Oncogenic roles of the lncRNA LINC00460 in human cancers

Min Su1,2,3,4†, Jinming Tang1,2†, Desong Yang1,2, Zhining Wu1,2, Qianjin Liao3, Hui Wang4, Yuhang Xiao2,5* and Wenxiang Wang1,2*

Abstract
Long noncoding RNAs (lncRNAs) represent an important group of endogenous RNAs with limited protein-encoding capability, with a length of more than 200 nucleotides. Emerging evidence has demonstrated that lncRNAs are greatly involved in multiple cancers by playing critical roles in tumor initiation and progression. Long intergenic non-protein coding RNA 460 (LINC00460), a novel cancer-related lncRNA, exhibits abnormal expression and oncogenic function in multiple cancers, and positively correlates with poor clinical characteristics of cancer patients. LINC00460 has also been shown to be a promising biomarker for diagnosis as well as prognostic evaluation in cancer patients. In this review, we briefly summarized recent knowledge on the expression, functional roles, molecular mechanisms, and diagnostic and prognostic values of LINC00460 in human malignancies.

Keywords: Long noncoding RNA, LINC00460, Human cancer, Oncogenic function, Functional role, Molecular mechanism

Introduction
Deep sequencing of mammalian transcriptomes has revealed that approximately 98% of RNA sequences are noncoding RNAs (ncRNAs) that comprise two groups based on length, including small (<200 nucleotides) and long (lncRNAs; >200 nucleotides) ncRNAs [1, 2]. Over the past two decades, an increasing number of studies have assessed lncRNAs because of their potential involvement in many pathologies, including malignancies [3]. LncRNAs contribute to multiple biological functions in cancer, ranging from cell proliferation, invasion, stemness, angiogenesis, to chemotherapy resistance [4, 5]. LncRNAs were demonstrated to mediate diverse molecular cellular events such as genetic transcription, nuclear compartment formation, alternative splicing and epigenetic modification [6, 7]. For example, lncRNA metastasis-associated lung adenocarcinoma transcript1 (MALAT1) has high expression in non-small cell lung cancer (NSCLC), and promotes proliferation progression of NSCLC cells through stabilizing FOXP3 by inhibited its ubiquitination induced by STUB1 [8]. Glucose transporter 1 (GLUT1) associated lncRNA (GAL) was upregulated in colorectal cancer liver metastasis (CRLM) tissues and associated with the overall survival (OS) rates of CRLM patients. GAL promoted colorectal cancer cell migration and invasion. GAL served as an oncogene through interacting with the GLUT1 protein to increase GLUT1 SUMOylation, inhibiting the effect of the ubiquitin-proteasome system on the GLUT1 protein [9].

Recent evidence reveals the long intergenic non-protein coding RNA 460 (LINC00460, NR_034119) plays a
critical role in tumor progression [10]. LINC00460 (on chromosome 13q33.2), is a novel cancer-related lncRNA with a transcript length of 935 nucleotides that contains 3 exons [11, 12]. In the present review, we summarize current research on the expression, functions, underlying mechanism and clinical significance of LINC00460 in human malignancies. Moreover, these provide support for the potential of LINC00460 as a novel biomarker and as a therapeutic target for cancers.

LINC00460 expression in malignancies
LINC00460 is generally upregulated in multiple tumor cells in comparison to that in control cells (Table 1), including bladder [13, 14], breast [15], cervical [16, 17], colon [18, 19], colorectal [10, 20–24], esophageal [25], gastric [26, 27], ovarian [28], lung [11, 29–31], pancreatic [32] and papillary thyroid cancers [33–35], as well as acute myeloid leukemia (AML) [36], glioma [37], head and neck squamous cell carcinoma (HNSCC) [38–42], hepatocellular carcinoma [43–45], laryngeal squamous cell carcinoma [46], meningioma [47], nasopharyngeal carcinoma [48] and osteosarcoma [49]. In addition, LINC00460 is also overexpressed in these tumor tissues compared with adjacent normal tissues. Its expression level is significantly associated with several clinical characteristics, including tumor size [10, 15, 32, 44, 49], tumor differentiation [25, 41, 42, 44, 45], lymph node metastasis [10, 13, 22, 25, 27, 34, 39, 41, 45], and TNM stage [10, 25, 27, 33, 34, 42, 44, 45].

Regulation of LINC00460 in cancer
The expression of LINC00460 has been reported to be regulated by genetic and epigenetic methods. A study performed by Zhang and colleagues [50] revealed LINC00460 is increased in colorectal cancer HCT116 cells following irradiation at 2 or 4 Gy. The critical region controlling LINC00460 transcription after irradiation was shown to be between −240 and −44 bp upstream of the LINC00460 transcription initiating site. In addition, C-jun was identified as a positive regulator of LINC00460 expression post-irradiation.

Nakano et al. [51] demonstrated that cells transfected with active EGFR mutations have elevated LINC00460 amounts. Furthermore, EGFR activation induced by EGFR treatment also caused LINC00460 upregulation, the EGFR-induced increase in LINC00460 expression could be significantly attenuated by gefitinib pre-treatment induced EGFR inactivation. These results suggested that overexpression of LINC00460 was associated with the the abnormal activation of EGFR.

In a report by Zhang et al. [18], LINC00460 showed significant hypomethylation in colorectal cancer tissue samples in comparison with adjacent noncancerous tissue specimens, which had a negative correlation with its expression. In addition, treatment with 5-aza-2’-deoxycytidine resulted in LINC00460 overexpression and demethylation in LOVO and SW620 cells, demonstrating that LINC00460 could be activated by DNA methylation.

In another study, Liang et al. [25] revealed elevated acetyl-histone H3 (Lys18 and Lys27) enrichment signals in the LINC00460 promoter. The chromatin immunoprecipitation (CHIP)-qPCR assay indicated CBP (CREB-binding protein) and P300 (histone acetyltransferase) individually and directly interact with the LINC00460 promoter, and CBP/P300 downregulation decreased LINC00460 amounts in ESCC cells. In addition, both CBP and P300 suppression downregulated LINC00460. These results indicated CBP/P300 interaction with the LINC00460 promoter induces LINC00460 transcription via histone H3 acetylation.

LINC00460 functions in malignancies
Studies have proposed that multiple properties contribute to tumor initiation and progression, including sustaining cell growth, resisting cell death, activating invasive and metastatic pathways, and increasing resistance to chemotherapy [52]. Recently, LINC00460 was described for its critical role in controlling oncopgenes [11, 13, 15, 19, 21–23, 33, 35, 36, 39, 42–45, 47, 49, 51, 53] and tumor suppressors [10], generally modulating the above mentioned cancer cell features (Fig. 1).

LINC00460 in cell viability and proliferation
LINC00460 expression is tightly correlated with tumor size in patients with several cancers such as osteosarcoma, and breast, colorectal, liver and pancreatic cancers. such as breast [15], colorectal [10], liver [44], pancreatic [32] cancer, and osteosarcoma [49]. In vitro gain- or loss- of function experiments demonstrated LINC00460 could promote cancer cell proliferation, including acute myeloid leukemia [36], bladder [13, 14], breast [15], cervical [16, 17], colon [19], colorectal [10, 20–24], esophageal [25], gastric [26, 27], ovarian [28], lung, pancreatic [32] and papillary thyroid cancers [33–35], glioma [37], HNSCC [38, 39, 41, 42], hepatocellular carcinoma [43–45], meningioma [47], nasopharyngeal carcinoma [48] and osteosarcoma [49]. Additionally, in vivo tumor xenograft models also demonstrated that silencing LINC00460 reduces tumor volume and lowers tumor weight (Table 2).

Studies have shown that LINC00460 knockdown significantly suppressed cancer cell progression at the G1 phase of the cell cycle. The function of LINC00460 on cell cycle progression might be related to the regulation of LINC00460 on protein proteins relevant to cell cycle,
| Cancer type                      | Expression in tissue | Sample size | Expression in cancer cells | Cancer cell lines | Relative normal cell lines | Functional role                  | Refs. |
|----------------------------------|----------------------|-------------|-----------------------------|-------------------|---------------------------|-----------------------------------|-------|
| Acute myeloid leukemia           | Up                   | 80          | Up                          | THP1, KG1, ME1, HL60 | HSS                       | Proliferation, apoptosis, cell cycle | [36]  |
| Bladder cancer                   | Up                   | 43          | Up                          | T-24, 5637, SW780, RT-112 | SV-HUC-1                  | Proliferation, migration, invasion | [13]  |
|                                  | −                    | −           | −                           | 5637, T24          | SV-HUC-1                  | Proliferation, migration, invasion | [14]  |
| Breast cancer                    | Up                   | 42          | Up                          | MCF-7, BT-474, MDA-MB-231, BT-549 | MCF-10 A                 | Proliferation, migration, invasion | [15]  |
| Cervical cancer                  | Up                   | 20          | Up                          | HeLa, CaSkI        | −                         | Proliferation, invasion, cell cycle | [16]  |
|                                  | Up                   | 30          | −                           | SiHa, C-33 A, HeLa, CaSkI | −                         | Proliferation, apoptosis, cell cycle | [17]  |
| Colon cancer                     | Up                   | 30          | −                           | HT-29, HCT-116, SW480, LOVO | NCM-460                   | Proliferation, invasion, EMT      | [19]  |
| Colorectal cancer                | Up                   | 60          | Up                          | HCT116, SW480, HT-29, Lovo | HcoEpC                    | Proliferation, apoptosis           | [10]  |
|                                  | Up                   | 92          | Up                          | SW620, HCT116, CX-1, HT29 | NCM460                    | Proliferation, cell cycle          | [24]  |
|                                  | Up                   | 74          | Up                          | HT29, HCT116, SW480, and LOVO | NCM460                  | Proliferation, migration, invasion, apoptosis | [21]  |
|                                  | Up                   | 62          | Up                          | HCT-15, HCT-116, SW480, SW620, RKO, LoVo, HT-29 | CCD841CoN | Proliferation, migration, invasion, EMT | [60]  |
|                                  | Up                   | 74          | Up                          | HT29, HCT116, SW480, LOVO | NCM460                    | Migration, invasion                | [22]  |
|                                  | Up                   | 498         | Up                          | SW480, SW620, HCT116, DLD1, LOVO, HT29 | FHC                     | Proliferation, migration, invasion | [20]  |
|                                  | Up                   | 40          | Up                          | HCT116, HT-29      | FHC                       | Migration, invasion               | [23]  |
|                                  | Up                   | 21          | −                           | −                  | −                         | Chemoresistance                   | [64]  |
|                                  | Up                   | 98          | Up                          | SKOV3, A2780, OVCAR, HO–8910 | HOSEpiC                  | −                                   | [28]  |
| Epithelial ovarian cancer        | Up                   | 15          | Up                          | EC1, EC9706, KYSE70, TE1, TE13 | Het-1 A                  | Migration, EMT                     | [61]  |
| Esophageal cancer                | Up                   | 60          | Up                          | MGC803, BGC823 and GSE1 | GSE1                     | Proliferation, migration, invasion, cell cycle | [53]  |
|                                  | Up                   | 80          | Up                          | (BGC823, AGS, GSE1, and MGC803) | GSE1 | Proliferation, apoptosis, cell cycle | [26]  |
|                                  | Up                   | 90          | Up                          | BGC-823, GSE-7901, MKN-28, MKN-45 | GES-1 | Proliferation, invasion, cell cycle | [27]  |
| Gastric cancer                   | Up                   | 42          | Up                          | U87, U251, LN229, A172 | NHA                       | Proliferation, migration, invasion, apoptosis | [37]  |
| Gloma                            | Up                   | 15          | Up                          | CAL-27, WSU-HN4, Wsu-HN6 | HOEC                      | Proliferation, migration, EMT, apoptosis | [38]  |
| Head and neck squamous cell cancer | Up                  | 60          | Up                          | HSC3, Fadu, SAS | HACA                     | Proliferation, migration, invasion, EMT | [39]  |
|                                  | Up                   | 123         | Up                          | WSU–HN4, Wsu-HN6, Wsu-HN30, SCC-4, SCC-9, SCC-25 and CAL-27 | Normal oral epithelial cells | −                                   | [41]  |
including cyclin D1 [17, 44, 54], CDK2 [26], CDK4/CDK6 [54], CCNG2 [26], CCND1 [53].

**LINC00460 in cell death**

Apoptotic, autophagic and necrotic cell deaths are the main mechanisms of cell death [55]. Cell apoptosis is the common process of programmed cell death [56]. LINC00460 has been reported to inhibit apoptosis in various cancers. The anti-apoptotic function of LINC00460 might be related to the regulation of the apoptotic proteins caspase-3 [21, 36], caspase-9 [10], PARP [17], Bcl-2 and Bax [10, 44].

LINC00460 could also regulate autophagy in cancer cells [42]. Knockdown of LINC00460 resulted in increased amounts of autophagosomes in HNSCC cells, along with increased LC3 II/LC3 I ratio and Beclin 1 amounts. Meanwhile, overexpression of LINC00460 restrains autophagy, with reduced number of autophagosomes and decreased LC3 II/LC3 I ratio and Beclin 1 amounts.

**LINC00460 in cancer metastasis**

Metastasis is the major cause results in the high mortality rate of diverse types of cancer, and high rates of metastasis are characteristic of advanced malignancies [57, 58]. LINC00460 has been reported to be positively associated with lymph node and distant metastases as well as TNM stage in diverse malignancies, including bladder [59], colorectal [21, 22, 24], esophageal [25], gastric [27], head and neck [39, 41, 42], liver [45] and papillary thyroid [34] cancers, as well as osteosarcoma [49]. In vitro experiments demonstrated LINC00460 could regulate migratory and invasive pathways in malignant cells. A role for LINC00460 in metastasis has

---

**Table 1 (continued)**

| Cancer type                       | Expression in tissue | Sample size | Expression in cancer cells | Cancer cell lines | Relative normal cell lines | Functional role                                      | Refs. |
|----------------------------------|---------------------|-------------|---------------------------|------------------|---------------------------|------------------------------------------------------|-------|
| Laryngeal squamous cell carcinoma| Up                  | 68          | –                         | –                | –                         | –                                                   | [46]  |
| Lung cancer                      | Up                  | 50          | Up                        | H157, 95D, SPC-A-1, A549, SK-LU-1, Calu-3, HCC-78, H1299, H1975 | 16HBE            | Proliferation              | [11]      |
|                                  |                     |             |                           |                  |                           |                                                     |       |
|                                  | Up                  | 52          | Up                        | A549, H226, H1915, SPCA-1, PC-9 | 16HBE            | Proliferation, migration, invasion, EMT | [29]  |
|                                  |                     |             |                           |                  |                           |                                                     |       |
|                                  | Up                  | 36          | Up                        | H460, A549, SK-MES-1, and H1299 | NHBE            | Proliferation, invasion, chemoresistance | [30]  |
|                                  |                     |             |                           |                  |                           |                                                     |       |
|                                  | Up                  | 8           | Up                        | A549, H1299, H1975, H460, PC9, SPC-A1 | Beas-2B         | Migration, invasion, EMT | [31]  |
| Meningioma                       | Up                  | 33          | Up                        | (IOMM-Lee, CH157-MN) | Ben–Men-1             | Proliferation, invasion, apoptosis | [47]  |
| Nasopharyngeal carcinoma         | Up                  | 50          | Up                        | SUNE-1, CNE-1, HNE-1, CNE-2, C666-1, HONE-1 | NP69          | Proliferation              | [48]  |
| Osteosarcoma                     | Up                  | 31          | Up                        | Saos-2, HOS, U2OS, MG63 | hFOB 11.19    | Proliferation, migration, invasion | [49]  |
| Pancreatic cancer                | Up                  | 59          | –                         | –                | –                         | –                                                   | [32]  |
| Papillary thyroid cancer         | Up                  | 58          | Up                        | SFTPCC1, BCPAP, FTC-133, 8505 C | Nthyori 3-1    | Proliferation, migration, invasion, EMT | [33]  |
|                                  | Up                  | 48          | Up                        | TPC-1, BCPAP, JHH-4 | Nthyori 3-1 | Proliferation, migration, invasion | [34]  |
|                                  | –                   | –           | Up                        | K1, TPC-1         | Nthyori 3-1 | Proliferation, invasion, apoptosis | [35]  |
**Table 2** In vivo functional characterization of LINC00460 in cancer

| Cancer type                               | Cancer cell lines | Animal                | Role in tumor growth | Refs. |
|-------------------------------------------|-------------------|-----------------------|----------------------|-------|
| Bladder Cancer                            | T-24              | BALB/c nude mice      | Promote              | [59]  |
| Breast cancer                             | MCF-7             | Nude mice             | Promote              | [15]  |
| Cervical cancer                           | HeLa, CaSki       | Nude mice             | Promote              | [16]  |
|                                            | SiHa              | Nude mice             | Promote              | [17]  |
| Colon cancer                              | HCT-116, LOVO     | BALB/c nude mice      | Promote              | [19]  |
| Colorectal cancer                         | HCT116, SW480     | BALB/c nude mice      | Promote              | [10]  |
|                                            | HT29              | BALB/c nude mice      | Promote              | [20]  |
|                                            | RKO               | BALB/c nude mice      | Promote              | [60]  |
| Gastric cancer                            | BGC823            | Athymic mice nude mice| Promote              | [26]  |
|                                            | MKN-45            | Nude mice             | Promote              | [27]  |
| Head and neck squamous cell carcinoma     | CAL-27            | BALB/c nude mice      | Promote              | [41]  |
|                                            | Fadu              | BALB/c nude mice      | Promote              | [39]  |
| Hepatocellular carcinoma                  | Hep3B             | BALB/c nude mice      | Promote              | [44]  |
|                                            | HepG2             | BALB/c nude mice      | Promote              | [45]  |
|                                            | HuH7              | BALB/c nude mice      | Promote              | [43]  |
| Lung cancer                               | AS49, SPC-A-1     | BALB/c nude mice      | Promote              | [11]  |
|                                            | AS49              | Nude mice             | Promote              | [30]  |
| Nasopharyngeal carcinoma                  | S-8 F             | BALB/c nude mice      | Promote              | [62]  |
|                                            | CNE-1, SUNE-1     | BALB/c nude mice      | Promote              | [48]  |
| Papillary thyroid cancer                   | TPC1              | BALB/c nude mice      | Promote              | [33]  |
also been documented, primarily involving the regulation of epithelial-to-mesenchymal transition (EMT), in which epithelial cells undergo diverse modifications to acquire a mesenchymal phenotype. Several studies have demonstrated that LINC00460 knockdown inhibits EMT development and regulates the expression of proteins relevant to EMT (upregulate E-cadherin, downregulate N-cadherin and vimentin) [19, 22, 29, 38, 39, 41, 50, 54, 60–62].

LINC00460 in chemotherapeutic or radiation resistance
At present, intrinsic or acquired resistance is the main cause of chemotherapy failure in many cancers [63]. LINC00460 has been demonstrated to be involved in chemoresistance. Zhang et al. [18] investigated the associations of IncRNAs and antitumor drug response, and demonstrated that LINC00460 could distinguish responses to AZD6244 and PD-0325901 in colon cancer samples. Meng and colleagues [64] demonstrated that LINC00460 is upregulated in colorectal cancer cells with oxaliplatin resistance and p53 mutations, compared with parental oxaliplatin-sensitive cells. LINC00460 silencing sensitized oxaliplatin-resistant colorectal cancer cells to this drug via p53 regulation.

The expression of LINC00460 was shown to be elevated in gefitinib-resistant NSCLC and cells [30]. Gain-and loss of function assays showed LINC00460 induces gefitinib resistance by increasing the expression of EGFR and the multidrug-resistance-associated proteins P-gp, MRP1, and BCRP. In another study, Nakano and collaborators [51] demonstrated that LINC00460 amounts are markedly elevated in cancer with wild-type or mutated (exon 19 deletion and L858R) EGFR in comparison with noncancerous tissues. It was also upregulated in NSCLC cells with gefitinib resistance in comparison with gefitinib-sensitive cells. EGFR activation, induced by transfection with active EGFR mutations or treatment with EGF, resulted in higher LINC00460 expression, suggesting LINC00460 contributes to resistance against EGFR-TKIs.

Radiation therapy is broadly utilized for treatment of some solid tumors, and recent advances enable direct tumor targeting, without harming adjacent noncancerous tissues [65]. Radiation treatment is mostly hampered by tumor resistance, and decreasing recurrence post-radiotherapy represents an important challenge [66]. LINC00460 was shown to be markedly upregulated following irradiation at 2 or 4 Gy in HCT116 cells [50]. Transient LINC00460 silencing remarkably reduced HCT116 cell proliferation and EMT induced by irradiation. Thus, LINC00460 was considered to mediate the sensitization of HCT116 cells to ionizing radiation.

Mechanisms underlying LINC00460’s effects in malignancies
Mounting evidence suggests the regulatory mechanisms of IncRNAs include modulating epigenetic alterations, regulating transcription or splicing, interacting with RNA binding proteins, and acting as miRNA sponges [4]. LncRNAs are involved in the regulation of various biological functions in the nucleus and cytoplasm [67]. LINC00460 was shown to be subcellular distributed in both cytoplasm and nucleus, thus playing important modulatory roles at the transcriptional and post-transcriptional levels [10, 11, 25, 48, 60] (Fig. 1). The following sections mainly focus on the molecular mechanisms of LINC00460 in regulating biological functions of malignancies.

LINC00460 serves as a ceRNA
One important mechanism of IncRNA is function as competing endogenous RNA (ceRNA), through sponging miRNA from target mRNA of the miRNAs and constructing a triple network of IncRNA-miRNA-mRNA. Several studies have shown LINC00460 is primarily expressed in cytoplasm of cells, and thus could act as a ceRNA through interaction with miRNAs, including miR-1224-5p [61], miR-149-5p [10], miR-206 [42], miR-302c-5p [11], miR-320b [36], miR-342-3p [53], miR-433-3p [19], miR-539 [35], and so on (Table 3). In addition, several assays, such as luciferase reporter assays and RNA immunoprecipitation (RIP) and/or RNA pull-down assays, were performed to identify miRNA-binding sites on LINC00460. Furthermore, functional assays indicated the miRNA and its target mRNA control LINC00460’s effects.

LINC00460 interacts with RNA binding proteins
LncRNAs has been shown to control gene expression by interacting with RNA binding proteins (RBPs) [68]. RNA pull-down assays and mass spectroscopy are generally performed in sequence for identifying RBPs for IncRNAs. Utilizing this method, Jiang et al. revealed PRDX1 as an RBP that binds LINC00460 [41]. The interaction between PRDX1 and LINC00460 was confirmed by RIP assays. In a further report, Li and co-workers [31] showed hnRNP K is a RBP that binds to LINC00460, and confirmed LINC00460 interacts with hnRNP K by immunoblot.

Apart from mass spectrometry, bioinformatics is also generally carried out for predicting the odds of LINC00460 interacting with RBPs, followed by confirmation by the RIP assay. Using this method, Yang and collaborators [26] showed LINC00460 interacts with EZH2 and LSD1, inducing H3K27 trimethylation and H3K4 demethylation of target gene promoters, thereby suppressing transcription. In addition, LINC00460 interactions with
EZH2 and LSD1 were also confirmed by the ChIP assay. In another report, Lian et al. [10] predicted LINC00460 could potentially bind to EZH2, SUZ12, DNMT1, and AGO2, by using bioinformatics analysis. They further confirmed that LINC00460 interacts with EZH2 through RIP assays, and further regulates the expression of KLF2.

**LINC00460 as a cancer biomarker**

**LINC00460 as a molecular marker for cancer diagnosis**

It is now widely accepted that the early diagnosis is crucial for achieving a lower mortality rate of tumors [69]. The detection and identification of IncRNAs in body fluids, including serum and plasma, may provide a novel tool for early noninvasive diagnosis of cancer [70]. Serum LINC00460 amounts were markedly elevated in 80 AML or CN-AML cases compared with 67 healthy control cases [36]. Receiver operating characteristic (ROC) curve analysis revealed serum LINC00460 amounts provided a clear separation of AML and healthy controls, with an area under the curve (AUC) of 0.8488 (95% CI, 0.7697–0.9279). Additionally, serum LINC00460 reliably differentiated CN-AML cases from healthy control cases (AUC = 0.7591). Serum LINC00460 amounts were also markedly reduced in patients after complete remission. These findings suggested that LINC00460 might be a potential diagnostic biomarker for patients with AML. However, LINC00460 is expressed in a broad range of cancer types, making it less specific in distinguishing the origin of tumors. Further studies for the expression, sensitivity and stability of LINC00460 in non-invasive body fluids should be further investigated for are required to make LINC00460 an ideal tool for disease diagnosis. In addition, LINC00460 in body fluids are required to investigate for its diagnostic value alongside other specific molecular markers, and further investigations with larger clinical sample sizes are still required.

### Table 3 CeRNA function of LINC00460 in cancer

| LINC00460 target miRNA | Validated method | miRNA target gene | Cancer type | Refs. |
|------------------------|------------------|-------------------|-------------|-------|
| miR-1224-5p            | Luciferase reporter assay | –               | Esophageal cancer | [61] |
| miR-1224-5p            | Luciferase reporter assay, RIP | FADS1          | osteosarcoma | [49] |
| miR-149-5p             | Luciferase reporter assay, RIP | CUL4A         | colorectal cancer | [10] |
| miR-149-5p             | Luciferase reporter assay, RNA pull-down | IL6          | nasopharyngeal carcinoma | [48] |
| miR-149-5p             | Luciferase reporter assay | BGN            | colorectal cancer | [23] |
| miR1495p               | Luciferase reporter assay, RIP | IL6          | Lung adenocarcinoma | [51] |
| miR-149-5p, miR-150-5p | Luciferase reporter assay, RNA pull-down | p53          | Colorectal Cancer | [64] |
| miR-206                | Luciferase reporter assay, RNA pull-down | STC2         | Head and neck squamous cell carcinoma | [42] |
| miR-302c-5p            | Luciferase reporter assay, RNA pull-down | FOXA1        | Lung adenocarcinoma | [11] |
| miR30a3p               | Luciferase reporter assay, RNA pull-down | –            | Nasopharyngeal carcinoma | [62] |
| miR-320a               | Luciferase reporter assay | –              | Gloma        | [37] |
| miR-338-3p             | Luciferase reporter assay, RNA pull-down | PBX3         | Acute myeloid leukemia | [36] |
| miR-342-3p             | Luciferase reporter assay, RIP | KDM2A        | Epithelial ovarian cancer | [28] |
| miR-342-3p             | Luciferase reporter assay, RNA pull-down | AGR2         | Hepatocellular carcinoma | [45] |
| miR-342-3p             | Luciferase reporter assay | AGR2          | Hepatocellular carcinoma | [43] |
| miR3613p               | Luciferase reporter assay | Gli1          | Cervical cancer | [16] |
| miR-433-3p             | Luciferase reporter assay, RNA pull-down | ANXA2        | Colon cancer | [19] |
| miR-4443               | Luciferase reporter assay | –              | Head and neck squamous cell carcinoma | [38] |
| miR-485-5p             | Luciferase reporter assay | Raf1          | Papillary thyroid cancer | [33] |
| miR-485-5p             | Dual luciferase reporter assay, RNA pull-down assay, RIP | PAK1         | Hepatocellular carcinoma | [44] |
| miR-489-5p             | Luciferase reporter assay, RNA pull-down | FGF7, AKT    | Breast cancer | [15] |
| miR-5035p              | Luciferase reporter assay | AKT2, HMGA2, SHOX2 | Cervical cancer | [17] |
| miR-539                | Luciferase reporter assay | MMP-9        | Meningioma | [47] |
| miR-539                | Luciferase reporter assay | MMP-9        | Papillary thyroid carcinoma | [35] |
| miR-612                | Luciferase reporter assay, RIP | AKT2         | Head and neck squamous cell carcinoma | [39] |
| miR-612                | Luciferase reporter assay | FOXK1        | Bladder Cancer | [59] |
| miR-613                | Luciferase reporter assay, RIP | SphK1        | Colorectal cancer | [21] |
| miR-939-5p             | Luciferase reporter assay, RNA pull-down | LIMK2        | Colorectal cancer | [22] |
LINC00460 serves as a biomarker for cancer prognosis

Recently, aberrant expression of LINC00460 has been considered an independent prognostic factor in diverse cancers. Indeed, elevated LINC00460 amounts were significantly associated with poor OS in bladder cancer [13, 71], cervical cancer [16, 17], colorectal cancer [10, 20–22], esophageal cancer [25, 72], gastric cancer [27], HNSCC [39, 40], liver cancer [45], lung cancer [30, 31, 51], osteosarcoma [49, 54], pancreatic cancer [32] and papillary thyroid carcinoma [33]. In addition, upregulation of LINC00460 was also associated with poor progression free survival (PFS) in AML [36], colorectal cancer [20, 23, 24], gastric cancer [26, 27], glioma [37], hepatocellular carcinoma [45] and lung adenocarcinoma [51] and osteosarcoma [54]. Besides survival data, other clinical features including tumor size, histological grade, differentiation degree, lymph node metastasis and TNM stage, are related to LINC00460 expression, (Table 4).

The prognostic value of LINC00460 was further investigated in combination with other lncRNAs. Cao and colleagues [73] identified an lncRNA trio (LINC00460, KTN1-AS1 and RP5-894A10.6) jointly showing an AUC of 0.68 (95% CI 0.60–0.76, P < 0.0001). In addition, Kaplan-Meier analysis of HNSCC cases, categorized into the high- and low-risk groups according to lncRNA signature-based risk score, revealed marked OS differences between the high- (43.9 months) and low- (25.6 months) risk groups (P = 0.002 in the log-rank test). The findings suggested the three-lncRNA panel-based signature could effectively predict patient survival in HNSCC.

Zhang et al. [74] conducted a lncRNA prognostic model with another lncRNA trio, comprising LINC00460, MIAT and LINC00443, which could independently distinguish kidney renal clear cell carcinoma cases at low- and high-risk of poor OS, with AUCs for 1-, 5- and 10-year OS of 0.723, 0.714 and 0.826, respectively. The model had independent and great prognostic value in these patients.

In another study, Huang et al. [72] identified another lncRNA trio, comprised of RP11-366H4.1.1, LINC00460 and AC093850.2, as an efficient predictive factor of OS and DFS in patients with ESCC. The authors utilized multivariable Cox regression analysis to generate a risk score as (0.882 \times \text{AC093850.2}) + (1.219 \times \text{LINC00460}) + (0.921 \times \text{RP11-366H4.1.1}), whose cutoff was 48.48. Median OS was markedly reduced in high-risk cases compared with the low-risk group in the training set (23.1 months vs. 39.1 months, P < 0.001), the test set (23 months vs. 59 months, P < 0.001) and an independent esophageal squamous cell carcinoma dataset (GSE53624) (22.4 months vs. 60.4 months, P < 0.001). In addition, the three-lncRNA signature could also be used for predicting DFS, with median DFS times of 15.2 and 33.3 months in high- and low-risk cases of the training set, respectively (P < 0.001), versus 16.4 and 50.8 months in the test set, respectively (P < 0.001). The above findings demonstrated the prognostic capability of the three-lncRNA signature to predict survival and recurrence risk.

Therefore, LINC00460 in combination with other lncRNAs or specific biomarkers can function as an independent prognostic indicator in diverse cancer types.

### Table 4 Involvement of LINC00460 in cancer prognosis

| Cancer type                        | Prognostic indicator | Associated clinical features                                                                 | Refs. |
|------------------------------------|----------------------|------------------------------------------------------------------------------------------------|-------|
| Acute myeloid leukemia             | OS, PFS              | FAB classification, cytogenetics                                                                 | [36]  |
| Bladder cancer                     | OS                   | Tumor stage, lymph nodes metastasis                                                             | [59, 71] |
| Breast cancer                      | OS                   | Tumor size, WHO stage                                                                              | [15]  |
| Cervical cancer                    | OS                   | –                                                                                                 | [16, 17] |
| Colon cancer                       | OS                   | –                                                                                                 | [18]  |
| Colorectal cancer                  | OS, DFS              | Tumor stage, metastasis classification, lymph node metastasis, TNM stage                         | [10, 20–24] |
| Esophageal squamous cell carcinoma | OS                   | TNM stage, lymph node metastasis, differentiation degree                                          | [25]  |
| Gastric cancer                     | OS, DFS              | TNM stage, lymph node metastasis                                                                | [26, 27] |
| Head and neck squamous cell carcinoma| OS                  | Tumor stage, tumor differentiation, lymph node metastasis, TNM stage                            | [39–42] |
| Hepatocellular carcinoma           | OS, PFS              | Tumor differentiation degree, TNM stages, lymph node metastasis                                  | [44, 45] |
| Lung cancer                        | OS, PFS              | –                                                                                                 | [30, 31, 51] |
| Nasopharyngeal carcinoma           | OS                   | –                                                                                                 | [48, 62] |
| Osteosarcoma                       | OS, DFS              | Tumor size, distant metastasis                                                                   | [49, 54] |
| Pancreatic cancer                  | OS                   | Tumor size                                                                                       | [32]  |
| Papillary thyroid carcinoma        | OS                   | TNM stage, lymph node metastasis                                                                | [33, 34] |
Conclusion and future perspectives

Numerous studies have confirmed that lncRNAs play critical roles in tumor development and progression in humans. This review mainly discusses research progress of the role, mechanism and clinical value of LINC00460 in a variety of human tumors. LINC00460 has been demonstrated to be upregulated in major types of human malignancies, regulating cellular events such as cell proliferation, apoptosis, migration, invasion, and chemoresistance. Thus, LINC00460 might be a potential candidate for treating diverse cancer types. Mechanistically, LINC00460 might modulate genes via a ceRNA mechanism or by interacting with RBPs. However, how LINC00460 is dysregulated in cancer remains incompletely defined. Regarding clinical application, LINC00460 dysregulation is associated with patient survival in many cancer types, and may also constitute a potent noninvasive molecular marker for diagnosing malignancies, indicating LINC00460 might represent a potential diagnostic and prognostic molecular marker. Overall, the above data indicate upregulation of and an oncogenic role for LINC00460 in human cancer.

However, there is a need for additional basic and clinical experimental results before LINC00460 can be applied in the clinic. Firstly, the actual molecular mechanism and regulatory effect of LINC00460 needs to be further explored. Secondly, many of these findings were established in tissues and cancer cell lines, lacking clinical correlation. Thirdly, although strategies such as lentivirus or plasmid containing siRNA have been used to target LINC00460 in vitro, the in vivo delivery vector for therapeutic IncRNA is still need to be developed. In summary, basic research on LINC00460 has shown encouraging results, it is expected to achieve breakthroughs in diagnosis, prognosis evaluation, and treatment in clinical trials.

Abbreviations
AML: Acute myeloid leukemia; AUC: Area under the curve; ceRNA: Competing endogenous RNA; ChIP: Chromatin immunoprecipitation; CRLM: Colorectal cancer liver metastasis; EMT: Epithelial-to-mesenchymal transition; GAL: GLUT1 associated IncRNA; GLUT1: Glucose transporter 1; HNSCC: Head and neck squamous cell carcinoma; LINC00460: Long intergenic non-protein coding RNA 460; lncRNAs: Long noncoding RNAs; ncRNAs: Noncoding RNAs; MALAT1: Metastasis-associated lung adenocarcinoma transcript1; NSCLC: Non-small cell lung cancer; OS: Overall survival; PFS: Progression free survival; RBP: RNA binding protein; RIP: RNA immunoprecipitation; ROC: Receiver operating characteristic; TNM: Tumor Node Metastasis.

Acknowledgements
Not applicable.

Author contributions
YX and WW designed the manuscript. MS and JT wrote a complete draft and first version of the manuscript. DY, ZW, QL, and HW edited and reviewed the manuscript. All authors approved final the version and contributed to the principal layout of the article. All authors read and approved the final manuscript.

Funding
This study was supported by Hunan Clinical Medical Research Center of Accurate Diagnosis and Treatment for esophageal carcinoma (2020SK4005); Changsha Science and Technology Board (ky2004128); Health and Family Planning Commission of Hunan Province (2020ZCK05355, 20201699); Hunan Cancer Hospital Climb Plan (2021NSFC-002, ZX2020005); Natural Science Foundation of Hunan Province (2020J5337).

Availability of data and materials
Not applicable.

Declarations
Ethics approval and consent to participate
Not applicable.

Consent for publication
All the co-authors agreed to publish the final version of this manuscript.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Thoracic Surgery Department 2, The Affiliated Cancer Hospital of Xiangya School of Medicine, Hunan Cancer Hospital, Central South University, Changsha, Hunan 410013, People’s Republic of China. 2 Hunan Clinical Medical Research Center of Accurate Diagnosis and Treatment for Esophageal Carcinoma, The Affiliated Cancer Hospital of Xiangya School of Medicine, Hunan Cancer Hospital, Central South University, Changsha, Hunan 410013, People’s Republic of China. 3 Hunan Key Laboratory of Cancer Metabolism, Hunan Cancer Hospital and The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, Hunan 410013, People’s Republic of China. 4 Hunan Key Laboratory of Translational Radiation Oncology, The Affiliated Cancer Hospital of Xiangya School of Medicine, Hunan Cancer Hospital, Central South University, Hunan 410013 Changsha, People’s Republic of China. 5 Department of Pharmacy, Xiangya Hospital of Xiangya School of Medicine, Central South University, Changsha, Hunan 410013, People’s Republic of China.

Received: 22 December 2021   Accepted: 17 July 2022
Published online: 29 July 2022

References
1. Lu W, Cao F, Feng L, Song G, Chang Y, Chu Y, et al: LncRNA Snhg6 regulates the differentiation of MDSCs by regulating the ubiquitination of EZH2. J Hematol Oncol. 2021;14(1):196.
2. Iyer MK, Niknafs YS, Malik R, Singhal U, Sahu A, Hosono Y, et al: The landscape of long noncoding RNAs in the human transcriptome. Nat Genet. 2015;47(3):199–208.
3. Jiang W, Pan S, Chen X, Wang ZW, Zhu X: The role of lncRNAs and circRNAs in the PD-1/PD-L1 pathway in cancer immunotherapy. Mol Cancer. 2021;20(1):116.
4. Su M, Xiao Y, Ma J, Cao D, Zhou Y, Wang H, et al: Long non-coding RNAs in esophageal cancer: molecular mechanisms, functions, and potential applications. J Hematol Oncol. 2018;11(1):118.
5. Huang Z, Zhou JK, Peng Y, He W, Huang C: The role of long noncoding RNAs in hepatocellular carcinoma. Mol Cancer. 2020;19(1):77.
6. Liu Y, Yang Y, Zhang L, Lin J, Li B, Yang M, et al: LncRNA ASAP1-IT1 enhances cancer cell stemness via regulating miR-509-3p/YAP1 axis in NSCLC. Cancer Cell Int. 2021;21(1):572.
7. Hua Q, Wang D, Zhao L, Hong Z, Ni K, Shi Y, et al: AL355338 acts as an oncogenic IncRNA by interacting with protein ENO1 to regulate EGFR/AKT pathway in NSCLC. Cancer Cell Int. 2021;21(1):525.
8. Li M, Shi M, Hu C, Chen B, Li S. MALAT1 modulated FOXP3 ubiquitination then affected GINS1 transcription and driven NSCLC proliferation. Oncogene. 2021;40(22):3870–84.

9. Li B, Kang H, Xiao Y, Du Y, Song G, Zhang Y, et al. lncRNA GAL promotes colorectal cancer liver metastasis through stabilizing GLUT1. Oncogene. 2022;41(13):1882–94.

10. Lian Y, Yan C, Xu H, Yang J, Yu Y, Zhou J, et al. A novel IncRNA, LINC00460, affects cell proliferation and apoptosis by regulating KLF2 and CUL4A expression in colorectal cancer. Mol Ther Nucleic Acids. 2018;12:684–97.

11. Ye JJ, Cheng YL, Deng J, Tao WP, Wu L. LncRNA LINC00460 promotes tumor growth of human lung adenocarcinoma by targeting miR-302c-5p/FoxA1 axis. Gene. 2019;685:76–84.

12. Chen X, Song J, Wang X, Sun D, Liu Y, Jiang Y. LncRNA LINC00460 function and mechanism in human cancer. Thorac Cancer. 2021. https://doi.org/10.1111/1759-7714.14238.

13. Li J, Huang S, Zhang Y, Zhuo W, Tong B, Cai F. LINC00460 enhances bladder carcinoma cell proliferation and migration by modulating miR-612/FOXK1 axis. Pharmacology. 2021;106(1–2):79–90.

14. Wen L, Zhang X, Bian J, Han L, Huang H, He M, et al. The long non-coding RNA LINC00460 predicts the prognosis and promotes the proliferation and migration of cells in bladder urothelial carcinoma. Oncol Lett. 2019;17(4):3874–80.

15. Zhu Y, Yang L, Chong QY, Yan H, Zhang W, Qian W, et al. Long non-coding RNA LINC00460 promotes breast cancer progression by regulating the miR-489-5p/FGF7/AXT axis. Cancer Manag Res. 2019;11:5983–6001.

16. Li F, Zhu W, Wang Z. Long noncoding RNA LINC00460 promotes the progression of cervical cancer via regulation of the miR-361-3p/Gli1 axis. Hum Cell. 2021;34(11):229–37.

17. Lin L, Xin B, Jiang T, Wang XL, Yang H, Shi TM. Long non-coding RNA LINC00460 promotes proliferation and inhibits apoptosis of cervical cancer cells by targeting microRNA-503-5p. Mol Cell Biochem. 2020;475(1–2):1–13.

18. Zhang J, Shen Z, Song Z, Luan J, Li Y, Zhao T. Drug response associated with and prognostic IncRNAs mediated by DNA Methylation and transcription factors in colon cancer. Front Genet. 2020;11:554833.

19. Hong W, Ying H, Lin F, Ding R, Wang W, Zhang M. IncRNA LINC00460 silencing represses EMT in colon cancer through downregulation of ANXA2 via upregulating miR-433-3p. Mol Ther Nucleic Acids. 2018;12:684–97.

20. Hou P, Meng S, Li M, Lin T, Chu S, Li Z, et al. LINC00460/DOX9/GF2BP2 complex promotes colorectal cancer proliferation and metastasis by mediating HMGAI1 mRNA stability depending on m6A modification. J Exp Clin Cancer Res. 2021;40(31):52.

21. Wang L, Chen X, Sun X, Suo J. Long noncoding RNA LINC00460 facilitates colorectal cancer progression by negatively regulating miR-613. Oncol Targets Ther. 2020;13:555–69.

22. Zhang Y, Liu X, Li Q. IncRNA LINC00460 promoted colorectal cancer cell metastasis via miR-939-5p sponging. Cell Transplant. 2020;29:63689720927405.

23. Xie X, Xiong G, Wang Q, Ge Y, Cui X. Long non-coding RNA LINC00460 promotes head and neck squamous cell carcinoma cell progression by sponging miR-612 to up-regulate AKT2. Am J Transl Res. 2019;11(10):6326–40.

24. Chaudhary R, Wang X, Cao B, De La Iglesia J, Masanat J, Song F, et al. Long noncoding RNA, LINC00460, as a prognostic biomarker in head and neck squamous carcinoma (HNSCC). Am J Transl Res. 2020;12(2):684–96.

25. Yang J, Cao W, Wu K, Qin X, Wang X, Li Y, et al. LncRNA LINC00460 promotes EMT in head and neck squamous cell carcinoma by facilitating peroxiredoxin-1 into the nucleus. J Exp Clin Cancer Res. 2019;38(1):365.

26. Xue K, Li J, Nan S, Zhao X, Xu C. Downregulation of LINC00460 decreases ST2C and promotes autophagy of head and neck squamous cell carcinoma by up-regulating microRNA-206. Life Sci. 2019;231:116459.

27. Hong H, Sui C, Qian T, Xu X, Fei Q, et al. Long noncoding RNA LINC00460 conduces to tumor growth and metastasis of hepatocellular carcinoma through miR-342-3p/A2R2 up-regulation. Aging. 2020;12(11):10544–55.

28. Tu J, Zhao Z, Xu M, Chen M, Wang Q, Ji J. LINC00460 promotes hepatocellular carcinoma development through sponging miR-485-5p to up-regulate PAK1. Biomed Pharmacother. 2019;118:109213.

29. Yang J, Li K, Chen J, Hu X, Wang H, Zhu X. Long noncoding RNA LINC00460 promotes hepatocellular carcinoma progression via regulation of miR-342-3p/A2R2 axis. Oncol Targets Ther. 2020;13:1979–91.

30. Ge SS, Wu YY, Gao W, Zhang CM, Hou J, Wen SX, et al. [Expression of long non-coding RNA LINC00460 in laryngeal squamous cell carcinoma tissue and its clinical significance]. Xin Chung Er Bi Yan Hou Jing Wai Ke Za Zhi. 2018;32(11):18–22.

31. Xing H, Wang S, Li Q, Ma Y, Sun P. Long noncoding RNA LINC00460 targets miR-339/MMP-9 to promote meningioma progression and metastasis. J Cell Biochem. 2019;120(6):9556–63.

32. Li M, Zhang X, Ding X, Zheng Y, Du H, Li H, et al. Long non-coding RNA LINC00460 promotes cell progression by sponging miR-4443 in Head and neck squamous cell carcinoma. Cell Transpl. 2020;29:63689720927405.

33. Kong YG, Cui M, Chen SM, Xu Y, Tao ZZ. LncRNA-LINC00460 facilitates NSCLC proliferation and mechanism in human cancer. Thorac Cancer. 2021. https://doi.org/10.1111/1759-7714.14238.

34. Xing H, Wang S, Li Q, Ma Y, Sun P. Long noncoding RNA LINC00460 targets miR-539/MMP-9 to promote meningioma progression and metastasis. J Cell Biochem. 2019;120(6):9556–63.

35. Hong W, Ying H, Lin F, Ding R, Wang W, Zhang M. IncRNA LINC00460 silencing represses EMT in colon cancer through downregulation of ANXA2 via upregulating miR-433-3p. Mol Ther Nucleic Acids. 2018;12:684–96.
54. Jiang JJ, Wang FC, Han LP. Long intergenic nonprotein coding RNA 00460 predicts a poor prognosis and correlates with poor prognosis in hepatocellular carcinoma. Cancer Cell Int. 2020;20:234.

55. Wang F, Liang S, Liu X, Han L, Wang J, Du Q. LINC00460 modulates KDM2A to promote cell proliferation and migration by targeting miR-342-3p in gastric cancer. Oncotargets Ther. 2018;11:6383–94.

56. Yuan B, Yang J, Gu H, Ma C. Down-regulation of LINC00460 represses metastasis of colorectal cancer via WWC2. Dig Dis Sci. 2020;65(2):442–56.

57. Cui Y, Zhang C, Lian H, Xie L, Xue J, Yin N, et al. LncRNA linc00460 sponges miR-1224-5p to promote esophageal cancer metastatic potential and epithelial-mesenchymal transition. Pathol Res Pract. 2020;216(7):153026.

58. Hu X, Liu W, Jiang X, Wang B, Li L, Wang J, et al. Long noncoding RNA LINC00460 aggravates invasion and metastasis by targeting miR-30a-3p/Rap1A in nasopharyngeal carcinoma. Hum Cell. 2019;32(4):465–76.

59. Yan W, Chung CY, Xie T, Ozeck M, Nichols TC, Frey J, et al. Intrinsic and acquired drug resistance to LSD1 inhibitors in small cell lung cancer occurs through a TEAD4-driven transcriptional state. Mol Oncol. 2021. https://doi.org/10.1002/1878-0261.13124.

60. Meng X, Sun W, Yu J, Zhou Y, Gu Y, Han J, et al. LncRNA SNHG17 regulates cell proliferation and invasion by targeting miR-338-3p/SOX4 axis in esophageal squamous cell carcinoma. Cell Death Dis. 2021;12(9):806.

61. Yuan B, Yang J, Gu H, Ma C. Down-regulation of LINC00460 represses metastasis of colorectal cancer via WWC2. Dig Dis Sci. 2020;65(2):442–56.

62. Cui Y, Zhang C, Lian H, Xie L, Xue J, Yin N, et al. LncRNA linc00460 sponges miR-1224-5p to promote esophageal cancer metastatic potential and epithelial-mesenchymal transition. Pathol Res Pract. 2020;216(7):153026.

63. Hu X, Liu W, Jiang X, Wang B, Li L, Wang J, et al. Long noncoding RNA LINC00460 aggravates invasion and metastasis by targeting miR-30a-3p/Rap1A in nasopharyngeal carcinoma. Hum Cell. 2019;32(4):465–76.

64. Chen W, Wang L, Li X, Zhao C, Shi L, Zhao H, et al. LncRNA SNHG17 regulates cell proliferation and invasion by targeting miR-338-3p/SOX4 axis in esophageal squamous cell carcinoma. Cell Death Dis. 2021;12(9):806.

65. Shi L, Yang Y, Li M, Li C, Zhou Z, Tang G, et al. LncRNA IFITM4P promotes immune escape by up-regulating PD-L1 via dual mechanism in oral carcinogenesis. Mol Ther. 2022;30(4):1564–77.

66. Huang Y, Qiao Y, Zhao Y, Li Y, Yuan J, Zhou J, et al. Large scale RNA-binding proteins/LncRNAs interaction analysis to uncover lncRNA nuclear localization mechanisms. Brief Bioinform. 2021. https://doi.org/10.1093/bib/bbab195.

67. Chen Y, Zelitto E, Guo R, Deng Y. The function of LncRNAs and their role in the prediction, diagnosis, and prognosis of lung cancer. Clin Transl Med. 2021;11(4):e367.

68. Xiu Z, Wang C, Xiang X, Li J, Huang J. Characterization of mRNA expression and endogenous RNA profiles in bladder cancer based on the cancer genome atlas (TCGA) database. Med Sci Monit. 2019;25:3041–60.

69. Huang GW, Xue YJ, Wu ZY, Xu XE, Wu JY, Cao HH, et al. A three-lncRNA signature predicts overall survival and disease-free survival in patients with esophageal squamous cell carcinoma. BMC Cancer. 2018;18(1):147.

70. Cao W, Liu JN, Liu Z, Wang X, Han ZG, Ji T, et al. A three-lncRNA signature derived from the Atlas of mRNA in cancer (TANRIC) database predicts the survival of patients with head and neck squamous cell carcinoma. Oral Oncol. 2017;65:94–101.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.