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ORIGINAL ARTICLE

miR-146a and miR-152 in prostate cancer and clinicopathological parameters

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Summary

Purpose: *To investigate the expression of miR-146a and miR-152 in the serum of patients with prostate cancer (PCa) and the relationship between their expression and clinicopathologic parameters.*

Methods: *56 patients with prostate cancer and 56 healthy volunteers were included in this study and the relationship between the expression levels of miR-146a and miR-152 and the clinicopathological parameters of the patients with PCa were analyzed. ROC curve was used to evaluate the diagnostic value of each indicator.*

Results: *The expression of miR-146a in patients in the cancer group was significantly higher than that in the normal group ($p<0.05$). The expression of miR-152 in the cancer group was significantly lower than that in the normal group ($p<0.05$). The expression level of miR-146a in patients with PCa was closely related to clinical staging, the presence or absence of bone metastasis, tPSA and pathological staging ($p<0.001$) and the expression level of miR-152 in patients with PCa was closely related to clinical staging, the presence or absence of bone metastasis and pathological staging ($p<0.001$).*

Conclusion: *The expression level of miR-146a showed a trend for up-regulation in PCa, and the expression level of miR-152 had a trend for down-regulation in PCa , and the results of partial correlation analysis showed that the expression level of miR-146a and miR-152 was negatively correlated with each other in the serum of the patients with PCa.*

Key words: *miR-146a, miR-152, clinicopathological parameters, diagnostic value, prostate cancer*

Introduction

Prostate cancer (PCa) is the most common cancer in males in Europe and North America [1]. Its incidence increases continually, and its morbidity ranks second among all cancers in males worldwide [2], while mortality ranks sixth worldwide [12]. Currently, serum prostate-specific antigen (PSA) is the gold standard for the diagnosis of PCa, but it also has some limitations. Its prognostic ability is limited [3], therefore it is necessary to find better biomarkers to improve existing diagnostic methods. In recent years, microRNAs (miRs) have received increasing attention in the research of cancer. Studies have shown that miRs play a key role in the development of PCa [4]. For example, miR-143 has been identified as a biomarker with a high sensitivity and specificity in PCa [5], which also provides new clues for the study of this disease.

miR-146a and miR-152 are miRs that have attracted much attention as potential tumor markers, but their biological functions are not identical

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in different tumor cells. Studies have found that miR-146a is up-regulated in thyroid cancer [6] and cervical cancer [7], suggesting that miR-146a is a "carcinogenic microRNA" in thyroid and cervical cancer. Related studies also have found that the expression of miR-146a is low in pancreatic cancer [8] and gastric cancer [9], which also indicates that miR-146a is an "anticancer microRNA" in pancreatic and gastric cancer. Studies have demonstrated that the expression of miR-152 in nasopharyngeal cancer is significantly lower than the expression in normal tissue [10], while the expression of miR-152 is up-regulated in neuroblastoma [11]. Thus, the effects of miR-146a and miR-152 vary according to the type of cancer.

Since currently the reports about miR-146a and miR-152 in PCa are few, we planned to study their expression in the serum of PCa patients and clarify their diagnostic value.

Methods

Clinical data

From May, 2009 to April, 2017, 56 patients diagnosed with PCa in the surgical department of our hospital were included in the cancer group. Their age ranged from 42 to 70 years (mean 55.01±12.09). Meanwhile, 56 healthy individuals were included in the normal group, with age range from 44 to 71 years (mean 54.31±11.54).

All the patients with PCa were diagnosed according to the WHO prostate cancer diagnostic criteria. Patients with diabetes mellitus, high blood pressure, cardiovascular and cerebrovascular diseases, and tuberculosis were excluded from the study. Fasting blood for performing the different tests was taken in the morning and the serum was separated and stored in a refrigerator at -80 °C. No significant differences in age, height and body mass index (BMI) existed between the patients with PCa and the healthy controls (p>0.05). The patients and their families were informed over the study in advance before the study entry and signed informed consent form. The general data are shown in Table 1 in detail.

Experimental materials

Real-time quantitative PCR (qRT-PCR) instrument was purchased from BioRad Co, Hercules, CA, USA; TRIzol was purchased from Invitrogen Co, Waltham, MA, USA; qRT-PCR kit and minScript reverse transcription kit were purchased from Dalian TaKaRa Co, Dalian, China.

Experimental methods

The serum was taken out from the refrigerator and thawed. TRIzol was added and RNA was extracted from the serum. Ultraviolet spectrophotometer was used to test the purity and concentration of RNA on 1 μl of total RNA according to the instructions of the manufacturer. Reverse transcription cDNA reaction parameters: 16°C for 15 min, 42°C for 60 min, and 85°C for 5 min. cDNA that had been transcribed was used to carry out the PCR amplification. The PCR amplification system was config-

Table 1. Comparison of the general data

Factors	*Cancer group (n=56) n (%)*	*Normal group (n=56) n (%)*	x^2	*P*
Age. years				
<50	29 (51.79)	28 (50.00)	0.036	0.850
≥50	27 (48.21)	28 (50.00)		
Height (cm)				
<170	22 (39.29)	25 (44.64)	0.330	0.566
≥170	34 (60.71)	31 (55.36)		
BMI (kg/m^2)				
≤18.25	32 (57.14)	30 (53.57)	0.145	0.704
>18.25	24 (44.64)	26 (46.43)		
Smoker				
Yes	34 (60.71)	31 (55.36)	0.330	0.566
No	22 (39.29)	25 (44.64)		
Drinker				
Yes	36 (64.29)	32 (57.14)	0.599	0.439
No	20 (35.71)	24 (42.86)		
Clinical staging				
A	10 (17.86)	-		
B	15 (26.79)	-	-	-
C	17 (30.35)	-		
D	14 (25.00)	-		

ured according to the instructions of the manufacturer and used U6 as internal reference. The primer sequences are shown in Table 2. The PCR reaction conditions: predenaturation at 95°C for 12 min, then 95°C for 15 s and 65°C for 30s, and the cycle was performed 40 times. PCR instrument was used to carry out real-time fluorescent quantitative PCR, and the experiment was repeated 3 times. The relative expression level of the genes was expressed in the form of $2^{-\Delta CT}$ (ΔCT=serum CT in prostate cancer group - serum CT in the normal group.

Statistics

In this study, SPSS 20.0 software package (Boyi Zhixun, Beijing Information Technology Co., Ltd.) was used to statistically analyze the experimental data, and GraphPad Prism 7 software was used to draw the experimental graphs. The measurement data were expressed in the form of mean value±standard deviation, log rank test was used to analyze the difference between the two groups and chi-square test was used to analyze the numerical data. The diagnostic value of miR-146a, miR-152 in PCa was analyzed with ROC curve. P<0.05 indicated statistically significant differences.

Results

Comparison of the expression of miR-146a and miR-152 in the serum of patients with PCa and in healthy individuals

The mean expression level of miR-146a in the serum of patients in the cancer group and in the normal group was 1.64±0.32 and 0.14±0.24, respectively and was significantly up-regulated in the cancer group compared with that in the normal group (p<0.05). The expression level of miR-152 in the serum of patients in the cancer group and in the normal group was 0.38±0.18 and 0.64±0.39, respectively and was significantly down-regulated in the cancer group compared with the normal group (p<0.05; Table 3).

The relationship between the expression level of miR-146a and the clinicopathological features of patients with PCa

The expression level of miR-146a in the serum of patients with PCa was significantly correlated with clinical staging, presence or absence of bone metastasis, tPSA and pathological staging (p<0.001), whereas was not significantly correlated with age (p>0.05).

The mean expression level of miR-146a in the serum of patients in the cancer group in clinical stage A, B, C and D was 0.98±0.27, 1.32±0.41, 1.57±0.37 and 1.82±0.777, respectively. The expression level of miR-146a in the serum of patients in clinical stage A was significantly lower than that in the serum of the patients in clinical stage B, clinical stage C and clinical stage D, the differences being statistically significant (p<0.05); the expression level of miR-146a in the serum of patients in clinical stage B was significantly lower than that in the serum of patients in clinical stage C, the differences being not statistically significant (p>0.05); the expression level of miR-146a in the serum of patients in clinical stage B was significantly lower than that in the serum of the patients in clinical stage D, the differences being not statistically significant (p>0.05); the expression level of miR-146a in the serum of patients in clinical stage C was significantly lower than that in the serum of the patients in clinical stage D, the differences being not statistically significant (p>0.05). The mean expression level of miR-146a in patients with or without bone metastasis in the cancer group was 1.81±0.87 and 1.42±0.52, respectively. The expression level of miR-146a in patients with bone metastasis in the cancer group was significantly higher than that in patients without bone metastasis (p<0.05); the mean expression level of miR-146a in grade (G) G1,

Table 2. RT-PCR of miRs related primers

Primers	*Forward primer*	*Reverse primer*
mir-146a	5'-CAACACCAGTCGATGGG CTGT-3'	5'-CCCAUGGAAUUCAGUUCUC AUU-3'
mir-152	5'-CCAGCTGAGTGGATGAC AGA-3'	5'-GTGCAGGGTCCGAGGTATTC-3'
U6	5'-GCTTCGGCAGCACATATA CTAAAAT-3	5'-CGCTTCACGAATTTGCGTGT CAT-3'

Table 3. The mean expression of miR-146a and miR-152 in the serum of the patients with prostate cancer and in the serum of healthy individuals

Groups	*Cancer group (n=56)*	*Healthy group (n=56)*	*t*	*p*
miR-146a	1.64±0.32	1.14±0.24	9.354	<0.05
miR-152	0.38±0.18	0.64±0.39	4.530	<0.05

G2 and G3 of the pathological staging of the patients in the cancer group was 1.05±0.42, 1.58±0.54 and 1.75±0.74 respectively. The expression level of miR-146a in G3 was significantly higher than that in G1, and the expression level of miR-146a in G2 was significantly higher than that in G1 (p<0.05); the mean expression level of miR-146a in G1 was significantly lower than that in G2 (p<0.05). When the expression level of tPSA was ≤10μg/L, the mean expression level of miR-146a in patients in the cancer group was 1.37±0.54 and when the expression level of tPSA was >10μg/L, the expression level of miR-146a in patients in the cancer group was 1.78±0.85; the expression level of miR-146a when tPSA≤10μg/L was significantly lower than that when tPSA >10μg/L (p<0.05; Table 4).

The relationship between the expression level of miR-152 and the clinicopathological features of patients with PCa

The mean expression level of miR-152 in the serum of patients with PCa was significantly correlated with clinical stage, presence or absence of bone metastasis and pathological stage (p<0.001), and was not significantly correlated with age and tPSA (p>0.05).

The mean expression level of miR-152 in the serum of patients in the cancer group in clinical stage A, B, C and D was 0.85±0.23, 0.71±0.19, 0.67±0.17 and 0.57±0.12, respectively. The expression level of miR-152 in the serum of patients in clinical stage D was significantly lower than that in the serum of patients in clinical stage A and clinical stage B (p<0.05); the expression level of miR-146a in the serum of the patients in clinical stage B was significantly lower than that in the serum of patients in clinical stage A (p<0.05); the expression level of miR-146a in the serum of the patients in clinical stage C was significantly lower than that in the serum of the patients in clinical stage A (p<0.05); the expression level of miR-146a in the serum of the patients in clinical stage D was significantly lower than that in the serum of patients in clinical stage B (p<0.05). The mean expression levels of miR-152 in patients with or without bone metastasis in the cancer group were 0.54±0.25 and 0.71±0.19, respectively and the expression level of miR-152 in patients with bone metastasis in the cancer group was significantly lower than that in patients without bone metastasis (p<0.05); the mean expression level of miR-152 in G1, G2 and G3 of the pathological staging of patients in the cancer group were 0.82±0.27, 0.69±0.21 and 0.55±0.18, respectively; the expression level in G1 was significantly higher than that in G3 (p<0.05), and the expression level of miR-146a in G2 was significantly lower than that in G1 (p<0.05); the expression level of miR-146a in G3 was significantly lower than that in G2 (p<0.05; Table 5).

Table 4. The mean relationship between the expression level of miR-146a and the clinicopathological features of patients with prostate cancer

Groups	*n*	*miR-146a*	*t/F*	*P*
Age, years			0.433	0.666
<50	29	1.64±0.65		
≥50	27	1.57±0.55		
Clinical staging			6.115	<0.001
A	10	0.98±0.27		
B	15	1.32±0.41*		
C	17	1.57±0.37*		
D	14	1.82±0.77*		
Bone metastasis			2.107	0.040
Yes	27	1.81±0.87		
No	29	1.42±0.52		
Pathological grading			5.342	0.008
G1	25	1.05±0.42		
G2	16	1.58±0.54#		
G3	15	1.75±0.74#		
tPSA(μg/L)			2.116	0.039
≤10μg/L	30	1.37±0.54		
>10μg/L	26	1.78±0.85		

*p<0.05 compared with clinical stage A

Table 5. The relationship between the expression level of miR-152 and the clinicopathological features of the patients with prostate cancer

Groups	*n*	*miR-152*	*t/F*	*P*
Age, years			0.932	0.356
<50	29	0.59±0.21		
≥50	27	0.64±0.19		
Clinical staging			5.119	0.004
A	10	0.85±0.23*		
B	15	0.71±0.19*		
C	17	0.67±0.17		
D	14	0.57±0.12		
Bone metastasis			2.849	0.006
Yes	27	0.54±0.25		
No	29	0.71±0.19		
Pathological grading			5.296	
G1	25	0.82±0.27		0.009
G2	16	0.69±0.21[a]		
G3	15	0.55±0.18[b]		
tPSA, μg/L			1.148	0.256
≤10	30	0.62±0.11		
>10	26	0.58±0.15		

*p<0.05 compared with clinical stage D. [a]p<0.05 compared with pathological grade 1. [b]p<0.05 compared with pathological grade 2.

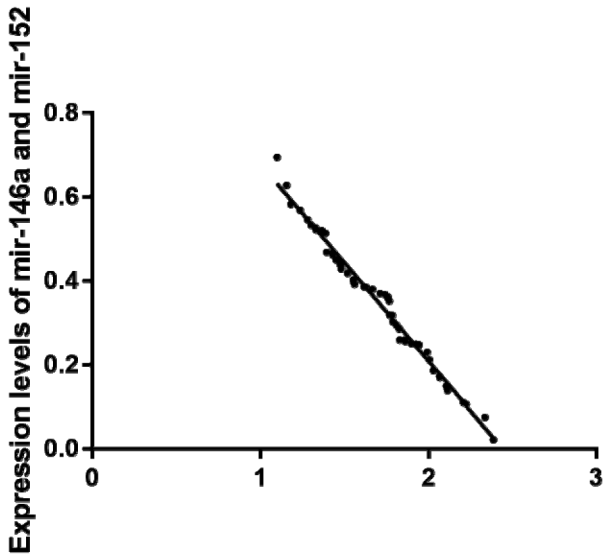

Figure 1. The correlation between the expression of miR-146a and the expression of miR-152 in the serum of the patients with prostate cancer. The results of partial correlation analysis showed that the expression level of miR-146a and the expression level of miR-152 were negatively correlated with each other in the serum of patients with prostate cancer (r=0.984, p<0.001).

The correlation between the expression of miR-146a and the expression of miR-152 in the serum of patients with PCa

The results of partial correlation analysis showed that the expression level of miR-146a and of miR-152 were negatively correlated with each other in the serum of patients with PCa (r=0.984, p<0.001; Figure 1).

The clinical diagnostic value of miR-146a and miR-152 in the serum of patients with PCa

The results of ROC analysis showed that miR-146a diagnosed PCa with 0.887 of AUC, the best cut-off point for the diagnosis of PCa was 0.932, the specificity was 79%, the sensitivity 89.29%, the positive predictive value 80.95%, the negative predictive value 89.80% and the accuracy 84.82%, whereas miR-152 diagnosed PCa with 0.699 of AUC, the best cut-off point for the diagnosis of PCa was 1.230, the specificity was 94.64% and the sensitivity was 48.21%, the positive predictive value 90.00%, the negative predictive value 64.63% and the accuracy 71.43%; miR-146a combined with miR-152 diagnosed PCa with 0.892 of AUC, and the best cut-off point for the diagnosis of PCa was 0.934, for specificity was 82.15% and for sensitivity was 92.86%. The positive predictive value was 83.87%, the negative predictive value 92.00% and the accuracy 87.50% (Figures 2-4).

Discussion

The morbidity of PCa ranks second and its mortality ranks sixth in the world [12]. It is also the second reason of death in males with cancer in the

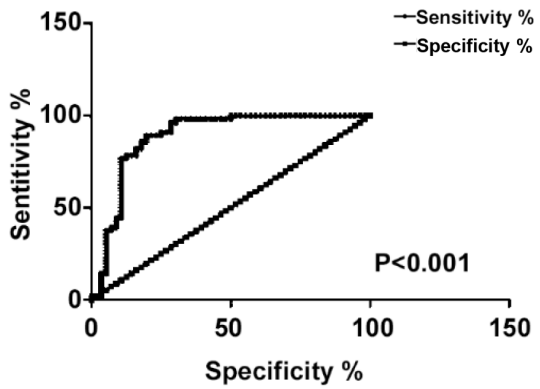

Figure 2. The clinical diagnostic value of miR-146a in the serum of patients with prostate cancer. The results of ROC analysis showed that miR-146a diagnosed prostate cancer with 0.887 of AUC and the best cut-off point for the diagnosis of prostate cancer was 0.932, the specificity was 79%, and the sensitivity was 89.29%.

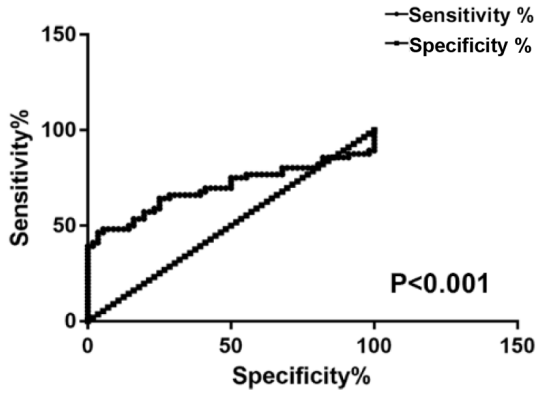

Figure 3. The clinical diagnostic value of miR-152 in the serum of the patients with prostate cancer. The results of ROC analysis showed that miR-152 diagnosed prostate cancer with 0.699 of AUC. The best cut-off point for the diagnosis of prostate cancer was 1.230, the specificity was 94.64%, and the sensitivity was 48.21%.

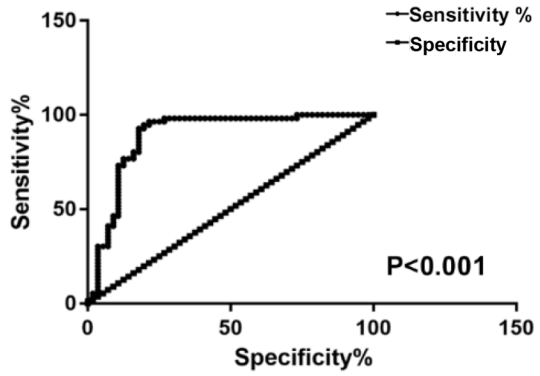

Figure 4. The clinical diagnostic value of miR-146a and miR-152 in the serum of the patients with prostate cancer. The results of ROC analysis showed that miR-146a combined with miR-152 diagnosed prostate cancer with 0.892 of AUC, and the best cut-off point for the diagnosis of prostate cancer was 0.934, the specificity was 82.15% and the sensitivity was 92.86%.

United States [13]. PCa has been reported to be one of the main reasons of death in diseases related to males in Nigeria [14]. miR derives from lncRNA and SnoRNA [15]. The dysregulation of miR in PCa contributes to the occurrence of cancers and the progression of metastasis [16]. miR can also be a good biomarker of prognosis results in the diagnosis and prediction of PCa [16]. Increasing evidence suggests that miR is involved in many types of cancers and helps diagnose the dysregulated miR and prognosis in patients [17,18]. Studies have shown that miR-152 is down-regulated in rheumatoid arthritis (RA) [19]. In contrast, miR-152 is up-regulated in neuroblastoma, and down-regulates proapoptotic genes, such as the conserved helix-loop-helix ubiquitin kinase, Cullin-5, growth retardation and DNA injury factors to negatively control apoptosis [20]. A study has found that the expression of miR-146a is significantly up-regulated in progressive oral precancerous lesions compared with its non-progressive counterpart [21]. In another study, miR-146a was down-regulated in head and neck squamous cell cancers [22]. However, the studies concerning the expression and mechanism of miR-152 and miR-146a in PCa are sparse, thus, this paper investigated the expression of miR-152 and miR-146a in the serum of patients with PCa and the relationship between their expression and clinicopathologic parameters, and analyzed the diagnostic value of miR-152 and miR-146a in PCa.

Firstly, we investigated the expression level of miR-152 and miR-146a in the serum of the patients with PCa by using PCR. The results showed that the expression of miR-146a in the serum of patients in the cancer group was significantly up-regulated than in the serum of patients in the normal group ($p<0.05$), while the expression of miR-152 in the serum of patients in the cancer group was significantly down-regulated than in the serum of patients in the normal group ($p<0.05$). This indicated that miR-146a was highly expressed in PCa while miR-152 was lowly expressed in PCa. Studies have also shown that the expression of miR-152 is suppressed in PCa, and miR-152 is a promising molecular target that can inhibit the migration and invasion of PCa cells [23].

Next, we analyzed the relationship between the expression level of miR-146a and miR-152 and the clinicopathological features of patients in the cancer group. The results showed that the expression level of miR-146a in the serum of patients with PCa was significantly related with clinical staging, presence or absence of bone metastasis, tPSA and pathological staging ($p<0.001$); the expression level of miR-152 in the serum of the patients with PCa

was significantly correlated with clinical staging, presence or absence of bone metastasis and pathological staging ($p<0.001$). Then, we analyzed the correlation between the expression of miR-146a and miR-152 in the serum of patients with PCa, and the results of partial correlation analysis showed that the expression level of miR-146a and miR-152 was negatively correlated with each other in the serum of patients with PCa ($r=-0.984$, $p<0.001$); thus, we speculated that the clinicopathological features of PCa were closely related to the expression level of miR-146a and miR-152, moreover, the high expression of miR-146a in the serum of patients with PCa promotes the occurrence and development of this malignancy; while the low expression of miR-152 in PCa may inhibit the disease, which complements the credibility of the results of this study [24,25]. At present, the reports about the relationship and the correlation between the expression level of miR-146a and miR-152 and the clinicopathological features of patients with PCa are few, but some reports, indicate that miR-146a inhibits the expression of epithelial growth factor receptors in PCa cells, thus inhibiting the cell viability and proliferation of PCa. Finally, we used ROC to detect the diagnostic value of the single detection of miR-146a, the single detection of miR-152 and the combined detection of the two in PCa. The results showed that the sensitivity of the combined detection of miR-146a and miR-152 for PCa detection was significantly greater than that of the single detection of miR-146a or the single detection of miR-152.

In summary, the high expression of miR-146a has a stimulating effect on PCa , and the low expression of miR-152 has a suppressive effect on PCa. The clinicopathological features of PCa are closely related to the expression level of miR-146a and miR-152. Monitoring the expression changes of miR-146a and miR-152 in the serum can improve the diagnostic rate of PCa. However, there are some limitations in this experimental work, for example, the biological functions of miR-146a and miR-152 in the serum of patients with all kinds of PCa were not investigated, therefore, it is desirable for researchers to expand the sample size and further investigate the effects of miR-146a and miR-152 in this malignancy.

Conflict of interests

The authors declare no conflict of interests.

References

1. Grönberg H. Prostate cancer epidemiology. Lancet 2003;361:859-64.
2. Center MM, Jemal A, Lortet-Tieulent J et al. International variation in prostate cancer incidence and mortality rates. Eur Urol 2012;61:1079-92.
3. Schroder FH, Hugosson J, Roobol MJ et al. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med 2009;360:1320-8.
4. Wang X, Shi Z, Liu X et al. Upregulation of miR-191 promotes cell growth and invasion via targeting TIMP3 in prostate cancer. JBUON 2018;23:444-52.
5. Wach S, Nolte E, Szczyrba J et al. MicroRNA profiles of prostate carcinoma detected by multiplatform microRNA screening. Int J Cancer 2012;130:611-21.
6. He H, Jazdzewski K, Li W et al. The role of microRNA genes in papillary thyroid carcinoma. Proc Natl Acad Sci USA 2005;102:19075-80.
7. Wang X, Tang S, Le SY et al. Aberrant expression of oncogenic and tumor-suppressive microRNAs in cervical cancer is required for cancer cell growth. PLoS One 2008;3:e2557.
8. Li Y, Vandenboom TG, Wang Z et al. miR-146a suppresses invasion of pancreatic cancer cells. Cancer Res 2010;70:1486-95.
9. Kogo R, Mimori K, Tanaka F, Komune S, Mori M. Clinical significance of miR-146a in gastric cancer cases. Clin Cancer Res 2011;17:4277-84.
10. Yu R, Zhang Y, Xu Z et al. Potential antitumor effects of panaxatriol against DU-15 human prostate cancer cells is mediated via mitochondrial mediated apoptosis, inhibition of cell migration and sub-G1 cell cycle arrest. JBUON 2018;23:200-4.
11. Liu X, Li J, Qin F, Dai S. miR-152 as a tumor suppressor microRNA: Target recognition and regulation in cancer. Oncol Lett 2016;11:3911-16.
12. Jemal A, Bray F, Center MM et al. Global cancer statistics. CA Cancer J Clin 2011;61:69-90.
13. Coman RT, Crisan N, Kadula PA et al. Neutrophil-to-lymphocyte ratio above 2 advocates for lymph node dissection in prostate cancer. J BUON 2018;23:275-6.
14. Awodele O, Adeyomoye AA, Awodele DF, Fayankinnu VB, Dolapo DC. Cancer distribution pattern in south-western Nigeria. Tanzan J Health Res 2011;13:125-31.
15. Ronnau CG, Verhaegh GW, Luna-Velez MV, Schalken JA. Noncoding RNAs as novel biomarkers in prostate cancer. Biomed Res Int 2014;2014:591703.
16. Hamilton MP, Rajapakshe KI, Bader DA et al. The landscape of microRNA targeting in prostate cancer defined by AGO-PAR-CLIP. Neoplasia 2016;18:356-70.

17. Bartel DP. MicroRNAs: target recognition and regulatory functions. Cell 2009;136:215-33.
18. Hayes J, Peruzzi PP, Lawler S. MicroRNAs in cancer: biomarkers, functions and therapy. Trends Mol Med 2014;20:460-69.
19. Guo J, Du J, Fei D, Xing J, Liu J, Lu H. miR-152 inhibits rheumatoid arthritis synovial fibroblast proliferation and induces apoptosis by targeting ADAM10. Int J Mol Med 2018;42:643-50.
20. Ragusa M, Majorana A, Banelli B et al. MIR152, MIR200B, and MIR338, human positional and functional neuroblastoma candidates, are involved in neuroblast differentiation and apoptosis. J Mol Med 2010;88:1041-53.
21. Cervigne NK, Reis PP, Machado J et al. Identification of a microRNA signature associated with progression of leukoplakia to oral carcinoma. Hum Mol Genet 2009;18:4818-29.
22. Lerner C, Wemmert S, Bochen F et al. Characterization of miR-146a and miR-155 in blood, tissue and cell lines of head and neck squamous cell carcinoma patients and their impact on cell proliferation and migration. J Cancer Res Clin Oncol 2016;142:757-66.
23. Zhu C, Li J, Ding Q et al. miR-152 controls migration and invasive potential by targeting TGFα in prostate cancer cell lines. Prostate 2013;73:1082-9.
24. Theodore SC, Davis M, Zhao F et al. MicroRNA profiling of novel African American and Caucasian prostate cancer cell lines reveals a reciprocal regulatory relationship of miR-152 and DNA methyltranferase 1. Oncotarget 2014;5:3512-25.
25. Xu B, Wang N, Wang X et al. MiR-146a suppresses tumor growth and progression by targeting EGFR pathway and in a p-ERK-dependent manner in castration-resistant prostate cancer. Prostate 2012;72:1171-8.