peng C, Ran K, Mu R, Ao Y. LncRNA CRNDE promotes hepatocellular carcinoma progression by upregulating SIX1 through modulating miR-337-3p. *J Cell Biochem* (2019) 120(9):16128–42. doi: 10.1002/jcb.20949

66. Chen Z, Zhang Z, Zhao D, Feng W, Meng F, Han S, et al. Long noncoding RNA (LncRNA) FOXD2-AS1 Promotes Cell Proliferation and Metastasis in Hepatocellular Carcinoma by Regulating MiR-185/AKT Axis. *Med Sci Monitor Int J Exp Clin Res* (2019) 25:9618. doi: 10.26599/MSM.918230

67. Lei T, Zhu X, Zhu K, Jia F, Li S. EGFR-induced upregulation of LncRNA FOXD2-AS1 promotes the progression of hepatocellular carcinoma via epigenetically silencing DKK1 and activating Wnt/β-catenin signaling pathway. *Cancer Biol Ther* (2019) 20(7):1007–16. doi: 10.1080/15384047.2019.1595276

68. Gao J, Yin X, Yu X, Dai C, Zhou F. Long noncoding RNA LINC00488 functions as a ceRNA to regulate hepatocellular carcinoma cell growth and angiogenesis through miR-330-3p. *Digestive Liver Dis* (2019) 51(7):1050–9. doi: 10.1016/j.jdlid.2019.03.012

69. Kang CL, Qi B, Cai QQ, Fu LS, Wang F, Yin Y-Z, Zhang X-Y. Long non-coding RNA HOTTIP is frequently up-regulated in hepatocellular carcinoma and is targeted by tumour suppressive miR-125b. *Liver Int* (2015) 35(5):1597–606. doi: 10.1111/liv.12746

70. Zhang Y, Zhang J, Zhou C, Qiu G, Wang G, Wang S, et al. Long non-coding RNA FOXD2-AS1 plays an oncogenic role in hepatocellular carcinoma by targeting miR-206. * Oncol Rep* (2018) 40(6):3625–34. doi: 10.3892/or.2018.76572

71. Lou Y, Yu Y, Xu X, Zhou S, Shen H, Fan T, et al. Long non-coding RNA LUCAT1 promotes tumourigenesis by inhibiting ANXA2 phosphorylation in hepatocellular carcinoma. *J Cell Mol Med* (2019) 23(3):1873–84. doi: 10.1111/jcmm.14088

72. Han Q, Chen B, Zhang K, Xia S, Zhong W, Zhao Z. The long non-coding RNA AK001796 contributes to poor prognosis and tumor progression in hepatocellular carcinoma. *Eur Rev Med Pharmacol Sci* (2019) 23(5):2013–9. doi: 10.26355/eurrev_201903_17240

73. Wang Y-D, Sun X-J, Yin J-Y, Yin M, Wang W, Nie Z-Q, et al. Long non-coding RNA FEZF1-AS1 promotes cell invasion and epithelial-mesenchymal transition through JAK2/STAT3 signaling pathway in human hepatocellular carcinoma. *Biomed Pharmacother* (2018) 106:134–41. doi: 10.1016/j.biopha.2018.05.116

74. Jin X, Liang J, Guan Y. Overexpression of long non-coding RNA MINCR contributes to progressive clinicopathological features and poor prognosis of human hepatocellular carcinoma. *Eur Rev Med Pharmacol Sci* (2018) 22 (23):8197–202. doi: 10.26355/eurrev_201812_16512

75. Gao J, Zhang D, Zeng L. Long non-coding RNA CRNDE regulates cellular proliferation, migration, and invasion in hepatocellular carcinoma. *Biomed Pharmacother* (2018) 102:102–6. doi: 10.1016/j.biopha.2018.03.041

76. Chen T, Pei J, Wang J, Luo R, Liu W, et al. HBx-related long non-coding RNA 01152 promotes cell proliferation and survival by IL-23 in hepatocellular carcinoma. *Biomed Pharmacother* (2019) 115:108877. doi: 10.1016/j.biopha.2019.108877

77. Mo Y, Lu Y, Wang P, Huang S, He L, Li D, et al. Long non-coding RNA XIST promotes cell growth by regulating miR-139-5p/PI3K/AKT axis in hepatocellular carcinoma. *Tumor Biol* (2017) 39(2):101428317690999. doi: 10.1177/1010428317690999

78. Kong Q, Zhang S, Liang C, Zhang Y, Kong Q, Chen S, et al. LncRNA XIST functions as a molecular sponge of miR-194-5p to regulate MAPK1 expression in hepatocellular carcinoma cell. *J Cell Biochem* (2018) 119 (6):4458–68. doi: 10.1002/jcb.26540

79. Xu C, Huang Q, Zhang C, Xu W, Xu G, Zhao X, et al. Long non-coding RNA TRPM2-AS as a potential biomarker for hepatocellular carcinoma. *Irish J Med Sci (1971-)* (2018) 187(3):821–8. doi: 10.1111/18145-017-1692-y

80. Huang L, Li X, Gao W. Long non-coding RNA linc-TGFB1 promotes cell proliferation, migration, and invasion in human hepatoma carcinoma by up-regulating ROCK1. *Biosci Rep* (2018) 38(5). doi: 10.1042/BSR20181289

81. Li O, Li Z, Tang Q, Li Y, Yuan S, Shen Y, et al. Long Stress Induced Non-Coding Transcripts 5 (LSINCT5) promotes hepatocellular carcinoma progression through interaction with high-mobility group AT-hook 2 and MiR-4516. *Med Sci Monitor: Int J Exp Clin Res* (2018) 24:8510. doi: 10.12659/MSP.911179
114. Yao X, Li J, Liu B, Zhang R, Gu F, Zhao J, et al. Long Noncoding RNA AK021443 Promotes Cell Proliferation and Migration by Regulating Epithelial–Mesenchymal Transition in Hepatocellular Carcinoma Cells. DNA Cell Biol (2018) 37(6):481–90. doi: 10.1089/dna.2018.4030

109. Liu J, Lu C, Xiao M, Jiang F, Qu L, Ni R. Long non-coding RNA SNHG20 promotes tumor progression by regulating miR-210 in hepatocellular carcinoma. Tumor Biol (2017) 38(10):1–11. doi: 10.1007/s13277-017-6356-1

108. 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 sponging miR-149-5p and predicts tumor recurrence in hepatocellular carcinoma. World J Gastroenterol (2019) 25(38):5789–99. doi: 10.3748/wjg.v25.i38.5789

115. Yang X, Sun L, Wang L, Yao B, Mo H, Yang W. lncRNA SNHG7 accelerates the proliferation, migration and invasion of hepatocellular carcinoma cells via regulating miR-132-5p and RPLA. Biomed Pharmacother (2019) 118:103936. doi: 10.1016/j.biopha.2019.103936

116. Dong J, Teng F, Gui W, Yang J, Dong 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):2262–74. doi: 10.1159/000495871

110. Li Y, Guo D, Zhao Y, Ren M, Lu G, Wang Y, et al. Long non-coding RNA SNHG5 promotes human hepatocellular carcinoma progression by regulating miR-26a-5p/GSK3β axis. Eur Rev Med Pharmacol Sci (2019) 23(9):3733–41. doi: 10.18632/eurrev_201905_17799

128. Liu J, Wang Z, Yin Y, Li N, Ye N, Bao B, et al. Long noncoding RNA TPTE2P1 contributes to cell proliferation, migration and apoptosis in hepatocellular carcinoma. Mol Med Rep (2016) 13(5):4481–6. doi: 10.3892/mmr.2016.5075

129. Wang Y, Hu Y, Wu G, Yang Y, Tang Y, Zhang W, et al. Long noncoding RNA RUSC1-AS-N indicates poor prognosis and increases cell viability in hepatocellular carcinoma. DNA Cell Biol (2018) 37(7):525–33. doi: 10.1080/01912121.2017.1384299
132. Koo JI, Lee H-J, Jung JH, Im E, Kim J-H, Shin N, et al. The Pivotal Role of Long Noncoding RNA RAS5F in the Proliferation of Hepatocellular Carcinoma via LGR5 Mediated β-Catenin and c-Myc Signaling. *Biomolecules* (2019) 9(11):718. doi: 10.3390/bi9110718

133. Xu J-H, Chang W-H, Hu W, Shu W-Q, Yuan T, Chen P. Upregulated long non-coding RNA LOC90784 promotes cell proliferation and invasion and is associated with poor clinical features in HCC. *Biochem Biophys Res Commun* (2017) 490(3):920–6. doi: 10.1016/j.bbrc.2017.06.141

134. Ding C, Cheng S, Yang Z, Lv Z, Xiao H, Du C, et al. Long non-coding RNA HOTAIR promotes cell migration and invasion via down-regulation of RNA binding motif protein 38 in hepatocellular carcinoma cells. *Int J Mol Sci* (2014) 15(3):4060–76. doi: 10.3390/ijms15034060

135. Cheng D, Deng J, Zhang B, He X, Meng Z, Li G, et al. LncRNA HOTAIR epigenetically suppresses miR-122 expression in hepatocellular carcinoma via DNA methylation. *EBioMedicine* (2018) 36:159–70. doi: 10.1016/j.ebiom.2018.08.055

136. Wang W, Chen G, Wang B, Yuan Z, Liu G, Niu B, et al. Long non-coding RNA BZRAP1-AS1 silencing suppresses tumor angiogenesis in hepatocellular carcinoma by mediating THBS1 methylation. *J Trans Med* (2019) 17(1):1–15. doi: 10.1186/s12967-019-02145-6

137. Li Y, Guo D, Ren M, Zhao Y, Wang X, Chen Y, et al. Long non-coding RNA SNA3-AS1 promotes the proliferation and metastasis of hepatocellular carcinoma by regulating the UPI1/Smad7 signaling pathway. *J Cell Mol Med* (2019) 23(9):6271–82. doi: 10.1111/jcmm.14513

138. Li S, Huang Y, Huang Y, Fu Y, Tang D, Kang R, et al. The long non-coding RNA TP73-AS1 modulates HCC cell proliferation through miR-200a-dependent HMGB1/RAGE regulation. *J Exp Clin Cancer Res* (2019) 38(1):1–12. doi: 10.1186/s13046-018-0519-z

139. Song W, Zhang J, Xia Q, Sun M. Down-regulated IncRNA TP73-AS1 reduces radioresistance in hepatocellular carcinoma via the PTEN/Akt signaling pathway. *Cell Cycle* (2019) 18(22):3177–88. doi: 10.1002/ccg2.1701908

140. Xiao J, Lv Y, Jin F, Liu Y, Ma Y, Xiong Y, et al. LncRNA HANR promotes tumorigenesis and increase of chemoresistance in hepatocellular carcinoma. *Cell Physiol Biochem* (2017) 43(5):1926–38. doi: 10.1007/s00296-017-4419-0

141. Huang X, Gao Y, Liu Y, Wang Y, Kan H. LncRNA CDKN2B-AS1 promotes metastasis via the miR-153-5p/ARHGAP18 signaling axis. *Biomolecules* (2018) 8(2):76. doi: 10.3390/ijms15034060

142. Zhao L, Hu K, Cao J, Wang P, Li J, Zeng K, et al. LncRNA MIAT functions as a prognostic indictor, inhibits tumor metastasis by regulating the HNRNPA2B1/NF-kB pathway in hepatocellular carcinoma. *Theranostics* (2018) 8(10):2814–24. doi: 10.7150/thno.23012

143. Zhang W-L, Zhao Y-N, Shi Z-Z, Gu G-Y, Cong D, Wei C, et al. HOXA11-AS1 promotes the migration and invasion of hepatocellular carcinoma cells by inhibiting miR-124 expression by binding to EZH2. *Hum Cell* (2019) 32(4):504–14. doi: 10.1007/s13577-019-00269-z

144. Zhang Y, Xu J, Zhang S, An J, Zhang J, Huang J, et al. HOXA-AS2 promotes proliferation and induces epithelial-mesenchymal transition via the miR-250-3p/GPC3 axis in hepatocellular carcinoma. *Cell Physiol Biochem* (2018) 50(6):2124–38. doi: 10.1007/1878-0261.12556

145. Zhang X, Chen H, Zhou B, Zhang Q, Liao Y, Wang J, et al. IncRNA HOXB-AS3 promotes hepatoma by inhibiting p53 expression. *Eur Rev Med Pharmacol Sci* (2018) 22(20):6784–92. doi: 10.26355/eurrev_201810_16145

146. Xu X, Gu J, Ding X, Ge G, Zhang X, Ji R, et al. LINC00978 promotes the progression of hepatocellular carcinoma by regulating EZH2-mediated silencing of p21 and E-cadherin expression. *Cell Death Dis* (2019) 10(1):1–15. doi: 10.1038/s41419-019-1990-6

147. Wang C-Z, Yan G-X, Dong D-S, Xin H, Liu Z-Y. LncRNA-ATB promotes autophagy by activating Yes-associated protein and inducing autophagy-related protein 5 expression in hepatocellular carcinoma. *World J Gastroenterol* (2019) 25(35):5310. doi: 10.3748/wjg.v25.i35.5310

148. Huang H, Chen J, Ding CM, Jin X, Jia ZM, Peng J. Lnc RNA NR2F1-AS1 regulates hepatocellular carcinoma oxalipatin resistance by targeting ARCC1 via miR-363. *J Cell Mol Med* (2018) 22(6):3238–45. doi: 10.1111/jcmm.13605

149. Guo D, Li Y, Chen Y, Zhang D, Wang X, Lu G, et al. DANCN promotes tumor progression and regulates EMT by sponging miR-27a-3p via ROCK1/LIMKi/COFILIN1 pathway. *Cell Proliferation* (2019) 52(4):e12628. doi: 10.1111/cpr.12628

150. Wang J, Pu J, Zhang Y, Yao T, Luo Z, Li W, et al. DANCN contributed to hepatocellular carcinoma malignancy via sponging miR-216a-5p and modulating KLF12. *J Cell Physiol* (2019) 234(6):9408–16. doi: 10.1002/jcp.27625

151. Zhang L, Wang Y, Sun S, Ma H, Guo C. LINC00205 promotes proliferation, migration and invasion of HCC cells by targeting miR-122-5p. *Pathology-Research Pract* (2019) 215(9):1525515. doi: 10.1016/j.prp.2019.15251

152. Fan J, Zhang J, Huang S, Li P. LncRNA OSER1-AS1 acts as a ceRNA to promote tumorigenesis in hepatocellular carcinoma by regulating miR-372-3p/Rab23 axis. *Biochem Biophys Res Commun* (2020) 521(1):196–203. doi: 10.1016/j.bbrc.2019.10.105

153. Guo Y, Bai M, Lin L, Huang J, An Y, Liang L, et al. LncRNA DLEU2 aggravates the progression of hepatocellular carcinoma by binding to EZH2. *Biomed Pharmacother* (2019) 118:109272. doi: 10.1016/j.biopha.2019.109272

154. Huang J-L, Ren T-Y, Cao S-W, Zheng S-H, Hu X-M, Hu Y-W, et al. HBx-related long non-coding RNA DBH-AS1 promotes cell proliferation and survival by activating MAPK signaling in hepatocellular carcinoma. *Oncotarget* (2015) 6(32):33791. doi: 10.18632/oncotarget.5667

155. Bao J, Chen X, Hou Y, Kang G, Li Q, Xu Y. LncRNA DBH-AS1 facilitates the tumorigenesis of hepatocellular carcinoma by targeting miR-138 via FAK/Src/ERK pathway. *Biomed Pharmacother* (2018) 107:824–33. doi: 10.1016/j.biopha.2018.08.079

156. Wang J, Zhang Y, Lu L, Yu T, Tang Q, Pu J. Insight into the molecular mechanism of LINC00152/miR-215/CDK13 axis in hepatocellular carcinoma progression. *J Cell Biochem* (2019) 120(11):18816–25. doi: 10.1002/jcb.29197

157. Li S-Q, Chen Q, Qin H-X, Yu Y-Q, Weng J, Mo Q-R, et al. Long intergenic nonprotein coding RNA 0152 promotes hepatocellular carcinoma progression by regulating phosphatidylinositol 3-Kinase/Akt/Mammalian target of rapamycin signaling pathway through miR-139/PK3CA. *Am J Pathol* (2020) 190(5):1095–107. doi: 10.1016/j.ajpath.2019.11.010
167. Ma P, Wang H, Sun J, Liu H, Zheng C, Zhou X, et al. LINCO0152 promotes cell cycle progression in hepatocellular carcinoma via miR-193a-2/3-5p/CCND1 axis. Cell Cycle (2018) 17(10):974–84. doi: 10.1080/15384101.2018.1464834

168. Lu X, Zhou J, Li R, Liang Z, Zhai W, Zhao L, et al. Critical role for the long non-coding RNA AFAF1-AS1 in the proliferation and metastasis of hepatocellular carcinoma. Tumor Biol (2016) 37(7):9699–707. doi: 10.1007/s13237-016-4858-8

169. Chen H, Yang F, Li X, Gong Z-J, Wang L-W. Long noncoding RNA LNC473 inhibits the ubiquitination of survivin via association with USP9X and enhances cell proliferation and invasion in hepatocellular carcinoma cells. Biochem Biophys Res Commun (2018) 499(3):702–10. doi: 10.1016/j.bbrc.2018.03.215

170. Li Y, Li Y, Xu X. The long noncoding RNA cardiac hypertrophy-related factor plays oncogenic roles in hepatocellular carcinoma by downregulating microRNA-211. J Cell Biochem (2019) 120(8):13361–71. doi: 10.1002/jcb.28611

171. Yang X, Cai JF, Peng R, Wei CY, Lu JC, Gao C, et al. The long noncoding RNA NORAD enhances the TGF-β pathway to promote hepatocellular carcinoma progression by targeting miR-202-5p. J Cell Physiol (2019) 234(7):12031–60. doi: 10.1002/jcp.27869

172. Qi H, Lu Y, Lv J, Wu H, Lu J, Zhang C, et al. The long noncoding RNA LncPAP1 contributes to progression of hepatocellular carcinoma through up-regulation of PAP1. Biosci Rep (2018) 38(3):BSR20180703. doi: 10.1042/ bsor20180703

173. Li Y, Ye Y, Feng B, Qi Y. Long noncoding RNA lncARSR promotes doxorubicin resistance in hepatocellular carcinoma via modulating PTEN-PIK3/Akt pathway. J Cell Biochem (2019) 118(12):4498–507. doi: 10.1002/jcb.26107

174. Shin VJ, Chen J, Cheuk IW-Y, Siu M-T, Ho C-W, Wang X, et al. Long non-coding RNA NORAD enhances the TGF-β pathway to promote hepatocellular carcinoma progression by targeting miR-193a/b-3p/CCND1. Mol Cancer (2018) 17(8):974. doi: 10.1186/s12943-018-0845-4

175. Sui C-J, Zhou Y-M, Shen W-F, Dai B-H, Lu J-J, Zhang M-F, et al. Long non-coding RNA LINC00358 negatively modulates miR-140-5p and targets ENO1. Biochim Biophys Acta Biomembr (2019) 1866:32–6. doi: 10.1016/j.bbamem.2019.06.056

176. Jin W, Chen L, Cai X, Zhang Y, Zhang J, Ma D, et al. Long non-coding RNA TUC383 is functionally involved in sorafenib-sensitized hepatocellular carcinoma cells by targeting RASAL1. Oncol Rep (2017) 37(1):273–80. doi: 10.3892/or.2016.5248

177. Sui C-J, Zhou Y-M, Shen W-F, Dai B-H, Lu J-J, Zhang M-F, et al. Long noncoding RNA GHGC1 promotes hepatocellular carcinoma progression through epigenetically regulating miR-208b/a-429. J Mol Med (2016) 94(12):1381–96. doi: 10.1007/s00109-016-1442-3

178. Huang G, Jiang H, Lin Y, Wu Y, Cai W, Shi R, et al. lncAKHE enhances the TGF-β pathway to promote hepatocellular carcinoma progression via acting as a competing endogenous RNA of microRNA-122-5p. J Cell Physiol (2019) 234(7):12092–100. doi: 10.1002/jcp.28787

179. Tang T, Guo C, Xia T, Zhang R, Zen K, Pan Y, et al. LncCCT1A1 promotes breast cancer stem cell function through activating WNT/β-catenin signaling. Theranostics (2019) 9(4):3784. doi: 10.7150/thno.37892

180. Xu X, Zhang Y, Tang J, Feng Y, Zhang Z, Yin Y, et al. The long non-coding RNA Lnc-GALH promotes hepatocellular carcinoma metastasis via epigenetically regulating Gankyrin. Cell Death Dis (2019) 10(2):1–13. doi: 10.1038/s41419-019-1348-0

181. Ma M, Xu H, Liu G, Wu J, Li C, Wang X, et al. Metabolism-induced tumor activator 1 (MITA1), an Energy Stress-Inducible Long Noncoding RNA, Promotes Hepatocellular Carcinoma Metastasis. Hepatology (2019) 70(1):215–30. doi: 10.1002/hep.30602

182. Wang YL, Liu JY, Yang JE, Yu XM, Chen ZL, Chen YJ, et al. Lnc-UCID promotes G1/S transition and hepatoma growth by preventing DHX9-mediated CDK6 down-regulation. Hepatology (2019) 70(1):259–75. doi: 10.1002/hep.30613

183. Xu Y, Yao B, Niu Y, Chen T, Mo H, Wang L, et al. Hypoxia-induced lncRNA EIF3J-AS1 accelerates hepatocellular carcinoma progression via targeting miR-122-5p/CNOT2D2 axis. Biochem Biophys Res Commun (2019) 518(2):239–45. doi: 10.1016/j.bbrc.2019.08.039

184. Fan H, Lv P, Mu T, Zhao X, Liu Y, Feng Y, et al. LncRNA n335586/miR-924/CKMT1A axis contributes to cell migration and invasion in hepatocellular carcinoma cells. Cancer Lett (2018) 429:89–99. doi: 10.1016/j.canlet.2018.05.010

185. Zhang W, Liu S, Liu K, Liu Y. Long non-coding RNA deleted in lymphocytic leukemia 1 promotes hepatocellular carcinoma progression by sponging miR-133a to regulate IGF-1R expression. J Cell Mol Med (2019) 23(8):5154–64. doi: 10.1111/jcmm.14384

186. Xu X, Yin Y, Tang J, Xie Y, Han Z, Zhang X, et al. Long non-coding RNA Myd88 promotes growth and metastasis in hepatocellular carcinoma via regulating Myd88 expression through H3K27 modification. Cell Death Dis (2017) 8(10):e3124–e. doi: 10.1038/cddis.2017.519

187. Tang T, Guo C, Xia T, Zhang R, Zen K, Pan Y, et al. LncCCT1A1 promotes breast cancer stem cell function through activating WNT/β-catenin signaling. Theranostics (2019) 9(4):3784. doi: 10.7150/thno.37892

188. Xu X, Zhang Y, Tang J, Feng Y, Zhang Z, Yin Y, et al. The long non-coding RNA Lnc-GALH promotes hepatocellular carcinoma metastasis via epigenetically regulating Gankyrin. Cell Death Dis (2019) 10(2):1–13. doi: 10.1038/s41419-019-1348-0

189. Mo J, Li B, Zhou Y, Xu Y, Jiang H, Cheng X, et al. LINCO00473 promotes hepatocellular carcinoma progression via acting as a ceRNA for microRNA-195 and increasing HMG2A expression. Biomed Pharmacother (2019) 120:109403. doi: 10.1016/j.biopha.2019.109403

190. Gao J, Yin X, Yu X, Dai C, Zhou F. Long noncoding lncRNA01551 promotes hepatocellular carcinoma cell proliferation, migration, and invasion by acting as a competing endogenous RNA of microRNA-122-5p to regulate ADAM10 expression. J Cell Biochem (2019) 120(10):16393–407. doi: 10.1002/jcb.28549

191. Yu S, Li N, Huang Z, Chen R, Yi P, Kang R, et al. A novel lncRNA, TCONS_00000619, represses hepatocellular carcinoma progression by inhibiting enzymatic activity of ENO1. Cell Death Dis (2018) 9(12):1–13. doi: 10.1038/s41419-018-1231-4

192. Wang R, Jiang J, Jiang T, Wang Y, Chen L. Increased long noncoding RNA LINCO0511 is correlated with poor prognosis and contributes to cell proliferation and metastasis by modulating miR-424 in hepatocellular carcinoma. Eur Rev Med Pharmacol Sci (2019) 23(8):3291–301. doi: 10.26355/eurrev_201904_17691

193. Hu W-Y, Wei H-Y, Li K-M, Wang R-B, Xu X-Q, Feng R. LINCO0511 as a ceRNA promotes cell malignant behaviors and correlates with prognosis of
hepatocellular carcinoma patients by modulating miR-195/50/EYA axis. *Biomed Pharmacother* (2020) 121:109642. doi: 10.1016/j.biopharma.2019.109642

201. Gong J, Qi X, Zhang Y, Yu Y, Lin X, Li H, et al. Long noncoding RNA linc00462 promotes hepatocellular carcinoma progression. *Biomed Pharmacother* (2017) 93:40–7. doi: 10.1016/j.biopha.2017.06.004

202. Chen Z, Zhou Z, He C, Zhang J, Wang J, Xiao Z. Down-regulation of LncRNA NR027113 inhibits cell proliferation and metastasis via PTEN/PI3K/AKT signaling pathway in hepatocellular carcinoma. *Eur Rev Med Pharmacol Sci* (2018) 22(21):7222–32. doi: 10.26355/eurrev_201811_16256

203. Chen Z, Xu D, Zhang T. Inhibition of proliferation and invasion of hepatocellular carcinoma cells by LncRNA-ASLC00525 silencing and the mechanism. *Int J Oncol* (2017) 51(3):851–8. doi: 10.3892/ijo.2017.4069

204. Zeng B, Liu Z, Ye H, Cheng D, Zhang G, Zhou J, et al. Up-regulation of LncDQ is associated with poor prognosis and promotes tumor progression via epigenetic regulation of the EMT pathway in HCC. *Cell Physiol Biochem* (2018) 46(3):1123–33. doi: 10.1159/000488841

205. Wu J, Tian X, An Q, Guan X, Hao C. LINC00963 promotes hepatocellular carcinoma progression by activating PI3K/AKT pathway. *Eur Rev Med Pharmacol Sci* (2018) 22(6):1645–52. doi: 10.26355/eurrev_201803_14574

206. Chen J, Wu D, Zhang Y, Yang Y, Duan Y, An Y. LncRNA DCST1-AS1 regulates the development of gastric cancer by sponging miR-203 and downregulating ROCK1. *Biochim Biophys Acta* (2020) 1866(12):118523. doi: 10.1016/j.bba-molcell.2019.118523

207. Hu M, Han Y, Zhang Y, Zhou Y, Ye L. LncRNA TINCR sponges miR-214-5p to up-regulate PAK1. *Biomed Pharmacother* (2018) 119:109213. doi: 10.1016/j.biopha.2019.109213

208. Chen J, Wu D, Zhang Y, Yang Y, Duan Y, An Y. LncRNA DCST1-AS1 regulates the development of gastric cancer by sponging miR-203 and downregulating ROCK1. *Biochim Biophys Acta* (2020) 1866(12):118523. doi: 10.1016/j.bba-molcell.2019.118523

209. Hu M, Han Y, Zhang Y, Zhou Y, Ye L. LncRNA TINCR sponges miR-214-5p to up-regulate PAK1 in hepatocellular carcinoma. *Mol Med Genet* (2020) 21(1):6–8. doi: 10.1186/s12881-019-0940-6

210. Hong Min, Z. Wei, W., Chao, Y., Yang, Y., et al. RHPN1-AS1 drives the progression of hepatocellular carcinoma via regulating miR-956/1F2B/P2 axis. *Curr Pharm Des* (2019) 25(43):4630–40. doi: 10.2174/13816256191105104549

211. Ni W, Zhang Y, Zhan Z, Ye F, Liang Y, Huang J, et al. A novel lncRNA uc.134 represses hepatocellular carcinoma progression by inhibiting ULA4-mediated ubiquitination of LATS1. *J Hematol Oncol* (2017) 10(1):91. doi: 10.1186/s13045-017-0449-4

212. Zhou CC, Yang F, Yuan SX, Ma JZ, Liu F, Yuan JH, et al. Systemic genome screening identifies the outcome associated focal loss of long noncoding RNA PRAL in hepatocellular carcinoma. *Hepatology* (2016) 63(3):850–63. doi: 10.1002/hep.28393

213. Yang F, Huo XS, Yuan SX, Zhang L, Zhou WP, Wang F, et al. Repression of the long noncoding RNA-LET by histone deacetylase 3 contributes to hypoxia-mediated metastasis. *Mol Cell* (2013) 49(6):1083–96. doi: 10.1016/j.molcel.2013.01.010

214. Zhang J, Li Z, Liu L, Wang Q, Li S, Chen D, et al. Long noncoding RNA TS1NC8 is a tumor suppressor that inactivates the interleukin-6/STAT3 signaling pathway. *Hepatology* (2018) 67(1):171–87. doi: 10.1002/hep.29405

215. Wang Y, Liu Z, Yao B, Li Q, Wang L, Wang C, et al. Long non-coding RNA CASC2 suppresses epithelial-mesenchymal transition of hepatocellular carcinoma cells through CASC2/miR-367/FOXO7 axis. *Mol Cancer* (2017) 16(1):123. doi: 10.1186/s12943-017-0702-z

216. Qin G, Tu X, Li H, Cao P, Chen X, Song J, et al. Long Noncoding RNA p53-Stabilizing and Activating RNA Promotes p53 Signaling by Inhibiting Heterogeneous Nuclear Ribonucleoprotein K deSUMOylation and Suppresses Hepatocellular Carcinoma. *Hepatology* (2020) 71(1):112–29. doi: 10.1002/hep.30793

217. Ding H, Liu J, Zou R, Cheng P, Su Y. Long non-coding RNA TPTEP1 inhibits hepatocellular carcinoma progression by suppressing STAT3 phosphorylation. *J Exp Clin Cancer Res* (2019) 38(1):189. doi: 10.1186/s13046-019-1193-0

218. Sun J, Liu L, Zou H, Yu W. The Long-Non-Coding RNA CASC2 Suppresses Cell Viability, Migration, and Invasion in Hepatocellular Carcinoma Cells by Directly Downregulating miR-183. *Yonsei Med J* (2019) 60(10):905–13. doi: 10.3349/ymj.2019.60.10.905

219. Gan Y, Han N, He X, Yu J, Zhang M, Zhou Y, et al. Long non-coding RNA CASC2 regulates cell biological behaviour through the MAPK signalling pathway in hepatocellular carcinoma. *Tumor Biol* (2017) 39(6):1014283717706229. doi: 10.1177/1010428317706229

220. Zhao L, Zhang Y, Zhang Y, Long noncoding RNA CASC2 regulates hepatocellular carcinoma cell oncogenesis through miR-362-5p/Nf-kB axis. *J Cell Physiol* (2018) 233(10):6661–70. doi: 10.1002/jcp.27396

221. Fan JG, Zeng F, Le YG, Xin L. LncRNA CASC2 inhibits the viability and induced the apoptosis of hepatocellular carcinoma cells through regulating miR-24-3p. *J Cell Biochem* (2018) 119(8):6391–7. doi: 10.1002/jcb.26479

222. Wang Y-G, Wang T, Shi M, Zhai B. Long noncoding RNA EPB41L4A-AS2 inhibits hepatocellular carcinoma development by sponging miR-30a-5p and targeting FOXL1. *J Exp Clin Cancer Res* (2018) 37(1):1–13. doi: 10.1186/s13046-019-1128-9

223. Cai K, Li T, Guo L, Guo H, Zhu W, Yan L, et al. Long non-coding RNA LINC00467 regulates hepatocellular carcinoma progression by modulating miR-9-5p/PPARA expression. *Open Biol* (2019) 9(9):190074. doi: 10.1098/rsob.190074

224. Wang X, Sun W, Shen W, Xia M, Chen C, Xiang D, et al. Long non-coding RNA DLIC regulates liver cancer stem cells via IL-6/STAT3 axis. *J Hepatol* (2016) 64(6):1283–94. doi: 10.1016/j.jhep.2016.01.019

225. Liu F, Yuan J, Huang J, Yang F, Wang T, Ma J, et al. Long non-coding RNA FTX inhibits hepatocellular carcinoma proliferation and metastasis by
binding MCM2 and miR-374a. Oncogene (2016) 35(41):5422–39. doi: 10.1038/onc.2016.80

238. Chen C, Zhang Q, Wang W, Yu C. Long non-coding RNA LINC00472 suppresses hepatocellular carcinoma cell proliferation, migration and invasion through miR-93-5p/PDCD4 pathway. Clinics Res Hepatol Gastroenterol (2019) 43(4):436–45. doi: 10.1016/j.clinre.2018.11.008

239. Zhu P, Li Y, Li P, Zhang Y, Wang X. c-Myc induced the regulation of long non-coding RNA TSLD8 inhibits hepatocellular carcinoma by stabilizing WWOX. Biochem Biophys Res Commun (2019) 516(2):526–32. doi: 10.1016/j.bbrc.2019.06.043

240. Xu F, Wang B, Liu M, Liu T, Zhang R. A long non-coding RNA GAS8-AS1 induces epithelial-mesenchymal transition in breast cancer by acting as a competing endogenous RNA of miR-421. J Cell Biochem (2019) 120(6):10633–42. doi: 10.1002/jcb.28353

241. Xu F, Wang B, Liu M, Liu T, Zhang R. A long non-coding RNA GAS8-AS1 induces epithelial-mesenchymal transition in breast cancer by acting as a competing endogenous RNA of miR-421. J Cell Biochem (2019) 120(6):10633–42. doi: 10.1002/jcb.28353

242. Wu J, Zhou X, Fan Y, Cheng X, Lu B, Chen Z. Long non-coding RNA RNP1 downregulates cyclin B1 and inhibits hepatocellular carcinoma cell proliferation in vitro and in vivo. Biochem Biophys Res Commun (2018) 497(1):173–80. doi: 10.1016/j.bbrc.2018.02.049

243. Chen C-L, Tseng Y-W, Wu J-C, Chen G-Y, Lin K-C, Hwang S-M, et al. Suppression of hepatocellular carcinoma by baclovirus-mediated expression of long non-coding RNA PENTP1 and MicroRNA regulation. Biomaterials (2015) 44(1):71–81. doi: 10.1016/j.biomaterials.2014.12.023

244. Sun Q-M, Hu B, Fu P-Y, Tang W-G, Zhang X, Zhan H, et al. Long non-coding RNA RNA 00607 as a tumor suppressor by modulating NF-kB signaling in hepatocellular carcinoma. Carcinogenesis (2018) 39(12):1438–46. doi: 10.1093/carcin/bgy113

245. Zhang H-F, Li W, Han Y-D. LINC00261 suppresses cell proliferation, metastasis and epithelial-mesenchymal transition. Biochem Biophys Res Commun (2018) 516(2):526–32. doi: 10.1016/j.bbrc.2019.06.043

246. Wu J, Zhou X, Fan Y, Cheng X, Lu B, Chen Z. Long non-coding RNA RNP1 downregulates cyclin B1 and inhibits hepatocellular carcinoma cell proliferation in vitro and in vivo. Biochem Biophys Res Commun (2018) 497(1):173–80. doi: 10.1016/j.bbrc.2018.02.049

247. Chen C, Zhang Q, Wang W, Yu C. Long non-coding RNA LINC00472 suppresses hepatocellular carcinoma cell proliferation, migration and invasion through miR-93-5p/PDCD4 pathway. Clinics Res Hepatol Gastroenterol (2019) 43(4):436–45. doi: 10.1016/j.clinre.2018.11.008

248. Xu F, Wang B, Liu M, Liu T, Zhang R. A long non-coding RNA TSLD8 inhibits hepatocellular carcinoma by stabilizing WWOX. Biochem Biophys Res Commun (2019) 516(2):526–32. doi: 10.1016/j.bbrc.2019.06.043

249. Wu J, Huang J, Wang W, Xu J, Yin M, Cheng N, et al. Long non-coding RNA GAS8-AS1 induces epithelial-mesenchymal transition in breast cancer by acting as a competing endogenous RNA of miR-421. J Cell Biochem (2019) 120(6):10633–42. doi: 10.1002/jcb.28353

250. Pan W, Zhang N, Liu W, Liu J, Zhou L, Liu Y, et al. The long noncoding RNA GAS8-AS1 suppresses hepatocarcinogenesis by epigenetically activating the tumor suppressor GAS8. J Biol Chem (2019) 294(44):17154–65. doi: 10.1074/jbc.RA118.003055

251. Peng C, Hu W, Weng X, Tong S, Ding C, et al. Over expression of lncRNA DGCR5 represses the development of hepatocellular carcinoma by targeting the miR-346/KLF14 axis. J Cell Physiol (2019) 234(1):572–80. doi: 10.1002/jcp.26779
272. Zhou Y, Huan L, Wu Y, Bao C, Chen B, Wang L, et al. LncRNA ID2-AS1 suppresses tumor metastasis by activating the HDAC8/ID2 pathway in hepatocellular carcinoma. Cancer Lett (2020) 469:399–409. doi: 10.1016/j.canlet.2019.11.007

273. Du J, Chen M, Liu J, Hu P, Guan H, Jiao X. Lncrna fn1-as1 suppresses liver hepatocellular carcinoma progression by competitively binding with mir-3146 to regulate pten expression. J Cell Biochem (2019) 120(10):18457–64. doi: 10.1002/jcb.29163

274. Wu J, Shuang Z, Zhao J, Tang H, Liu P, Zhang L, et al. Lnc00152 promotes tumorigenesis by regulating DNM1Ls in triple-negative breast cancer. Biomed Pharmacother (2018) 97:1275–81. doi: 10.1016/j.biopharm.2017.11.055

275. Zheng Z-K, Pang C, Yang Y, Duan Q, Zhang J, Liu W-C. Serum long noncoding RNA urorheiloma carcinoma-associated 1: A novel biomarker for diagnosis and prognosis of hepatocellular carcinoma. J Int Med Res (2018) 46(1):348–56. doi: 10.1177/0300060517764441

276. Zhang J, Wei H, Yang H. Long noncoding RNA SNHG15, a potential prognostic biomarker for hepatocellular carcinoma. Eur Rev Med Pharmacol Sci (2016) 20(9):1720–4.

277. Tu Z-Q, Li R-J, Mei J-Z, Li X-H. Down-regulation of long non-coding RNA GASS is associated with the prognosis of hepatocellular carcinoma. Int J Clin Exp Pathol (2014) 7(7):4303.

278. Fu C, Xu X, Lu W, Nie L, Yin T, Wu D. Increased expression of long non-coding RNA CCAAT2 predicts poorer prognosis in patients with hepatocellular carcinoma. Medicine (2019) 98(42):e17412. doi: 10.1097/MD.0000000000017412

279. Wang Y, Jing W, Ma W, Liang C, Chai H, Tu J. Down-regulation of long non-coding RNA SNHG15, a potential prognostic biomarker for hepatocellular carcinoma. Eur Rev Med Pharmacol Sci (2016) 20(9):1720–4.

280. Ma W, Wang H, Jing W, Zhou F, Chang L, Hong Z, et al. Down-regulated long non-coding RNA signature to improve the prognosis prediction for patients with hepatocellular carcinoma. Oncotarget (2018) 9(9):11348–56. doi: 10.18632/oncotarget.29348

281. Li S-Y, Wang H, Mai H-F, Li G-F, Chen S-J, Li G-S, et al. Down-regulated long non-coding RNA signature predicts recurrence-free survival in hepatocellular carcinoma. J Cell Biochem (2019) 120(9):14645–56. doi: 10.1002/jcb.28726

282. Zeng Z, Dong J, Li Y, Dong Z, Liu Z, Huang J, et al. The expression level and clinical significance of IncRNA X91348 in hepatocellular carcinoma. Artif Cells Nanomed Biotechnol (2019) 47(1):3067–71. doi: 10.1080/21694101.2019.1640228

283. Chen Q, Tian G, Wang C. Expression of IncRNA TCONS_00027978 in hepatocellular carcinoma and its influence on prognosis and survival. Eur Rev Med Pharmacol Sci (2017) 21(24):6555–60. doi: 10.26355/eurrev_201712_14009

284. Gu J-X, Zhang X, Miao R-C, Xiang X-H, Fu Y-N, Zhang J-Y, et al. Six-long non-coding RNA signature predicts recurrence-free survival in hepatocellular carcinoma. World J Gastroenterol (2019) 25(2):220. doi: 10.3748/wjg.v25.i2.220

285. Refai NS, Louka ML, Halim HY, Montasser I. Long non-coding RNAs (CASC2 and TUG1) in hepatocellular carcinoma: Clinical significance. J Gene Med (2019) 21(9):e3112. doi: 10.1002/jgme.3112

286. Zhao Q-J, Zhang J, Xu L, Li F-F. Identification of a five-long non-coding RNA signature to improve the prognosis prediction for patients with hepatocellular carcinoma. World J Gastroenterol (2018) 24(30):3426. doi: 10.3748/wjg.v24.i30.3426

287. Shaker OG, Abedelwahed MY, Ahmed NA, Hassan EA, Ahmed TI, Abouasrae MA, et al. Evaluation of serum long noncoding RNA NEAT and MiR-129-5p in hepatocellular carcinoma. JUBMB Life (2019) 71(10):1517–8. doi: 10.1002/jubm.2096

288. Guo S, Chen W, Luo Y, Ren F, Zhong T, Rong M, et al. Clinical implication of long non-coding RNA NEAT1 expression in hepatocellular carcinoma patients. Int J Clin Exp Pathol (2015) 8(5):5395.

289. Tang J, Jiang B, Deng L, Zhang X, Wang X, Sun B. Circulation long non-coding RNAs as act biomarkers for predicting tumorigenesis and metastasis in hepatocellular carcinoma. Oncotarget (2015) 6(6):4505. doi: 10.18632/oncotarget.2934
Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright © 2021 Ghafouri-Fard, Gholipour, Hussen and Taheri. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.