INTRODUCTION

Osteosarcoma is a common type of malignant bone tumor in adolescents, accounting for 5%-10% of all malignancies among adolescents. Osteosarcoma is the sixth most common cause of cancer-related deaths in adolescents. The main cause of death in osteosarcoma is lung metastasis. The 5-year survival rate of patients with osteosarcoma is below 20%, even after active treatment. Targeted therapy and immunotherapy have improved the treatment of malignant tumors. However, there are limited effective therapeutic targets for osteosarcoma. Therefore, there is a need to elucidate the molecular mechanism underlying the progression of osteosarcoma and identify new therapeutic targets for osteosarcoma to enhance prognosis.

Long noncoding RNAs (lncRNAs) are involved in the proliferation, migration, and invasion of tumors. In the current study, our aim was to explore the role of lncRNA plasmacytoma variant translocation gene 1 (PVT1) in osteosarcoma.

Methods: Quantitative real-time reverse transcription-polymerase chain reaction was used to detect the expression of lncRNA PVT1 in osteosarcoma tissues and cells. The relationship between lncRNA PVT1 expression status and the prognosis of patients with osteosarcoma was analyzed. The effect of lncRNA PVT1 on the malignant biological behavior of osteosarcoma cells in vitro was also analyzed.

Results: LncRNA PVT1 was upregulated in osteosarcoma. High lncRNA PVT1 expression indicated poor prognosis in patients with osteosarcoma. In vitro knockdown of lncRNA PVT1 inhibited the proliferation, migration, and invasion ability of osteosarcoma cells. In addition, we confirmed that lncRNA PVT1 affected the epithelial-mesenchymal transition of osteosarcoma cells.

Conclusion: LncRNA PVT1 is a potential therapeutic target for osteosarcoma.

KEYWORDS

EMT, lncRNA PVT1, osteosarcoma, prognosis
of tumor cells by regulating DNA rearrangement and interacting with other oncogenes. However, the role of lncRNA PVT1 in osteosarcoma has been evaluated in only a limited number of studies.

Epithelial-mesenchymal transition (EMT) of cells is known to play an indispensable role in the progression of tumors. EMT is a reversible cellular process that promotes invasiveness and is traditionally believed to be the prelude to the process of metastasis, wherein cells within a primary tumor lose their epithelial characteristics and acquire both the phenotype and a transcriptional program reminiscent of mesenchymal cells. Multiple studies have shown that lncRNAs are involved in the regulation of EMT in osteosarcoma cells. The expression of lncRNA PGM5-AS1 is upregulated in osteosarcoma. It regulates the expression of miR-140-5p and FBN1 through sponge adsorption, thereby promoting tumor EMT, invasion, and metastasis. LncRNA CCAT2, a marker of poor prognosis in patients with osteosarcoma, was found to promote EMT in osteosarcoma cells. Therefore, we also studied the relationship between lncRNA PVT1 and EMT in osteosarcoma cells.

Here, we investigated the expression and molecular function of lncRNA PVT1 in osteosarcoma. The findings of this study suggest that lncRNA PVT1 is a potential therapeutic target for osteosarcoma.

2 | METHODS

2.1 | Bioinformatics analysis

The GEO2R online analysis tool (https://www.ncbi.nlm.nih.gov/geo/geo2r/) was employed to examine five GeneChip expression microarrays of osteosarcoma (GSM954792, GSM954810, GSM954823, GSM954797, and GSM954825) to screen differentially expressed lncRNAs. The threshold for differentially expressed lncRNAs was set as follows: log2 (fold change) >2; adjusted P-value < .05. The differentially expressed lncRNA results from the five datasets were visualized on a volcano plot. The Gene Expression Profiling Interactive Analysis (GEPIA) online tool (http://geopia.cancer-pku.cn) was utilized to determine the expression of differentially expressed genes in osteosarcoma and their correlation with patient prognosis.

2.2 | Specimen collection

This study was approved by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University. In total, 78 pairs of surgically resected tumor and adjacent non-tumorous tissues were collected between January 2015 and December 2018. The resected tissue was snap-frozen in liquid nitrogen and stored at 80°C. All patients were diagnosed with osteosarcoma based on pathological analysis. The patients did not undergo chemotherapy, radiation therapy, or targeted therapy before surgery. All patients provided written informed consent to use the tissue specimens for the study.

2.3 | Cell culture and construction of stable cell lines

The osteosarcoma cell lines (MG-63, SW1353, Saos-2, and U2OS) and a human osteoblast cell line (hFOB1.19) were purchased from the American Type Culture Collection (ATCC). The cells were cultured in Dulbecco's modified Eagle's medium (DMEM; HyClone) supplemented with 10% fetal bovine serum (FBS; Thermo Fisher Scientific) and 1% penicillin (Biosharp) at 37°C and 5% CO2. The lentiviral vector containing the lncRNA PVT1 shRNA (shPVT1#1: 5'-GCCAACAGGWGGAGCAGCUUTTT-3'; shPVT1#2: 5'-GGACTTGAGAACTGTCCTTAC-3'; shPVT1#3: 5'-GCTCCACCCCCAGAACCTCA-3') was designed and synthesized by GENECHEM Biotech (http://genecem.bioon.com.cn/). The cells were cultured until the logarithmic phase and transfected with the lentiviral vector containing green fluorescent protein (GFP) (multiplicity of infection = 30). The empty virus vector was used as the negative control (shNC). The transfected cells were cultured in the presence of puromycin (Solarbio) for 5 days to screen for stable cell lines with low lncRNA PVT1 expression. The efficiency of lncRNA PVT1 knockdown was confirmed by quantitative real-time reverse transcription-polymerase chain reaction (qRT-PCR).

2.4 | RNA extraction and qRT-PCR

Total RNA was extracted from the cells or tissues using TRIzol reagent (Invitrogen). The purity of the extracted RNA was measured using a spectrophotometer (Unico). Next, the extracted RNA was subjected to reverse transcription to obtain cDNA using the PrimeScript RT-PCR kit (TaKaRa). qRT-PCR analysis was performed using SYBR™ Premix Ex Taq™ (TaKaRa) in the 7500 Fast Real-Time System (Applied Biosystems). GAPDH was used as a loading control. The relative expression of lncRNA PVT1 was calculated by the 2^-ΔΔCt method. The following primers were used for qRT-PCR analysis: lncRNA PVT1 forward, 5'-CCACTCTTGGAGGAC-3'; lncRNA PVT1 reverse, 5'-CAACAGGAGGAGCAACA-3'. GAPDH forward, 5'-ACTAGGCGCT-3'; GAPDH reverse, 5'-ATCCGTGACTCCGACCTC-3'.

2.5 | Western blotting

Total protein was extracted from the cells and tissues using radioimmunoprecipitation assay (RIPA) lysis buffer (Biosharp). The extracted protein was denatured using loading buffer (R&D Systems). The protein sample was subjected to sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) using a 10% gel. The resolved proteins were transferred onto a polyvinyl difluoride...
The membrane was incubated with the following primary antibodies (all from Abcam) at 4°C overnight: anti-GAPDH (ab181602), anti-E-cadherin (ab194982), anti-vimentin (ab92547), anti-N-cadherin (ab18203), and anti-Snail (ab229701). The membrane was then incubated with the secondary antibody at room temperature for 1 hour. The protein bands were visualized using enhanced chemiluminescence (ECL) solution.

2.6 | CCK-8 assay

Cell proliferation was analyzed using the CCK8 kit (Dojindo, Japan). Briefly, the cells (1 × 10⁵ cells/well) were inoculated into 96-well plates and cultured in DMEM at 37°C for 0, 24, 48, and 72 hours. Then, 10 μL of CCK-8 solution was added to each well. The absorbance of the solution was measured at 450 nm using a plate reader (Bio-Rad).

2.7 | Colony formation assay

Briefly, the cells were inoculated in a 6-well plate (500 cells/well) and cultured in complete DMEM for 8-12 days. The cells were washed with phosphate buffered saline (PBS), fixed in methanol for 15 minutes, and stained with 0.1% crystal violet for 15 minutes.

2.8 | Transwell assay

Migration and invasion assays were performed using a Transwell chamber. For the invasion assay, the upper Transwell chamber was pre-coated with Matrigel (BD Biosciences). For the migration assay, Matrigel was not added. Briefly, the cells (1 × 10⁵) were inoculated in the upper Transwell chamber in a serum-free medium. The lower chamber, medium containing 10% FBS was added. The cells were incubated at 37°C and 5% CO₂. The cells were fixed in methanol for 15 minutes, stained with 0.1% crystal violet for 15 minutes, and counted under a microscope.

2.9 | Wound healing assay

The wound healing assay was performed to evaluate the cell migration ability. Briefly, the cells were inoculated in a 6-well plate until they formed a monolayer. Next, a scratch wound was introduced in the monolayer using a 200-μL pipette tip. The cells were incubated in complete medium at 37°C and 5% CO₂. The representative images were captured at 0 and 24 hours to evaluate wound healing.

2.10 | Statistical analysis

All statistical analyses were performed using SPSS 20.0 software (SPSS Inc) and GraphPad Prism 7 (GraphPad Software Inc). The nominal data were analyzed by the chi-square test, whereas the enumeration data were analyzed by the t test. Moreover, the Chi-square test was used to analyze the relationship between IncRNA PVT1 expression and clinicopathological features of patients. Kaplan-Meier and log-rank tests were used to analyze the effects of clinicopathological characteristics on patient prognosis. In this study, the overall survival (OS) was used as the main endpoint. The difference was considered statistically significant when the P-value was <.05.

3 | RESULTS

3.1 | Bioinformatic prediction

We analyzed the five GeneChip microarrays of osteosarcoma and constructed a volcano plot of the differentially expressed IncRNAs (Figure 1A). In total, 237 differentially expressed IncRNAs were identified, including 57 downregulated IncRNAs and 180 upregulated IncRNAs. The expression of IncRNA PVT1 was markedly upregulated in osteosarcoma tissue. The GEPIA online analysis revealed that the osteosarcoma samples exhibited significantly higher expression of IncRNA PVT1 than that of the normal samples (Figure 1B). The survival analysis revealed that high IncRNA PVT1 expression was associated with poorer prognosis of osteosarcoma (Figure 1C,D).

3.2 | Upregulated expression of IncRNA PVT1 in osteosarcoma cells and tissues

The results of the bioinformatics analysis were validated by qRT-PCR. The expression of IncRNA PVT1 was analyzed in 78 pairs of osteosarcoma tissues and adjacent non-tumorous tissues. The osteosarcoma tissues exhibited significantly higher IncRNA PVT1 expression than that of the adjacent non-tumorous tissues (Figure 2A). The expression of IncRNA PVT1 was also determined in osteosarcoma cell lines. As shown in Figure 2B, the osteosarcoma cell lines exhibited higher IncRNA PVT1 expression than the normal osteoblast cell line hFOB1.19. Of the different osteosarcoma cell lines, the MG-63 and SW1353 cell lines displayed the highest expression of IncRNA PVT1 and were selected for the subsequent cell function assays.

3.3 | Correlation of IncRNA PVT1 expression with prognosis in patients with osteosarcoma

To investigate the correlation between IncRNA PVT1 expression and clinicopathological features of patients with osteosarcoma, 78 patients were categorized into the high IncRNA PVT1 (n = 48) and low
IncRNA PVT1 (n = 30) expression groups using the average expression of IncRNA PVT1 as a cutoff value. The enhanced expression of IncRNA PVT1 was strongly correlated with the degree of tumor differentiation, distant metastasis, and disease stage in patients with osteosarcoma (P < .05; Table 1). However, IncRNA PVT1 expression was not correlated with age, sex, tumor location, tumor size, or pathological grade (Table 1). The OS of patients with osteosarcoma after follow-up was plotted. The log-rank test analysis revealed that the high IncRNA PVT1 expression group had a poorer OS than that of the low IncRNA PVT1 expression group (Figure 3A). In addition, the main factors affecting the OS of patients with osteosarcoma were differentiation, distant metastasis, and disease stage (Figure 3B-D).

Cox regression analysis model was constructed to examine the effect of IncRNA PVT1 on the prognosis of patients with osteosarcoma. Univariate regression analysis revealed that tumor size, differentiation, historical grade, distant metastasis, and disease stage were highly correlated with OS in patients with osteosarcoma (Table 2). Multivariate regression analysis revealed that high expression of IncRNA PVT1 was an independent risk factor for the prognosis of patients with osteosarcoma (Table 2).
3.4 Effects of lncRNA PVT1 on the biological behavior of osteosarcoma cells

The role of lncRNA PVT1 in osteosarcoma cells was analyzed in vitro using the MG-63 and SW1353 cell lines. The expression of lncRNA PVT1 was silenced in MG-63 and SW1353 cells using lentiviral transfection and validated using qRT-PCR (Figure 2C). The effect of lncRNA PVT1 knockdown on the proliferation of osteosarcoma cells was evaluated by CCK-8 assay. The proliferation of shPVT1-transfected cells was significantly suppressed compared with that of shNC-transfected cells (Figure 3A). The colony formation capacity of shPVT1-transfected tumor cells was significantly lower than that of shNC-transfected cells (Figure 4B). The effect of lncRNA PVT1 knockdown on the migration and invasion of osteosarcoma cells was evaluated by the Transwell assay. The knockdown of lncRNA PVT1 significantly inhibited the migration and invasion abilities of osteosarcoma cells (Figure 4B). The migration of shPVT1-transfected cells was significantly suppressed compared with that of shNC-transfected cells.

3.5 Role of lncRNA PVT1 in the EMT of osteosarcoma cells

The EMT is a key step in tumor cell metastasis. Thus, the potential roles of lncRNA PVT1 in the EMT of osteosarcoma cells were analyzed. Silencing of lncRNA PVT1 affected the expression of EMT-associated molecules in osteosarcoma MG-63 and SW1353 cells. The lncRNA PVT1 knockdown cells exhibited enhanced expression of E-cadherin and decreased expression of N-cadherin, vimentin, and Snail (Figure 5).

4 DISCUSSION

LncRNA PVT1 is reported to be a common retrovirus integration site in mouse leukemia. The integration site is located in the sense strand of chromosome 8q24 spanning over a genomic region of 300 kb with a length of approximately 1716 nucleotides. Chromosome 8q24 region is the major target for DNA copy number amplification in tumor cells. The abnormal amplification of this region...
is generally predictive of a high risk of carcinogenesis. Several studies have revealed that abnormal lncRNA PVT1 expression plays a critical regulatory role in biological phenotypes, including cell proliferation, angiogenesis, cell cycle, migration, and invasion. Yang et al. showed that the lung cancer tissues and cells exhibit increased lncRNA PVT1 expression, which is closely correlated with the pathological stage and lymph node involvement in patients with lung cancer. In addition, they demonstrated that patients with high lncRNA PVT1 expression have a poor prognosis and that the down-regulation of lncRNA PVT1 expression can inhibit the invasion, migration, and proliferation of tumor cells. Chai et al. demonstrated that the overexpression of lncRNA PVT1 promotes the invasion, migration, and proliferation of colorectal cancer cells in vitro and that lncRNA PVT1, which functions as a competitive endogenous RNA, regulates tumor growth by sponging miR-455. Niu et al. demonstrated that gastric cancer tissues exhibit significantly enhanced expression of lncRNA PVT1 and that lncRNA PVT1 can regulate the invasion and proliferation of gastric cancer cells via targeted regulation of miR-125 activity. Zhang et al. revealed that lncRNA PVT1 expression was upregulated in glioma and that silencing of lncRNA PVT1 induces G0/G1 cell cycle arrest and suppresses cell invasion and proliferation.

There are limited studies on the role of lncRNA PVT1 in osteosarcoma. In 2017, Zhou et al. reported that osteosarcoma tissues overexpress lncRNA PVT1 and that silencing lncRNA PVT1 induces cell cycle arrest and apoptosis and suppresses migration, proliferation, and invasion of osteosarcoma cells by exerting a negative regulatory effect on miR-195. Song et al. reported that lncRNA PVT1 is also involved in glucose metabolism and proliferation of osteosarcoma cells through the miR-497/HK2 pathway. Sun et al. demonstrated that lncRNA PVT1 is involved in the resistance of osteosarcoma cells through activation of the c-MET/PI3K/AKT pathway. Recently, Chen et al. revealed that ALKBH5-mediated m6A modification of lncRNA PVT1 is involved in the occurrence of osteosarcoma. Consistent with these studies, the results of this study revealed that the expression of lncRNA PVT1 was upregulated in osteosarcoma cell lines and tissues. In addition, we demonstrated that lncRNA PVT1 expression was highly correlated with TNM stage, tumor differentiation, and distant metastasis in patients with osteosarcoma. Furthermore, high expression of lncRNA PVT1 can be utilized as an independent prognostic risk indicator for osteosarcoma. Knockdown of lncRNA PVT1 expression suppressed the invasion, migration, and proliferation of osteosarcoma cells.

| Characteristics | n   | Low expression (n = 30) | High expression (n = 48) | $\chi^2$ | P       |
|-----------------|-----|------------------------|-------------------------|---------|---------|
| Age (y)         |     |                        |                         |         |         |
| <18             | 30  | 9 (30.00)              | 21 (43.75)              | 1.475   | .225    |
| ≥18             | 48  | 21 (70.00)             | 27 (56.25)              |         |         |
| Gender          |     |                        |                         |         |         |
| Female          | 77  | 12 (40.00)             | 15 (31.25)              | 0.625   | .429    |
| Male            | 51  | 18 (60.00)             | 33 (68.75)              |         |         |
| Tumor site      |     |                        |                         |         |         |
| Femur/tibia     | 64  | 26 (86.67)             | 38 (79.17)              | 0.705   | .401    |
| Other           | 14  | 4 (13.33)              | 10 (20.83)              |         |         |
| Tumor size (cm) |     |                        |                         |         |         |
| <3              | 50  | 18 (60.00)             | 32 (66.67)              | 0.357   | .550    |
| ≥3              | 28  | 12 (40.00)             | 16 (33.33)              |         |         |
| Differentiation |     |                        |                         |         |         |
| Well/Median     | 27  | 17 (56.67)             | 10 (20.83)              | 10.474  | .001    |
| Poor            | 51  | 13 (43.33)             | 38 (79.17)              |         |         |
| Histological grade |   |                        |                         |         |         |
| G1-G2           | 38  | 18 (60.00)             | 20 (41.67)              | 2.484   | .115    |
| G3-G4           | 40  | 12 (40.00)             | 28 (58.33)              |         |         |
| Distant metastasis |   |                        |                         |         |         |
| No              | 62  | 28 (93.33)             | 34 (70.83)              | 5.732   | .017    |
| Yes             | 16  | 2 (6.67)               | 14 (29.17)              |         |         |
| Disease stage   |     |                        |                         |         |         |
| I               | 15  | 10 (33.33)             | 5 (10.42)               | 24.111  | .000    |
| II              | 28  | 17 (56.67)             | 11 (22.92)              |         |         |
| III             | 35  | 3 (10.00)              | 32 (66.67)              |         |         |
FIGURE 3  Survival curve of 78 cases patients with osteosarcoma. (A) Expression of lncRNA PVT1 and overall survival in patients with osteosarcoma; (B) degree of tumor differentiation and overall survival in patients with osteosarcoma; (C) distant metastasis and overall survival in patients with osteosarcoma; (D) disease stage and overall survival in patients with osteosarcoma

TABLE 2  Univariate and multivariate Cox regression of prognostic factors of patients with osteosarcoma

| Parameter                              | Univariate analysis | Multivariate analysis |
|----------------------------------------|---------------------|-----------------------|
|                                        | HR  | 95% CI        | P      | HR  | 95% CI        | P      |
| Age (≤18 y vs > 18 y)                  | 0.791 | 0.429-1.457    | .452   |      |                |        |
| Gender (Female vs male)                | 1.663 | 0.851-3.250    | .137   |      |                |        |
| Tumor site (Femur/tibia vs other)      | 1.755 | 0.861-3.575    | .121   |      |                |        |
| Tumor size (<3 vs > 3 cm)              | 1.969 | 1.071-3.622    | .029   | 1.755 | 0.93-3.314     | .083   |
| Differentiation (well/Median vs Poor)  | 7.881 | 2.793-22.238   | .000   | 1.759 | 0.896-3.454    | .101   |
| Histological grade(G1-G2 vs G3-G4)     | 1.888 | 1.011-3.523    | .046   | 2.930 | 1.006-8.529    | .049   |
| Distant metastasis (no vs yes)         | 4.221 | 2.195-8.119    | .000   | 2.091 | 1.018-4.296    | .045   |
| Disease stage (I-II vs III)            | 4.944 | 2.703-9.042    | .000   | 3.793 | 1.794-8.021    | .000   |
| LncRNA PVT1 expression (Low vs high)   | 4.695 | 2.075-10.621   | .000   | 1.308 | 1.088-3.504    | .039   |
EMT is involved in tumor metastasis and invasion. The hallmarks of EMT are decreased expression of E-cadherin and increased expression of vimentin and N-cadherin. Various studies have confirmed the correlation between lncRNAs and EMT key effectors during carcinogenesis: Zheng et al. revealed that lncRNA PVT1 can regulate the invasion of esophageal cancer cells by inducing EMT; Zhang et al. proposed that lncRNA PVT1 may play an oncogenic role by regulating EMT through the TGFβ/Smad pathway in pancreatic cancer. In this study, we demonstrated that knockdown of lncRNA PVT1 expression could enhance E-cadherin expression and decrease N-cadherin and vimentin expression. These results were consistent with those of Zhang et al. This indicated that lncRNA PVT1 promoted osteosarcoma by regulating EMT.
CONCLUSION

This study demonstrated the upregulation of lncRNA PVT1 expression in osteosarcoma cells and tissues and that lncRNA PVT1 is a potential therapeutic target for osteosarcoma. However, further studies are needed to elucidate the molecular mechanism by which lncRNA PVT1 promotes the progression of osteosarcoma.

REFERENCES

1. Longhi A, Errani C, De Paolis M, et al. Primary bone osteosarcoma in the pediatric age: state of the art. Cancer Treat Rev. 2006;32(6):423-436.
2. Mialou V, Philip T, Kalifa C, et al. Metastatic osteosarcoma at diagnosis: prognostic factors and long-term outcome—the French pediatric experience. Cancer. 2005;104(5):1100-1109.
3. Wilusz JE, Sunwoo H, Spector DL. Long noncoding RNAs: functional surprises from the RNA world. Genes Dev. 2009;23(13):1494-1504.
4. Lipovich L, Johnson R, Lin CY. MacroRNA underdogs in a microRNA world: evolutionary, regulatory, and biomedical significance of mammalian long non-protein-coding RNA. Biochim Biophys Acta. 2010;1799(9):597-615.
5. Shitivelman E, Henglein B, Groitl P, et al. Identification of a human transcription unit affected by the variant chromosomal translocations 2;8 and 8;22 of Burkitt lymphoma. Proc Natl Acad Sci USA. 1989;86(9):3257-3260.
6. Cory S, Graham M, Webb E, et al. Variant (6;15) translocations in murine plasmacytomas involve a chromosome 15 locus at least 72 kb from the c-myc oncogene. Embo j. 1985;4(3):675-681.
7. Tang J, Li Y, Sang Y, et al. LncRNA PVT1 regulates triple-negative breast cancer through KLF5/beta-catenin signaling. Oncogene. 2018;37(34):4723-4734.
8. Du P, Hu C, Qin Y, et al. LncRNA PVT1 mediates antiapoptosis and 5-fluorouracil resistance via increasing Bcl2 expression in gastric cancer. J Oncol. 2019;2019:1-10.
9. Shang AQ, Wang W, Yang YB, et al. Knockdown of long noncoding RNA PVT1 suppresses cell proliferation and invasion of colorectal cancer via upregulation of miRNA-214-3p. Am J Physiol Gastrointest Liver Physiol. 2019;317(2):G222-G232.
10. Cho SW, Xu J, Sun R, et al. Promoter of IncRNA gene PVT1 is a tumor-suppressor DNA boundary element. Cell. 2016;164(5):840-842.
11. Gupta S, Maitra A. EMT: matter of life or death? Cell. 2018;173(6):1398-1412.
12. Kalluri R, Weinberg RA. The basics of epithelial-mesenchymal transition. J Clin Invest. 2009;119(6):1420-1428.
13. Liu W, Liu P, Gao H, Wang X, Yan M. Long non-coding RNA PGM5-A51 promotes epithelial-mesenchymal transition, invasion and metastasis of osteosarcoma cells by impairing miR-140-5p-mediated FBN1 inhibition. Mol Oncol. 2020.
14. Yan L, Wu X, Yin X, Du F, Liu Y, Ding X. LncRNA CCAT2 promoted osteosarcoma cell proliferation and invasion. J Cell Mol Med. 2018;22(5):2592-2599.
15. Zeidler R, Joos S, Delecuse HJ, et al. Breakpoints of Burkitt’s lymphoma t(8;22) translocations map within a distance of 300 kb downstream of MYC. Genes Chromosom Cancer. 1994;9(4):282-287.
16. Tseng Y-Y, Bagchi A. The PVT1-MYC duet in cancer. Mol Cell Oncol. 2015;2(2):e974467.
17. Lee SC-W, Abdel-Wahab O. Therapeutic targeting of splicing in cancer. Nat Med. 2016;22(9):976-986.
18. Yang YR, Zang SZ, Zhong CL, et al. Increased expression of the IncRNA PVT1 promotes tumorigenesis in non-small cell lung cancer. Int J Clin Exp Pathol. 2014;7(10):6929-6935.
19. Chai J, Guo D, Ma W, et al. A feedback loop consisting of RUNX2/IncRNA-PVT1/miR-455 is involved in the progression of colorectal cancer. Am J Cancer Res. 2018;8(3):538-550.
20. Niu J, Song X, Zhang X. Regulation of IncRNA PVT1 on miR-125 in metastasis of gastric cancer cells. Oncol Lett. 2020;19(2):1261-1266.
21. Zhang Y, Yang G, Luo Y. Long non-coding RNA PVT1 promotes glioma cell proliferation and invasion by targeting miR-200a. Exp Ther Med. 2019;17(2):1337-1345.
22. Zhou Q, Chen F, Zhao J, et al. Long non-coding RNA PVT1 promotes osteosarcoma development by acting as a molecular sponge to regulate miR-195. Oncotarget. 2016;7(50):82620-82633.
23. Song J, Wu X, Liu F, et al. Long non-coding RNA PVT1 promotes glycolysis and tumor progression by regulating miR-497/HK2 axis in osteosarcoma. Biochem Biophys Res Commun. 2017;490(2):217-224.
24. Sun ZY, Jian YK, Zhu HY, et al. IncRNA PVT1 targets miR-152 to enhance chemoresistance of osteosarcoma to gemcitabine through activating c-MET/PI3K/AKT pathway. Pathol Res Pract. 2019;215(3):555-563.
25. Chen S, Zhou L, Wang Y. ALKBH5-mediated m(6)A demethylation of IncRNA PVT1 plays an oncogenic role in osteosarcoma. Cancer Cell Int. 2020;20(1):34.
26. Guo S, Xu X, Tang Y, et al. miR-15a inhibits cell proliferation and epithelial to mesenchymal transition in pancreatic ductal adenocarcinoma by down-regulating Bmi-1 expression. Cancer Lett. 2014;344(1):40-46.
27. Kitamura K, Seike M, Okano T, et al. MiR-134/487b/655 cluster regulates TGF-β1-induced epithelial-mesenchymal transition and drug resistance to gefitinib by targeting MAGI2 in lung adenocarcinoma cells. Mol Cancer Ther. 2014;13(2):444-453.
28. Zheng X, Hu H, Li S. High expression of IncRNA PVT1 promotes invasion by inducing epithelial-to-mesenchymal transition in esophageal cancer. Oncol Lett. 2016;12(4):2357-2362.
29. Zhang X, Feng W, Zhang J, et al. Long noncoding RNA PVT1 promotes epithelialmesenchymal transition via the TGFbeta/Smad pathway in pancreatic cancer cells. Oncol Rep. 2018;40(2):1093-1102.

How to cite this article: Xun C, Jiang D, Tian Z, Yunus A, Chen J. Long noncoding RNA plasmacytoma variant translocation gene 1 promotes epithelial-mesenchymal transition in osteosarcoma. J Clin Lab Anal2021;35:e23587. https://doi.org/10.1002/jcla.23587