Cellular and Molecular Biology
E-ISSN : 1165-158X / P-ISSN : 0145-5680
www.cellmolbiol.org
Original Research

LncRNA NORAD targets miR-410-3p to regulate drug resistance sensitivity of osteosarcoma

Xin Xie[1], Wenjun Liu[1], Zhiyuan Duan[1], Xu Li[2], Lide Zhang[1], Guanlin Yang[1*]

[1] Department of Teaching and Research Center, Liaoning University of Traditional Chinese Medicine, Shenyang, 110000, China
[2] Foot and Ankle Surgery, Central Hospital Affiliated to ShenYang Medical College, Shenyang, 110000, China

*Correspondence to: yangguanlin2019@126.com

Received February 24, 2020; Accepted May 17, 2020; Published June 5, 2020

Doi: http://dx.doi.org/10.14715/cmb/2020.66.3.22

Abstract: The current experiment was performed to investigate the effect of LncRNA NORAD on the sensitivity of miR-410-3p to drug resistance of osteosarcoma cells. The cisplatin-resistant cell line HOS/DDP was induced; si-NC, si-NORAD, miR-NC, miR-410-3p, pcDNA-NC, and pcDNA-NORAD were transfected into HOS/DDP cells, respectively; record as a si-NC group, si-NORAD group, miR-NC group, miR-410-3p group, pcDNA-NC group, pcDNA-NORAD group; si-NORAD was co-transfected into HOS/DDP cells with anti-miR-NC, anti-miR-410-3p, recorded as an anti-miR-NC+si-NORAD group and anti-miR-410-3p+si-NORAD group. Real-time quantitative PCR (RT-qPCR) was used to detect LncRNA NORAD, miR-410-3p and multidrug resistance protein 1 (MRP1) mRNA expression levels; Western blot was used to detect cyclin D1 (CyclinD1), MRP1, phosphorylated (p-p65), phosphorylated IκBα (p-IκBα) protein expression; cell counting kit 8 (CCK-8) was used to detect cell viability; dual luciferase report assay to detect targeting relationship between LncRNA NORAD and miR-410-3p. Compared with osteosarcoma cells HOS, the expression levels of LncRNA NORAD, MRP1 mRNA and protein in osteosarcoma resistant cells HOS/DDP were significantly increased, and miR-410-3p expression levels were significantly reduced (P<0.05). Low expression of NORAD or high expression of miR-410-3p, CyclinD1, MRP1 expression levels were significantly reduced, the cell survival rate was significantly reduced, and the half inhibitory concentration of cisplatin was significantly reduced (P<0.05). LncRNA NORAD targets and regulates miR-410-3p, and low expression of miR-410-3p can reverse the effects of low NORAD expression on HOS/DDP cell proliferation and cisplatin resistance. Low expressions of NORAD, p-p65, p-IκBα protein expression levels were significantly reduced; low expression of miR-410-3p could reverse the inhibitory effect of low NORAD expression on p-p65, p-IκBα protein expression. Inhibition of LncRNA NORAD expression can inhibit the proliferation of osteosarcoma HOS/DDP cells through targeted regulation of miR-410-3p, increasing its sensitivity to cisplatin, and it may be related to the NF-κB signaling pathway.

Key words: lncRNA NORAD; miR-410-3p; Osteosarcoma; Cisplatin; Drug resistance.

Introduction

Osteosarcoma is a primary malignant bone tumor with high disability and lethality, which is mainly treated with chemotherapy (1). However, chemotherapy resistance will lead to poor prognosis. Studying the chemical resistance mechanism of osteosarcoma to improve osteosarcoma sensitivity to chemotherapy resistance carries great significance for improving the chemotherapy effect of osteosarcoma (2). Osteosarcoma is recently found to resist cisplatin, a commonly used tumor chemotherapy drug (3). Studies have shown that long non-coding RNA (lncRNA) is involved in tumor development and progression and is related to the occurrence and development of osteosarcoma (4). NORAD is a cytoplasmic lncRNA that can play a potential oncogenic role by binding and inhibiting Pumilio protein. LncRNA NORAD up-regulates expression in colorectal cancer tissues, which is positively correlated with colorectal cancer metastasis and poor prognosis in patients. By regulating miR-202-5p, lncRNA NORAD significantly inhibits the proliferation, migration and invasion of colorectal cancer cells and induces apoptosis in vitro (5). lncRNA NORAD is highly expressed in breast cancer tissues, which promotes breast cancer cell proliferation, invasion and migration and indicates poor prognosis (6). Studies have found that miRNAs can regulate tumor cell development, reduce or even reverse tumor cell resistance to chemotherapeutic drugs. miRNA research provides a new therapeutic direction for changing the drug resistance mechanism of osteosarcoma (7). Studies have reported that miR-410 regulates autophagy-related 16-like 1 (ATG16L1) gene expression in osteosarcoma and enhances chemical sensitivity via autophagy inhibition (8). miR-410-3p can inhibit the proliferation and promote the apoptosis of prostate cancer cells (9). However, it remains unknown whether the effect of lncRNA NORAD on drug resistance of osteosarcoma and its mechanism is related to miR-410-3p. This experiment aims to investigate the effect of lncRNA NORAD on osteosarcoma sensitivity to cisplatin resistance and examine whether its mechanism is related to miR-410-3p.

Materials and Methods

Cells and main reagents

Osteosarcoma cells HOS were purchased from Shanghai Thermo Biotechnology Development Co., Ltd.; Cisplatin (DDP) was purchased from Sigma, USA; RPMI-1640 medium was purchased from Hyclone, USA; fetal bovine serum was purchased from Hangzhou Sijiqing Company; Trizol reagents, reverse transcription kits and fluorogenic quantitative PCR kits were purchased from Beijing Mairuibo Biotechnology Co., Ltd.; bicinchoninic acid (BCA) kit, RIPA protein lysate, cell counting kit 8 (CCK-8) were purchased from Beyotime Institute of Biotechnology; rabbit anti-human CyclinD1, rabbit anti-human MRP1, rabbit anti-human p-p65, rabbit anti-human p-IκBα, β-actin were purchased from Shanghai Xuanling Biotechnology Co., Ltd.; sheep anti-rabbit IgG-HRP was purchased from Shanghai Hengfei Biotechnology Co., Ltd.; dual-luciferase detection kit was purchased from Promega, USA.

Screening of cisplatin-resistant osteosarcoma cells HOS/DDP

The osteosarcoma cells HOS were induced by DDP in a stepwise increasing dose to establish a cisplatin-resistant cell line HOS/DDP. Both the osteosarcoma cells HOS and HOS/DDP cells were cultured in RPMI-1640 medium containing 10% fetal bovine serum in 5% CO_2, 37°C incubator. At the same time, amid culture, HOS/DDP cells were added with DDP at a final concentration of 1 μg/ml.

Cell transfection and grouping

si-NC, si-NORAD, miR-NC, miR-410-3p, pcDNA-NC and pcDNA-NORAD were transfected into HOS/DDP cells in a logarithmic growth phase and recorded as a si-NC group, si-NORAD group, miR-NC group, miR-410-3p group, pcDNA-NC group, pcDNA-NORAD group. si-NORAD was respectively transfected into HOS/DDP cells with anti-miR-NC, anti-miR-410-3p and recorded as anti-miR-NC + si-NORAD group, anti-miR-410-3p + si-NORAD group.

Detection of LncRNA NORAD, miR-410-3p and MRP1 mRNA expression levels by Real-time quantitative PCR (RT-qPCR)

Total RNA in glioma cell lines and clinical specimens was extracted by the Trizol method, reverse-transcribed into cDNA, and PCR was performed using the SYBR Green kit. LncRNA NORAD, MRP1 and miR-410-3p were internally referenced with GAPDH and U6, respectively. There were 3 repeats in each sample, LncRNA NORAD upstream primer sequence: 5'-TGATAGGATACATCTTGGACATGGA-3', downstream primer: 5'-AACCTAATGAACAAGTCCTGACATACA-3'; MRP1 upstream primer 5'-TCCAGTGCCTTCCCCTACGGC-3', downstream primer 5'-GCCGTAGGGGAAGGCAGTGGA-3'; GAPDH upstream primer 5'-GGAGCGAGATCCCTCCAAAAT-3', downstream primer 5'-GGCTGTTGTCATACTTCTCATGG-3'; miR-410-3p upstream primer 5'-CGCGAATATAACACAGATGGCCTGT-3', downstream primer 5'-GCTGTCAACGATACGCTACGTAACG-3'; U6 upstream primer 5'-CGCTTCGGCAGCACATATACTA-3', downstream primer: 5'-CGCTTCACGAATTTGCGTGTCA-3'. upstream primer

Primers were synthesized by Sangon Biotech (Shanghai) Co, Ltd.

Western blot detection of CyclinD1, MRP1, p-p65, p-IκBα protein expression

Total protein was extracted from each group of cells, and protein quantification was performed using a BCA kit. After polyacrylamide gel electrophoresis and transmembrane, it was blocked using a blocking solution, added with primary antibody and incubated at 4°C overnight, added with secondary antibody and incubated at room temperature for 2 h, followed by the development, fixation. The gray value of protein bands in each group was measured using Quantity One gel software, and the ratio of target band to the β-actin band was taken as the protein expression level.

Cell survival rate detection by cell counting Kit 8 (CCK-8)

Cells cultured for 48 h after transfection in each group were seeded in 96-well plate at 1×10^4 cells/well, and three repeats were set in each well. After inoculation, 10 μL CCK-8 reagent was added to each well, and absorbance value (OD) at 490 nm of cells in each group was detected on a microplate reader. Cell survival rate (%) = OD value of experimental group/OD value of blank control group×100%. The experiment was repeated three times.

Cells in the above groups were treated with DDP at 0, 2, 4, 6, 8, 16, 32 and 64 μg/ml, respectively. Cell growth inhibition rate was calculated using CCk-8, and growth curves were plotted to calculate median inhibitory concentration (IC50) against cisplatin.

Detection of LncRNA NORAD's targeted regulation of miR-410-3p by dual-luciferase reporter assay

Starbase prediction indicates a binding site between LncRNA NORAD and miR-410-3p. NORAD wild-type and mutant reporter gene vectors containing miR-410-3p binding sites were constructed and respectively co-transfected with miR-NC and miR-410-3p into osteosarcoma cells HOS/DDP using LipofectamineTM 2000. Luciferase activity was detected as stipulated in instructions, and the experiment was repeated 3 times.

Statistical analysis

SPSS 20.0 software was used for statistical analysis. The measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$). The two groups were compared by *t*-test. A comparison between multiple groups was analyzed by one-way analysis of variance. A pairwise comparison was made by the LSD *t*-test. $P<0.05$ suggests a statistically significant difference.

Results

LncRNA NORAD, miR-410-3p, MRP1 expression in osteosarcoma resistant cells HOS/DDP

Compared with osteosarcoma cells HOS, osteosarcoma resistant cells HOS/DDP have significantly increased LncRNA NORAD, MRP1 mRNA and protein expression levels, and significantly reduced miR-410-3p expression levels (P <0.05) (Figure 1, Table 1).

Lowly expressed NORAD inhibits HOS/DDP proliferation and reduces resistance to cisplatin

Compared with the si-NC group, HOS/DDP cells of the si-NORAD group have significantly reduced NORAD expression level, significantly reduced CyclinD1 and MRP1 expression levels, significantly reduced cell survival rate and significantly reduced median inhibitory concentration against cisplatin (P <0.05) (Figure 2, Table 2).

Highly expressed miR-410-3p inhibits HOS/DDP proliferation and reduces resistance to cisplatin

Compared with the miR-NC group, HOS/DDP cells of the miR-410-3p group have significantly increased miR-410-3p expression level, significantly reduced CyclinD1 and MRP1 expression level, significantly reduced cell survival rate and significantly decreased median inhibitory concentration against cisplatin (P <0.05) (Figure 3, Table 3).

NORAD targets miR-410-3p and regulates miR-410-3p expression

Starbase prediction indicates a binding site between NORAD and miR-410-3p (Figure 4). Luciferase report experiment shows that, compared with the miR-NC group, HOS/DDP cells transfected with WT-NORAD vector in the miR-410-3p group have significantly reduced luciferase activity (P <0.05); while HOS/DDP cells transfected with MUT-NORAD vectors have no significant difference in luciferase activity (Table 4). Compared with the pcDNA-NC group, the pcDNA-NORAD group has significantly reduced the miR-410-3p expression level (P<0.05). Compared with the si-NC group, the si-NORAD group has significantly increased miR-410-3p expression level (P <0.05) (Table 5).

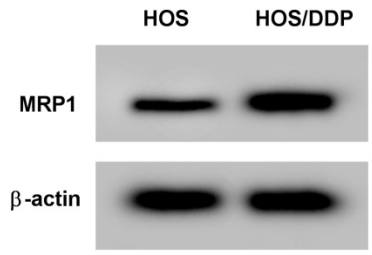

Figure 1. Western Blot detection of MRP1 protein expression.

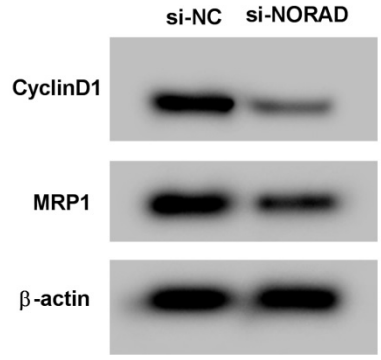

Figure 2. Western Blot detection of CyclinD1 and MRP1 protein expression.

Table 1. LncRNA NORAD, miR-410-3p, MRP1 expression in osteosarcoma resistant cells HOS/DDP ($\bar{x}$±s, n=9).

Group	LncRNA NORAD	miR-410-3p	MRP1 mRNA	MRP1 protein
HOS	1.00±0.10	1.05±0.11	1.02±0.12	0.30±0.03
HOS/DDP	3.03±0.30*	0.37±0.04*	3.46±0.35*	0.96±0.10*
t	19.258	17.429	19.784	18.965
P	0.000	0.000	0.000	0.000

Note: Compared with HOS, *P<0.05.

Table 2. Lowly expressed NORAD inhibits the proliferation of HOS/DDP and reduces the resistance.

Group	NORAD	CyclinD1	MRP1	Cell survival rate (%)	IC50 against cisplatin
si-NC	1.00±0.13	0.86±0.09	0.95±0.10	100.37±10.03	32.11±3.21
si-NORAD	0.42±0.04*	0.34±0.04*	0.40±0.04*	52.41±5.25*	10.27±1.03*
t	12.793	15.839	15.320	12.709	19.435
P	0.000	0.000	0.000	0.000	0.000

Note: Compared with si-NC, *P<0.05.

Table 3. Highly expressed miR-410-3p inhibits HOS/DDP proliferation and reduces resistance to cisplatin($\bar{x}$±s, n=9).

Group	miR-410-3p	CyclinD1	MRP1	Cell survival rate (%)	IC50 against cisplatin
miR-NC	1.01±0.10	0.88±0.09	0.96±0.08	100.89±10.10	33.08±3.31
miR-410-3p	2.68±0.27*	0.39±0.04*	0.32±0.03*	59.22±5.90*	8.05±0.80*
t	17.400	14.926	22.472	10.687	22.051
P	0.000	0.000	0.000	0.000	0.000

Note: Compared with miR-NC, *P<0.05.

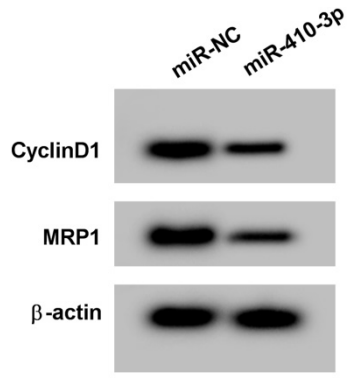

Figure 3. Western Blot detection of CyclinD1 and MRP1 protein expression.

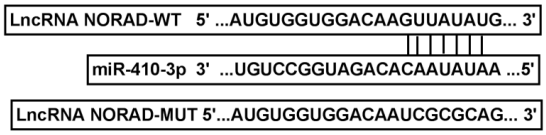

Figure 4. Prediction of the combined region of miR-410-3p and NORAD by starbase.

Lowly expressed miR-410-3p can reverse the effect of low NORAD expression on HOS/DDP cell proliferation and cisplatin resistance

Compared with the anti-miR-NC+si-NORAD group, HOS/DDP cells of the anti-miR-410-3p+si-NORAD group have significantly reduced miR-410-3p expression level, significantly increased CyclinD1 and MRP1 expression, significantly increased cell survival rate and significantly increased median inhibitory concentration against cisplatin (P <0.05) (Figure 5, Table 6).

Expression of NF-κB signaling pathway-related proteins

Compared with the si-NC group, the si-NORAD group has significantly reduced p-p65 and p-IκBα protein expression levels (P<0.05); compared with the anti-miR-NC+si-NORAD group, the anti-miR-410-3p+si-NORAD group has significantly increased p-p65 and p-IκBα protein expression levels (P <0.05).

Discussion

Osteosarcoma features high malignancy and early metastasis, which leads to its unsatisfactory treatment effect. Studies have shown that lncRNA is involved in regulating the occurrence and development of osteosarcoma (10). Other studies have reported that lncRNA is also involved in cisplatin resistance of osteosarcoma

Table 4. Detection of dual-luciferase activity after co-transfection of miR-NC or miR-410-3p with reporter plasmid in HOS/DDP cells.

Group	Luciferase activity	
	WT	MUT
miR-NC	1.00±0.11	1.03±0.10
miR-410-3p	0.42±0.04*	1.02±0.12
t	14.866	0.192
P	0.000	0.850

Note: Compared with miR-NC, *P<0.05.

Table 5. miRT-410-3p expression detection by qRT-PCR($\bar{x}$±s, n=9).

Group	miR-410-3p
pcDNA-NC	1.02±0.11
pcDNA-NORAD	0.45±0.04*
si-NC	1.05±0.10
si-NORAD	1.86±0.16#
F	245.574
P	0.000

Note: Compared with pcDNA-NC, *P<0.05, Compared with si-NC, #P<0.05.

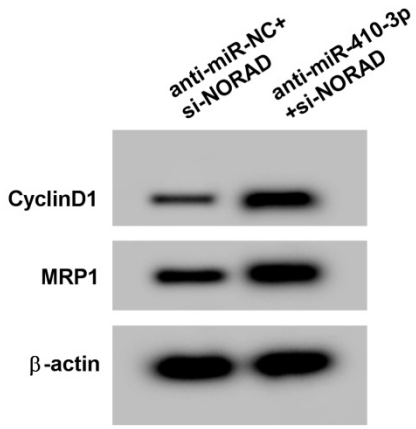

Figure 5. Western Blot detection of CyclinD1 and MRP1 protein expression.

(11). Studies have reported that lncRNA NORAD upregulates SIP1 expression to promote cervical cancer cell proliferation and invasion (12). High expression of lncRNA NORAD in pancreatic cancer tissues is related to the shorter overall survival of pancreatic cancer patients; NORAD overexpression promotes migration and invasion of pancreatic cancer cells (13). LncRNA NORAD down-regulation in lung cancer and breast cancer is related to lymph node metastasis and poor prognosis; inhibition of lncRNA NORAD expression can inhibit lung cancer and breast cancer metastasis (14). Nevertheless, the effect of lncRNA NORAD on osteo-

Table 6. Lowly expressed miR-410-3p can reverse the effect of NORAD low expression on HOS/DDP cell proliferation and cisplatin resistance (x±s, n=9).

Group	miR-410-3p	CyclinD1	MRP1	Cell survival rate (%)	IC50 against cisplatin
anti-miR-NC+si-NORAD	1.02±0.09	0.35±0.04	0.42±0.05	50.86±5.01	10.88±1.05
anti-miR-410-3p+si-NORAD	0.46±0.05*	0.76±0.07*	0.88±0.08*	89.11±8.92*	28.27±2.80*
t	16.318	15.256	14.628	11.216	17.446
P	0.000	0.000	0.000	0.000	0.000

Note: Compared with anti-miR-NC+si-NORAD, *P<0.05.

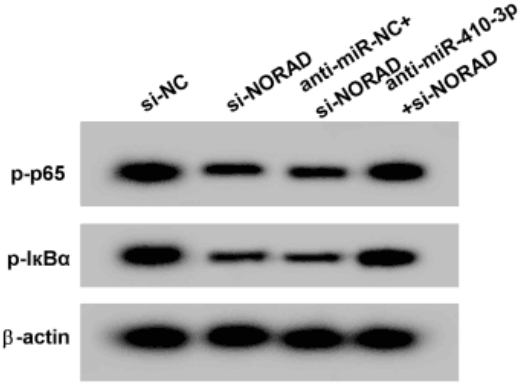

Figure 6. Western Blot detection of p-p65 and p-IκBα protein expressions.

Table 7. Expression of NF-κB signaling pathway-related proteins ($\bar{x}$±s,n=9).

Group	p-p65	p-IκBα
si-NC	0.82±0.09	0.73±0.07
si-NORAD	0.40±0.04*	0.32±0.03*
anti-miR-NC+si-NORAD	0.42±0.03	0.35±0.04
anti-miR-410-3p+si-NORAD	0.72±0.07#	0.60±0.06#
F	104.361	128.509
P	0.000	0.000

Note: Compared with si-NC, *P<0.05, Compared with anti-miR-NC+si-NORAD, #P<0.05.

sarcoma cell proliferation and cisplatin sensitivity is yet unknown. In this experiment, the resistance sensitivity of lncRNA NORAD to osteosarcoma resistant cells was studied by establishing cisplatin-resistant osteosarcoma cells. The results showed that osteosarcoma resistant cells HOS/DDP had significantly increased lncRNA NORAD expression level, and resistant cells HOS/DDP had significantly higher mRNA and protein expression levels of multidrug resistance protein 1 (MRP1) than HOS cells. This indicates that HOS/DDP cells are more resistant to DDP, while lncRNA NORAD is related to cisplatin resistance of osteosarcoma. In further NORAD expression inhibition, the results showed significantly reduced CyclinD1 and MRP1 expression levels, significantly reduced cell survival rate, significantly reduced median inhibitory concentration against cisplatin. This indicates that inhibition of NORAD expression can inhibit HOS/DDP cell survival and enhance its sensitivity to cisplatin.

In addition, studies have shown that miRNA is also involved in tumor occurrence and development, which is also related to chemotherapy resistance of tumor cells. For instance, significantly down-regulated miR-410-3p in glioma tissues is related to the poor prognosis of human gliomas; overexpression of miR-410-3p inhibits cell proliferation, migration and invasion, and accelerates apoptosis (15). miR-410-3p is down-regulated in breast cancer tissues, while overexpressed miR-410-3p inhibits breast cancer proliferation and epithelial-mesenchymal transition (EMT) by targeting Snail (16). miR-410-3p up-regulates the proliferation, invasion and migration of rhabdomyosarcoma cells, and promotes apoptosis (17). By inhibiting HMGB1-induced autophagy, miR-410-3p can enhance the sensitivity of pancreatic ductal adenocarcinoma to gemcitabine (18). Results of this experiment indicate that osteosarcoma resistant cells HOS/DDP have significantly reduced miR-410-3p expression level, while in the case of high expression of miR-410-3p, there are significantly reduced CyclinD1, MRP1 expression level, significantly reduced cell survival rate and significantly lowered median inhibitory concentration against cisplatin. It suggests that high expression of miR-410-3p can inhibit the survival of HOS/DDP cells and enhance their sensitivity to cisplatin. Moreover, this study also indicates that lncRNA NORAD can regulate miR-410-3p in a targeted manner. Further reversal experiments show that low expression of miR-410-3p can reverse the effects of low NORAD expression on HOS/DDP cell proliferation and cisplatin resistance.

Nuclear factor-kappa B (NF-κB) with an extensive presence in cells is related to tumor cell differentiation, proliferation and apoptosis. Activation of the NF-κB signaling pathway is closely related to the occurrence and development of various tumors and drug resistance of tumor cells (19). NF-κB signaling pathway inhibitor ACT001 can increase the cytotoxicity of tamoxifen to breast cancer tamoxifen-resistant cells MCF7R/LCC9 (20). The results of this experiment showed that inhibition of NORAD expression significantly reduced the expression levels of p-p65 and p-IκBα proteins, indicating that inhibition of NORAD expression can inhibit the NF-κB signaling pathway. On the other hand, lowly expressed miR-410-3p can reverse the inhibitory effect of NORAD low expression on the NF-κB signaling pathway. It suggests that the effect of NORAD expression inhibition on cisplatin-resistant osteosarcoma cells may be related to the NF-κB signaling pathway.

To conclude, via targeted regulation of miR-410-3p, inhibition of LncRNA NORAD expression can inhibit the proliferation of osteosarcoma HOS/DDP cells and increase their sensitivity to cisplatin, which may be related to NF-κB signaling pathway.

References

1. Zhang Jianfeng, Liu Yunxia. New advances in chemotherapy for osteosarcoma. Zhejiang Clinic Med J 2018; 20 (8): 1464-1466.
2. Chen Jinquan, Zhang. Research progress on the mechanisms of chemotherapy resistance of osteosarcoma. Chin J Bone Tumor Bone Dis 2017; 6 (12): 918-923.
3. Yong Lei, Liu Xiaoguang. Research progress on the mechanism of osteosarcoma tolerance to cisplatin. Chin J Bone Tumor Bone Dis 2019, 8 (5): 41-46.
4. Liu Yishu, Qu Guofan. Research progress on long-chain non-coding RNA in osteosarcoma. Pract Oncol J 2019; 23 (3): 266-270.
5. Zhang J, Li XY, Hu P, Ding YS. LncRNA NORAD contributes to colorectal cancer progression by inhibition of miR-202-5p. Oncology Research Featuring Preclinic Clinic Cancer Therapeutic 2018; 26(9):1411-8.
6. Zhou K, Ou Q, Wang G, Zhang W, Hao Y, Li W. High long non-coding RNA NORAD expression predicts poor prognosis and promotes breast cancer progression by regulating TGF-β pathway. Cancer Cell Int 2019;19(1):63.
7. Gui Peng. Research progress on MiRNA's targeted regulation of drug resistance mechanism of osteosarcoma. Chin Cancer 2019; 28 (9): 694-698.

8. Chen R, Li X, He B, Hu W. MicroRNA-410 regulates autophagy-related gene ATG16L1 expression and enhances chemosensitivity via autophagy inhibition in osteosarcoma. Mol Med Rep 2017; 15(3): 1326-1334.
9. Zhao Zhenling, Shao Huanjun, Hao Lina. Effect of miR-410-3p on prostate cancer cell proliferation and apoptosis and its mechanism of action. Int J Urology Nephrol 2018; 38 (5): 754-758.
10.Bai Guangjian, Han Zhitao, Liu Ge. Research progress on osteosarcoma related lncRNA. Chin J Clinic Oncology 2018; 45 (6): 297-300.
11.Li Yuchun. Effect of long non-coding RNA H19 on cisplatin chemotherapy sensitivity of osteosarcoma and its mechanism of action. Chin J Gerontolog 2017; 37 (24): 6043-6046.
12.Huo H, Tian J, Wang R, Li Y, Qu C, Wang N. Long non-coding RNA NORAD upregulate SIP1 expression to promote cell proliferation and invasion in cervical cancer. Biomed Pharmac. 2018; 106:1454-60.
13.Li H, Wang X, Wen C, Huo Z, Wang W, Zhan Q, Cheng D, Chen H, Deng X, Peng C, Shen B. Long noncoding RNA NORAD, a novel competing endogenous RNA, enhances the hypoxia-induced epithelial-mesenchymal transition to promote metastasis in pancreatic cancer. Mol Cancer 2017; 16(1):169.
14.Tan BS, Yang MC, Singh S, Chou YC, Chen HY, Wang MY, Wang YC, Chen RH. LncRNA NORAD is repressed by the YAP pathway and suppresses lung and breast cancer metastasis by sequestering S100P. Oncogene 2019; 38(28): 5612-26.
15.Wang C, Huang S, Rao S, Hu J, Zhang Y, Luo J, Wang H. Decreased expression of miR-410-3p correlates with poor prognosis and tumorigenesis in human glioma. Cancer Manag Res, 2019; 11(1): 10581-10592.
16.Zhang YF, Yu Y, Song WZ, Zhang RM, Jin S, Bai JW, Kang HB, Wang X, Cao XC. miR-410-3p suppresses breast cancer progression by targeting Snail. Oncol Rep, 2016; 36(1): 480-486.
17.Zhang L, Pang Y, Cui X, Jia W, Cui W, Liu Y, Liu C, Li F. MicroRNA-410-3p upregulation suppresses proliferation, invasion and migration, and promotes apoptosis in rhabdomyosarcoma cells. Oncol Lett, 2019, 18(1): 936-943.
18.Xiong J, Wang D, Wei A, Ke N, Wang Y, Tang J, He S, Hu W, Liu X. MicroRNA-410-3p attenuates gemcitabine resistance in pancreatic ductal adenocarcinoma by inhibiting HMGB1-mediated autophagy. Oncotarget 2017; 8(64):107500.
19.Jiang Y, Zhang D, Zhang T. Research progress on the role of nuclear factor κB (NF-κB) signaling pathway in inflammation and tumor. Chine J Cell Mol Immuno 2018; 34 (12): 78 -83.
20.Jin Xiaohan, Jia Yongsheng, Wu Zhongsheng. The role of nuclear factor κB in tamoxifen resistance of breast cancer. Tumor, 2018; 38 (7): 662-669.