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ORIGINAL ARTICLE

Association of *MALAT1* expression in gastric carcinoma and the significance of its clinicopathologic features in an Iranian patient

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ABSTRACT

Aim: The aim of this study was to evaluate the expression of *MALAT1* and the relationship between its expression with clinical characteristics in an Iranian gastric cancer patient.

Background: Long non-coding RNAs (LncRNAs) play critical roles in the initiation and development of gastric cancer. Metastasis-associated lung adenocarcinoma transcript 1 (*MALAT1*) is a highly conserved lncRNA and plays key roles in various types of human cancer. However, our understanding of the role of lncRNAs in the occurrence and development of gastric cancer is not fully clear.

Methods: This cross-sectional study was performed on 41 gastric tumor tissue samples with matched normal adjacent tumor tissues. The RNA level of lncRNA *MALAT1* gene was assessed using quantitative Real-time polymerase chain reaction. *B2M* was used as an internal control. The $2^{-\Delta\Delta Cq}$ method was adopted to determine expression fold changes.

Results A significant association was observed between the levels of *MALAT1* in gastric tumor tissues compared with normal adjacent tissues (mean= 1.558, p= 0.014). In addition, clinicopathologic data on *MALAT1* RNA expression levels in gastric cancer tissues was evaluated. No significant association was observed between the relative expression of *MALAT1* and the stage, grade, *H. pylori* infection, and tumor size groups among gastric cancer patients (p= 0.82, p= 0.904, p= 0.407, and p= 0.701, respectively).

Conclusion: The current results showed that *MALAT1* has a significant association in gastric cancer. The expression of *MALAT1* may be used as a diagnostic biomarker for monitoring gastric cancer patients.

Keywords: Gastric cancer, *MALAT1*, Lncrna, Clinicopathologic feature.

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Introduction

Gastric cancer (GC) is the second common malignant tumor leading to mortality among cancers worldwide. Whereas the occurrence trend of GC has fallen in most parts of the world, the impact of GC on public health and burden of disease still remains (1). GC is a heterogeneous disease with complicated mechanisms and geographical differences in prevalence and with which patient outcome is difficult to predict (2, 3). *Helicobacter pylori* (*H. pylori*) is known as an environmental risk factor for GC; genetic, epigenetic modifications, and various signaling pathways have been reported to contribute to the progress and development of GC (4, 5). To better recognize the pathogenesis of GC and detect more actual biomarkers in predicting prognosis and response to treatment, further investigation is required into all aspects of the disease. Long noncoding RNAs (lncRNAs) represent a class of noncoding RNAs (longer than 200 nucleotides)

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involved in gene regulation by molecular mechanisms, cell homeostasis, and cell fate (6). Long non-coding RNAs (lncRNAs) have received much attention as tumor biomarkers for early detection, prognosis, and responses to drug treatment in the past several years (7). To date, many studies on lncRNAs have focused on the underlying results and mechanisms of them and their potential as prognostic and diagnostic markers (4, 7-12). However, our understanding about the role of lncRNAs in the occurrence and development of GC is rather incomplete. Metastasis-associated lung adenocarcinoma transcript 1 (*MALAT1*) is a highly conserved lncRNA and plays important roles in various types of human cancer, such as regulating pre-messenger RNA splicing, histone modification enzymes, and transcription factors (13). According to a previous functional study, the knock-down of *MALAT1* in animal experiments led to the inhibition of migration, cell proliferation, and *MALAT1* downregulation entailing a lower expression of genes such as β-catenin, EMT, EZH2, Lin28, and OCT4 (14). Increasingly, studies have showed that *MALAT1* genes are overexpressed and associated with the occurrence and development of GC (15). Chemotherapy-resistant gastric cancer cells show silencing of *MALAT1* inhibited chemo-induced autophagy by acting as a ceRNA for miR-23b-3p (16). According to our two previous studies, the methylation frequency of *MALAT1* promoter methylation was significantly higher in colon lesions than in rectum lesions, and a significant association was observed between the expression of *MALAT1* and different polyp types and numbers of polyps. A correlation was also observed between the levels of *MALAT1* and *p53* in neoplasm tissues (17, 18). The aim of this study was to evaluate the expression of *MALAT1* and the relationship between its expression and clinical characteristics in an Iranian GC patient to gain further knowledge of the diagnostic and prognostic value of *MALAT1*.

Methods

Patients

In this case-control study, 41 gastric tumor tissue samples with matched normal tissues adjacent to the tumor were obtained from patients who underwent surgical resection at Imam Reza Hospital, Tehran, Iran, between January 2016 and April 2018. Histopathological surgical specimens were confirmed following evaluation by a pathologist. The participants had Iranian ethnicity and provided written informed consent for participation in the present study prior to the sampling procedure. Detailed information is provided on the clinicopathological parameters, including age, sex, tumor grade, tumor stage, tumor size, and H. pylori infection. The tumor stage was determined using the American Joint Committee on Cancer Staging Manual (7th edition) (19). This study was approved by the Ethics Committee of the Research Center for Cancer Screening and Epidemiology, AJA University of Medical Sciences, Tehran, Iran (IR.AJAUMS.REC.1398.128). The tissue samples were frozen in liquid nitrogen immediately following removal, and were stored at -80 ˚C.

RNA extraction and cDNA synthesis

Total RNA was extracted from the tumor samples of the patients using the Total RNA extraction mini kit (Favorgen, Cat No. FABRK001, Iran). RNA concentration was quantified by a Nanodrop ND-1000 spectrophotometer (Nanodrop Technologies), and its quality was measured by the A260/A280 and A260/A230 ratio. The concentrations of the samples were normalized, and 1 µg of total RNA was reverse-transcribed to cDNA using the RevertAid RT kit (Thermo Fisher Scientific, Waltham, Massachusetts, USA).

Quantitative real-time PCR analysis

qPCR was performed using a PCR cycler (Rotor-Gene

Table 1. Primer sequences used for Real-time PCR

Primer name		Sequence (5'–>3')	GC%	Tm	Reference
MALAT1	Forward	GGTAACGATGGTGTCGAGGTC	57.14	60	(18)
	Reverse	CCAGCATTACAGTTCTTGAACATG	41.67		
β2M	Forward	TGCTGTCTCCATGTTTGATGTATCT	40	60	(18)
	Reverse	CTCTGCTCCCCACCTCTAAGT	57.1		

Q MDx; Qiagen GmbH). cDNA fragments were used as templates to amplify the *MALAT1* and *B2M* genes through SYBR® Premix Ex Taq™ (Takara Bio, Inc.), according to the manufacturer's protocols. The experimental protocol was performed as follows: i) Thermocycling conditions consisted of an initial activation step for 30 sec at 94 ˚C, 35 cycles at 94 ˚C for 5 sec, and 60 ˚C for 35 sec; and ii) melting curve analysis. The primer sequences of the qPCR are listed in Table 1. The $2^{-\Delta\Delta Cq}$ method was adopted to determine expression fold changes (patient vs. normal).

Statistical analysis

Statistical analysis was carried out using SPSS 21 (IBM Corp., USA), and data was plotted via GraphPad Prism (v.5.04; GraphPad Software, Inc.). Significance was set at $p<0.05$ using the paired t-test.

Results

General statistical information

The study population comprised 41 patients with the diagnosis of gastric cancer. Thirty-four patients (82.9%) were male, 7 (17.1%) were smokers, and the mean age of the study group was 60.32 ± 14.185 years. All patients tested negative for an alcohol habit. Among the patients, 23 (56.1%) were positive for *H. pylori* infection. In addition, 4 (9.8%) patients were positive for lymphatic invasion, and 34 patients (82.9%) were negative. The tumor grade of 3, 16, and 22 patients was determined to be I, II, and III, respectively, and 4 (9.8%) patients presented with tumor stage I, 22 (53.7%) with tumor stage III, and 15 (36.6%) with the higher stage IV. In 16 (39.0%) gastric tumors, the size of the tumor was ≤ 5 cm and 20 (48.8 %) had a tumor size of >5. No treatment had been initiated for gastric cancer patients recruited in the current study. Demographic characteristics of the patients are detailed in Table 2.

Expression of lncRNAs *MALAT1* in the tumor tissue samples

To explore the role of lncRNAs *MALAT1* in GC tissue, expression levels were quantified in tumor tissues compared with healthy adjacent tissues. The qRT-PCR results showed that *MALAT1* expression was significantly upregulated in GC tissues compared with adjacent normal tissues (mean= 1.558, p= 0.014) (Fig 1).

Table 2. Demographic variables of the study population

Variable	Patients	
	Frequency	Percentage
Gender		
Male	34	82.9%
Female	7	17.1%
Smoking		
No	34	82.9%
Yes	7	17.1%
H. pylori infection		
No	18	43.9%
Yes	23	56.1%
Lymphatic invasion		
Negative	34	82.9%
Positive	4	9.8%
Stage		
I	4	9.8%
III	22	53.7%
IV	15	36.6%
Grade		
I	3	7.3%
II	16	39%
III	22	53.7%
Tumor size		
›5 cm	20	48.8%
‹5 cm	16	39%

Lack of associations between the expression of *MALAT1* and clinical characteristics

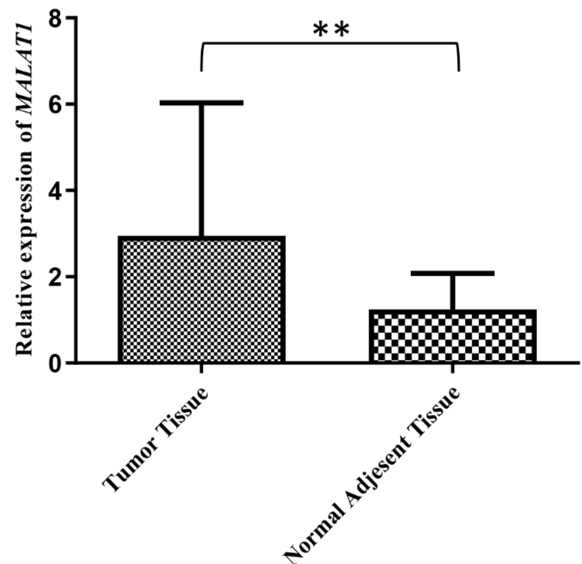

Figure 1. Real-time quantitative PCR analysis of *MALAT1* expression in gastric tissue; GC, gastric cancer; (*p< 0.05) (**p< 0.01) (***p< 0.001)

The role of lncRNA *MALAT1* in gastric cancer was further evaluated through investigation into the associations between the RNA levels of the gene and several clinicopathological features, including tumor stage, grade, size, and *H. pylori* infection.

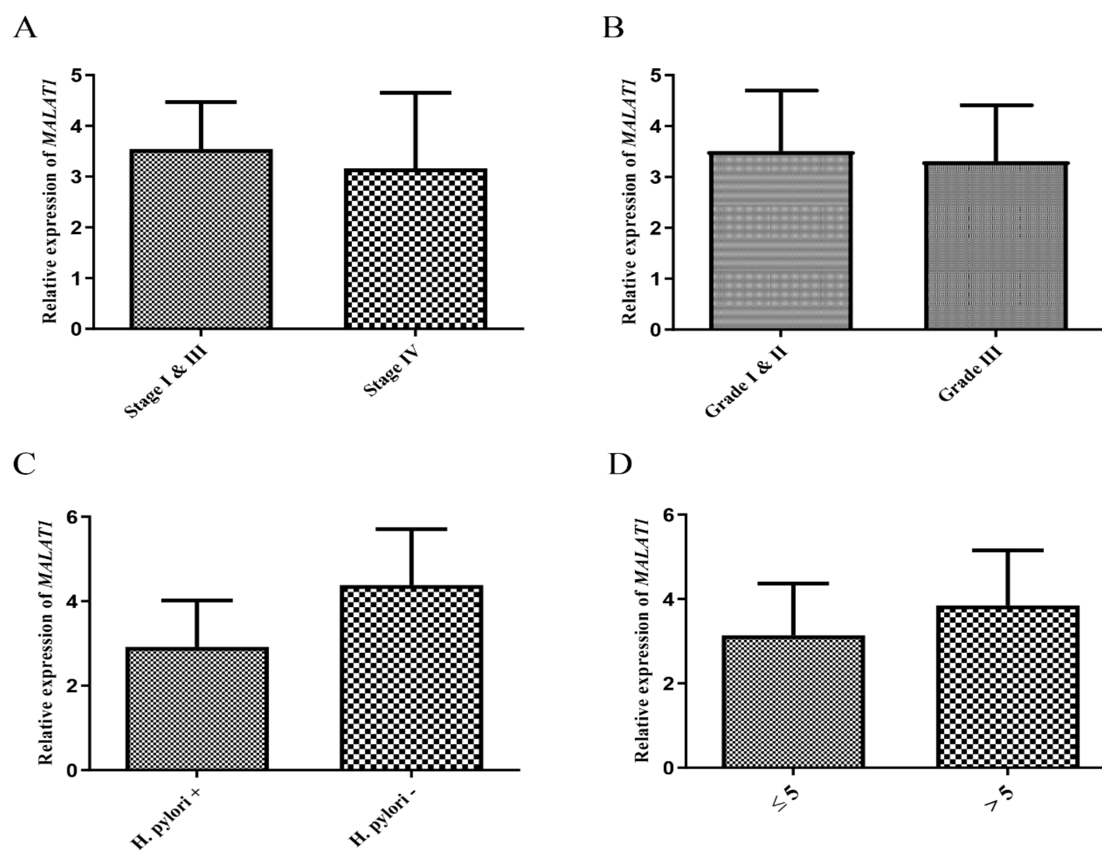

Figure 2. Relative RNA expression between the *MALAT1* gene and different clinicopathologic variables, including I&III and IV, grades I&II and III, *H. pylori* infection positive & negative, and tumor size <5 & >5 cm ($p > 0.05$)

Table 3. Diagnosis values of MALAT1 of GC patient and healthy control tissues

Variable	MALAT1
Cut-off	1.283
Specificity	62.16%
Sensitivity	72.97%
Area	0.7297
%95 CI	0.6128-0.8467

The relative expression of *MALAT1* demonstrated no statistically significant difference between stage I & III and IV, grade I & II and III, *H. pylori* infection positive & negative, and size <5 & >5 cm groups among *GC* patients (p= 0.82, p= 0.904, p= 0.407, and p= 0.701, respectively) (Fig. 2A-D).

Characteristics *MALAT1* as predictive GC-related biomarkers

To investigate the characteristics of *MALAT1* as potential biomarkers for GC, the receiver operating characteristics (ROC) curves and the area under the ROC curves (AUC) were performed on 41 UC patients and adjacent healthy controls. The ROC curve showed an area under the curve of 0.7297 (95% CI: 0.6128-0.8467; p= 0.0007) (Fig. 3) (Table 3).

Discussion

Despite advances in medicine and life science, GC remains a worldwide public health concern (20). Thus, it is essential to explore novel effective molecular mechanisms of GC progression for tumorigenesis prevention or improvement of survival rates. Accumulating evidence demonstrates that aberrantly expressed lncRNAs are implicated in GC tumorigenesis and progression; these lncRNAs are involved in numerous cell signal pathways and act as either tumor suppressors or oncogenes (7, 11, 12).

MALAT1, also called nuclear transcript 2, is a long intergenic non-coding RNA (lincRNA)> ~7 kb long, located on chromosome 11q13, and the *MALAT1* sequence is strongly conserved during evolution among

species, which predicts the potentially important biological function of *MALAT1* (21).

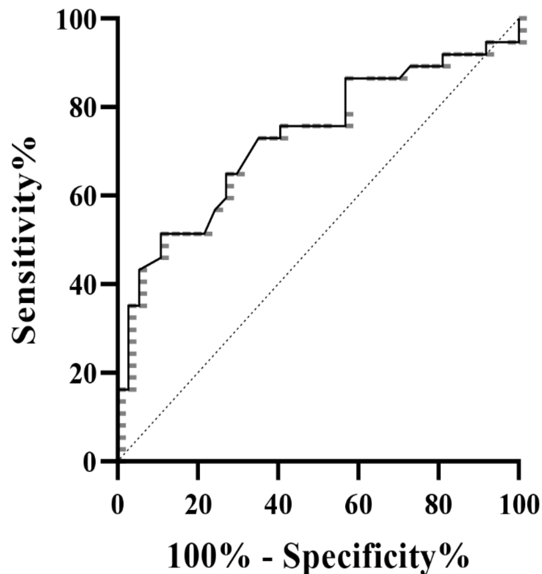

Figure 3. Receiver-operating characteristic (ROC) curves of normalized MALAT1 to distinguish GC patient tissue from normal tissue. The area under the curve (AUC) was determined for MALAT1.

MALAT1 was first identified in 2003 as significantly associated with early-stage lung cancer metastasis (NSCLC), and hence was suggested as a prognostic marker for NSCLC stage I (22). Aberrant expression and multiple biological functions of *MALAT1* have been reported in various cancer types (23-28). In addition, increased *MALAT1* expression contributes to brain metastasis by promoting epithelial mesenchymal transition (29). In HepG2 cells, the relationship between *MALAT1* and *Oct4* has shown that *MALAT1* suppression significantly decreases the expression levels of transcription factor Oct4, indicating that *MALAT1* could promote the stem-like properties of liver cancer cells (28). Undoubtedly, the activity of *MALAT1* in the gastrointestinal cancer system requires extensive attention.

In the current study, a significant association was found between *MALAT1* RNA levels in GC tissues. However, clinicopathologic data compared with *MALAT1* expression levels in GC tissues showed no significant association.

In recent years, interest in the *MALAT1* gene has been increasing. *MALAT1* is a chief lncRNA which is upregulated in various types of prostate, lung, ovarian, gastric, and colorectal cancer (15, 18, 30-32). Similar to previous studies, the current research found that *MALAT1* expression was significantly upregulated in GC tissues when compared with adjacent normal tissues, but no significant association was found between *MALAT1* and clinicopathologic features. The findings of the current study, however, are inconsistent with those of Li et al. (2017), who reported that *MALAT1* overexpression is positively correlated with TNM stage (33). Li et al. Also found that *MALAT1* level was significantly increased in GC tissues at the □+□ stage when compared with the □+□ stage (30). A recent clinical study showed that *MALAT1* was associated with colorectal cancer and its high expression may lead to a poor prognosis in patients with stage II/III CRC (34). In gastric cancer, high *MALAT1* expression levels have been reported to promote development and metastasis (35). *MALAT1* is also shown to have been upregulated in hepatocellular carcinoma, where the overexpression of *MALAT1* increases the risk of tumor recurrence after liver transplantation (36). In a clinical study on pancreatic cancer, abnormal overexpression of *MALAT1* was identified as an unfavorable prognosis for clinical progression and prognosis (37). According to previous research, in vitro experiments on seven cell lines of pancreatic cancer identified *MALAT1* as promoting growth, migration, and invasion of cells (38). A study on bladder cancer showed that *MALAT1* promotes EMT-related cell migration which may be activated through Wnt signaling (39). The upregulation of *MALAT1* was associated with the ability to increase proliferation, apoptosis, and motility in bladder cancer cells (40). In addition, in cervical cancer, the upregulation of *MALAT1* has been associated with human papillomavirus (HPV) infection (41). *MALAT1* has also been found in the promotion and invasion of cervical cancer cells (42).

In conclusion, the current study found that *MALAT1* expression is correlated with gastric cancer tissues compared with adjacent healthy tissues. However, further studies are needed on *MALAT1* molecular mechanisms such as transcriptional factors that are

affected by the *MALAT1* levels in gastric cancer tissues and cell lines.

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Conflict of interests

The authors declare that they have no conflict of interest.

References

1. Moradzadeh R, Anoushirvani AA. Trend of Gastric Cancer Incidence in an Area Located in the Center of Iran: 2009-2014. J Gastrointest Cancer 2020;51:159-64.

2. La Vecchia C, Conte P. Cancer Control in Central and Eastern Europe. Oncologist 2016;21:1161-2.

3. Riquelme I, Ili C, Roa JC, Brebi P. Long non-coding RNAs in gastric cancer: mechanisms and potential applications. Oncotarget 2016;5:17

4. Poursheikhani A, Bahmanpour Z, Razmara E, Mashouri L, Taheri M, Morshedi Rad D, et al. Non-coding RNAs underlying chemoresistance in gastric cancer. Cell Oncol 2020;43:961-88.

5. Sitarz R, Skierucha M, Mielko J, Offerhaus GJA, Maciejewski R, Polkowski WP, et al. Gastric cancer: epidemiology, prevention, classification, and treatment. Cancer Manag Res 2018;10:239.

6. Sanchez Calle A, Kawamura Y, Yamamoto Y, Takeshita F, Ochiya T. Emerging roles of long non□coding RNA in cancer. Cancer Sci 2018;109:2093-100.

7. Yuan L, Xu ZY, Ruan SM, Mo S, Qin JJ, Cheng XD. Long non-coding RNAs towards precision medicine in gastric cancer: early diagnosis, treatment, and drug resistance. Mol Cancer 2020;19:96.

8. Chaudhary R, Lal A. Long noncoding RNAs in the p53 network. Wiley Interdiscip Rev RNA. Wiley Interdiscip Rev RNA 2016;8:10.

9. Dragomir MP, Kopetz S, Ajani JA, Calin GA. Non-coding RNAs in GI cancers: from cancer hallmarks to clinical utility. Gut 2020;69:748-63.

10. Ghafouri-Fard S, Taheri M. Long non-coding RNA signature in gastric cancer. Exp Mol Pathol 2020;113:104365.

11. Tan H, Zhang S, Zhang J, Zhu L, Chen Y, Yang H, et al. Long non-coding RNAs in gastric cancer: New emerging biological functions and therapeutic implications. Theranostics 2020;10:8880-902.

12. Wei L, Sun J, Zhang N, Zheng Y, Wang X, Lv L, et al. Noncoding RNAs in gastric cancer: implications for drug resistance. Mol Cancer 2020;19:62.

13. Chen Q, Zhu C, Jin Y. The Oncogenic and Tumor Suppressive Functions of the Long Noncoding RNA MALAT1: An Emerging Controversy. Front Genet 2020;11:93.

14. Wang W, Zhu Y, Li S, Chen X, Jiang G, Shen Z, et al. Long noncoding RNA MALAT1 promotes malignant development of esophageal squamous cell carcinoma by targeting β-catenin via Ezh2. Oncotarget 2016;7:25668-82.

15. Guo F, Guo L, Li Y, Zhou Q, Li Z. MALAT1 is an oncogenic long non-coding RNA associated with tumor invasion in non-small cell lung cancer regulated by DNA methylation. Int J Clin Exp Pathol 2015;8:15903-10.

16. Zhang YF, Li CS, Zhou Y, Lu XH. Propofol facilitates cisplatin sensitivity via lncRNA MALAT1/miR-30e/ATG5 axis through suppressing autophagy in gastric cancer. Life Sci 2020;244:117280.

17. Chaleshi V, Iran S, Alebouyeh M, Mirfakhraie R, Aghdaei HA. Evaluation of MALAT1 promoter DNA methylation patterns in early colorectal lesions and tumors. Gastroenterol Hepatol Bed Bench 2019;12:S58.

18. Chaleshi V, Irani S, Alebouyeh M, Mirfakhraie R, Asadzadeh Aghdaei H. Association of lncRNA-p53 regulatory network (lincRNA-p21, lincRNA-ROR and MALAT1) and p53 with the clinicopathological features of colorectal primary lesions and tumors. Oncol Lett 2020;19:3937-49.

19. Washington K. 7th edition of the AJCC cancer staging manual: stomach. Ann Surg Oncol 2010;17:3077-9

20. Thrift AP, El-Serag HB. Burden of Gastric Cancer. Clin Gastroenterol Hepatol 2020;18:534-42.

21. Hutchinson JN, Ensminger AW, Clemson CM, Lynch CR, Lawrence JB, Chess A. A screen for nuclear transcripts identifies two linked noncoding RNAs associated with SC35 splicing domains. BMC Genomics 2007;1;8:39.

22. Ji P, Diederichs S, Wang W, Böing S, Metzger R, Schneider PM, et al. MALAT-1, a novel noncoding RNA, and thymosin β 4 predict metastasis and survival in early-stage non-small cell lung cancer. Oncogene 2003;22:8031-41

23. Chen Y, Huang W, Sun W, Zheng B, Wang C, Luo Z, et al. LncRNA MALAT1 promotes cancer metastasis in osteosarcoma via activation of the PI3K-Akt signaling pathway. Cell Physiol Biochem 2018;51:1313-26

24. Zhao M, Wang S, Li Q, Ji Q, Guo P, Liu X. MALAT1: A long non-coding RNA highly associated with human cancers. Oncol Lett 2018;16:19-26.

25. Guo J, Ding Y, Yang H, Guo H, Zhou X, Chen X, et al. Aberrant expression of lncRNA MALAT1 modulates radioresistance in colorectal cancer in vitro via miR-101-3p sponging. Exp Mol Pathol 2020;115:104448.

26. Liu X, Huang G, Zhang J, Zhang L, Liang Z. Prognostic and clinicopathological significance of long noncoding RNA MALAT-1 expression in patients with non-small cell lung cancer: A meta-analysis. PLoS One 2020;15:e0240321.

27. Pa M, Naizaer G, Seyiti A, Kuerbang G. Therapeutics CC. Long noncoding RNA MALAT1 functions as a sponge of MiR-200c in ovarian cancer. Oncol Res 2017;11.

28. Zhao L, Lou G, Li A, Liu Y. lncRNA MALAT1 modulates cancer stem cell properties of liver cancer cells by regulating YAP1 expression via miR-375 sponging. Mol Med Rep 2020;22:1449-57.

29. Shen L, Chen L, Wang Y, Jiang X, Xia H, Zhuang Z. Long noncoding RNA MALAT1 promotes brain metastasis by inducing epithelial-mesenchymal transition in lung cancer. J Neurooncol 2015;121:101-8.

30. Li X, Zhao J, Zhang H, Cai J. Silencing of LncRNA Metastasis-Associated Lung Adenocarcinoma Transcript 1 Inhibits the Proliferation and Promotes the Apoptosis of Gastric Cancer Cells Through Regulating microRNA-22-3p-Mediated ErbB3. Onco Targets Ther 2020;13:559-71.

31. Sebastian A, Hum NR, Hudson BD, Loots GG. Cancer-Osteoblast Interaction Reduces Sost Expression in Osteoblasts and Up-Regulates lncRNA MALAT1 in Prostate Cancer. Microarrays 2015;4:503-19.

32. Wu L, Wang X, Guo Y. Long non-coding RNA MALAT1 is upregulated and involved in cell proliferation, migration and apoptosis in ovarian cancer. Exp Ther Med 2017;13:3055-60.

33. Li J, Gao J, Tian W, Li Y, Zhang J. Long non-coding RNA MALAT1 drives gastric cancer progression by regulating HMGB2 modulating the miR-1297. Cancer Cell Int 2017;17:44.

34. Zheng HT, Shi DB, Wang YW, Li XX, Xu Y, Tripathi P, et al. High expression of lncRNA MALAT1 suggests biomarker of poor prognosis in colorectal cancer. Int J Clin Exp Pathol 2014;15;7:3174-81.

35. Okugawa Y, Toiyama Y, Hur K, Toden S, Saigusa S, Tanaka K, et al. Metastasis-associated long non-coding RNA drives gastric cancer development and promotes peritoneal metastasis. Carcinogenesis 2014;35:2731-9.

36. Lai MC, Yang Z, Zhou L, Zhu QQ, Xie HY, Zhang F, et al. Long non-coding RNA MALAT-1 overexpression predicts tumor recurrence of hepatocellular carcinoma after liver transplantation. Med Oncol 2012;29:1810-6.

37. Pang EJ, Yang R, Fu XB, Liu Ye-fu. Overexpression of long non-coding RNA MALAT1 is correlated with clinical progression and unfavorable prognosis in pancreatic cancer. Tumour Biol 2015;36:2403-7

38. Jiao F, Hu H, Yuan C, Wang L, Jiang W, Jin Z, et al. Elevated expression level of long noncoding RNA MALAT-1 facilitates cell growth, migration and invasion in pancreatic cancer. Oncol Rep 2014;32:2485-92.

39. Ying L, Chen Q, Wang Y, Zhou Z, Huang Y, Qiu F. Upregulated MALAT-1 contributes to bladder cancer cell migration by inducing epithelial-to-mesenchymal transition. Mol Biosyst 2012;8:2289-94.

40. Han Y, Liu Y, Nie L, Gui Y, Cai Z. Inducing cell proliferation inhibition, apoptosis, and motility reduction by silencing long noncoding ribonucleic acid metastasis-associated lung adenocarcinoma transcript 1 in urothelial carcinoma of the bladder. Urology 2013;81:209.

41. Jiang Y, Li Y, Fang S, Jiang B, Qin C, Xie P, et al. The role of MALAT1 correlates with HPV in cervical cancer. Oncol Lett 2014;7:2135-41.

42. Guo F, Li Y, Liu Y, Wang J, Li Y, Li G. Inhibition of metastasis-associated lung adenocarcinoma transcript 1 in CaSki human cervical cancer cells suppresses cell proliferation and invasion. Acta Biochim Biophys Sin 2010;15;42:224-9.