Int J Clin Exp Pathol 2024;17(2):29-38
www.ijcep.com /ISSN:1936-2625/IJCEP0154181

Original Article

RCOR1 is targeted by miR-23b-3p to modulate growth, colony formation, migration, and invasion of prostate cancer cells

Chenli Liu*, Zhong Dong*, Maozhang Li, Guangwei Bai, Zhixiang Zhao

*Department of Urology, Huizhou Central People's Hospital, Huizhou 516000, Guangdong, China. *Equal contributors.*

Received October 31, 2023; Accepted January 23, 2024; Epub February 15, 2024; Published February 28, 2024

Abstract: Objectives: Prostate cancer holds the second-highest incidence rate among all male malignancies, with a noticeable scarcity of effective treatment approaches. The REST Corepressor 1 (RCOR1) protein exhibits elevated expression across various tumors, acting as an oncogene. Nevertheless, its functions and mechanisms in prostate cancer have yet to be documented. While miR-23 demonstrates reduced expression in prostate cancer, the downstream genes it regulates remain unclear. Methods: RT-qPCR and Western blotting assays were utilized to elucidate the mRNA and protein levels of miR-23b-3p and RCOR1. The luciferase reporter assay was employed to unveil the targeting relationship between miR-23b-3p and RCOR1. Additionally, a CCK-8 assay demonstrated cell growth, while colony formation and Transwell assays were performed to observe clone formation, cell migration, and invasion. Results: In this study, we observed substantial mRNA and protein levels of RCOR1 in prostate cancer cells such as DU145, PC3, and LNCap. RCOR1 overexpression enhanced the growth, colony formation, migration, and invasion of prostate cancer cells, whereas genetic silencing of RCOR1 suppressed these processes. Bioinformatics analysis identified miR-23b-3p as a potential regulator of RCOR1, and luciferase assays validated RCOR1 as a downstream target of miR-23b-3p. Increasing miR-23b-3p mimics diminished RCOR1's mRNA and protein levels, while raising miR-23b-3p levels boosted RCOR1's expression. Moreover, the stimulatory impact of RCOR1 on prostate cancer cell development could be countered by elevating miR-23b-3p mimics. Conclusion: In summary, our findings confirm that RCOR1 is indeed under the influence of miR-23, shedding light on the miR-23/RCOR1 pathway's role in prostate cancer development. This offers novel theoretical and experimental support for comprehending the underlying mechanisms of prostate cancer and for targeted therapeutic avenues.

Keywords: ROCR1, miR-23b-3p, prostate cancer cells, cell growth, colony formation, migration and invasion

Introduction

Prostate cancer (PCa), being one of the most prevalent tumors in the urinary system, ranks second in incidence among male malignant tumors worldwide. It has emerged as a significant health concern for men, with its incidence steadily increasing annually [1, 2]. Surgery, radical radiotherapy, and other treatments have a good effect on early localized prostate cancer. However, later treatment can lead to the development of castration-resistant prostate cancer (CRPC). Prostate cancer has low sensitivity to chemotherapy, is prone to tumor metastasis, and presents challenges in clinical treatment, resulting in a poor prognosis and has a serious impact on the quality of life of patients [3]. Hence, there is an urgent need to explore the potential mechanisms underlying the occurrence and development of PCa and identify new prognostic biomarkers along with more effective treatment strategies.

In previous studies, it has been found that a small non-coding RNA called microRNA (miRNA) plays a crucial regulatory role in the occurrence and development of various human cancers, including prostate cancer. MiRNA binds to complementary loci on the target mRNA in its 3'-non-translation region (3'-UTRs), inhibiting the expression of the target gene at the post-transcriptional level. Additionally, miRNA can

regulate targeted oncogenes and tumor suppressor factors, highlighting that disorders and dysfunction in miRNA expression play a direct causal role in cancer etiology [4, 5]. MicroRNAs (miRNA or miR) have been studied as biomarkers for an extended time [6]. However, exploring the study of genes and proteins that regulate miRs, as well as the genes and proteins regulated by miRs, is a novel strategy for disease research. Therefore, it is crucial to gain a deeper understanding of the molecular functions of miRNA-targeted genes and proteins in prostate cancer.

Previous studies have identified the REST Corepressor 1 (RCOR1) as playing a role in cancer. When compared to the control group, differences in the expression levels of RCOR1 have been observed in patients with oral squamous carcinoma, breast cancer, ovarian cancer, lymphoma, and glioma [7]. The expression level of RCOR2 was decreased in lung adenocarcinoma cells treated with rhubarbrine [8]. In addition to differences in expression, some studies have suggested that RCOR1 may exert a functional impact on the occurrence and development of tumors. For instance, RCOR1 directly interacts with MED28, inhibiting cancer stem cell (CSC)-like characteristics in oral squamous cell carcinoma (OCSCC) cells [9]. The upregulation of RCOR1 can sustain the tumor stem-like phenotype in diffuse astrocytoma (DA), angioma (AO), and polymorphic glioblastoma (GBM) [10]. RCOR1 activates angiogenesis and the secretion of inflammatory factors, thereby enhancing tumor-induced angiogenesis and inflammation in breast cancer [11]. Although it is known that RCOR1 is expressed differentially in various cancers, its expression level, mechanism of action, and how it influences cell behavior through the miR-23/RCOR1 pathway in prostate cancer have not been clearly determined, despite being identified as the target gene of miR-23.

Our study confirms that RCOR1 promotes prostate cancer (PCa) cell proliferation and identifies the upstream miRNA, miR-23b-3p, targeting RCOR1. Furthermore, the current study explores the potential mechanism of miR-23b-3p in regulating PCa cell proliferation by targeting the 3'-UTR of RCOR1 mRNA. Identifying miRNAs targeting RCOR1 in PCa may aid in the development of PCa therapy based on RCOR1. This study may offer new insights and therapeutic targets for the treatment of PCa.

Materials and methods

Cell culture

DU145 cells were cultured in DMEM/F12 medium with 10% FBS and 1% penicillin/streptomycin solution, while PC3 cells were maintained in RPMI 1640 (Gibco, Shanghai, China) with 10% FBS and 1% penicillin/streptomycin (Gibco, Shanghai, China). The cells were cultivated in a humidified incubator with 5% CO_2 under normoxic conditions at 37°C.

Cell counting kit-8 (CCK8) assay for cell growth

Cell viability was assessed using CCK8 kits in accordance with the manufacturer's instructions (#C0037, Beyotime, Shanghai, China). A volume of 200 μL cell suspension was prepared and transferred to a 96-well plate (2-5 × 10^3/well) at a specific concentration. Subsequently, 10 μL of CCK8 solution was added to each well, and the plate was placed in an incubator with conditions set at 37°C and 5% CO_2 for 4 hours of culture. Following the incubation, the data were read at 450 nm on a microplate reader.

Transwell assay

According to the manufacturer's instructions (Corning, NY, USA), the 24-well Transwell chamber is used to measure cell migration capacity. Cells at 2.5 × 10^4, were starved for 12 hours in advance, and were suspended in 400 μl of serum-free medium and added to the upper chamber. Additionally, 600 μl of serum-containing medium was added to the lower chamber. Cultivated under the conditions of 37 degrees Celsius and 5% CO_2, and after 24 hours, cells in the upper chamber were counted for the migrated or invaded cells. The invasion experiment was identical to the migration experiment, except for the addition of 100 μl of matrix gel (Beyotime) to the upper chamber. The experiment was carried out in triplicate.

Western blotting

The tissue is ground and crushed, and cracking fluid is added for extraction. After centrifugation, the total protein sample is obtained. The protein concentration is determined using the

dioctoctanoic acid (BCA) method with a kit purchased from Beyotime. In 10% sodium dodecyl sulfate-polyacrylamide gel (SDS-PAGE), 40 mg (protein amount) is added to each lane, and proteins are separated at 80 mV and 100 mV voltages. Subsequently, the electrophoresis gel is transferred to a PVDF membrane. At 4°C, the PVDF membrane is sealed with 5% skim milk powder for 1 hour. Next, the primary antibodies (anti-RCOR1, 1:200, Novus Biologicals, #NB600-240; anti-β-tubulin, 1:1000, Abcam, Cambridge, UK; and anti-GAPDH, 1:7500 dilution, Proteinteintech, United States) are incubated overnight, followed by incubation with secondary antibodies (HRP-labeled goat anti-mouse or anti-rabbit antibodies, Beyotime) for 1 hour at room temperature. Finally, the Western lightning-electrochemical luminescence method (ECL; Beyotime) is employed for band visualization, using GAPDH as the internal loading control.

Quantitative polymerase chain reaction (RT-qPCR)

For RT-qPCR, Trizol® reagents (Cat#6-15596, Invitrogen, Carlsbad, California, United States) are utilized to extract total RNA from tissues. The absorbance of the total RNA sample at 260 nm/280 nm is measured to assess RNA quality. Reverse transcription is performed using the reverse cDNA synthesis kit (Promega, Madison, WI, USA), taking an equal amount of RNA as a template to synthesize cDNA. Subsequently, qPCR testing is conducted on Bio-Rad according to the manufacturer's instructions. The experiments are carried out in triplicate to ensure the reliability of the results.

Colony formation assay

Cells subjected to different treatments were cultured in 24-well plates at a density of 200 cells per well. After two weeks, colony formation was assessed. Clones were visualized and counted using Crystal Violet staining (Beyotime). The relative colony formation ability was measured to mimic the negative control (NC).

Dual-luciferase reporter assay

Cells were divided into the following treatments: a) pmirGLO/RCOR1-WT+miR-23b-3p mimic NC; b) pmirGLO/RCOR1-WT+miR-23b-3p mimic; c) pmirGLO/RCOR1-MUT+miR-23b-3p mimic NC; d) pmirGLO/RCOR1-MUT+miR-23b-3p mimic. Cells were seeded in triplicate in 96-well plates, then co-transfected with the above contents using Lipofectamine 2000 (Invitrogen, CA, USA). Luciferase and Renilla activity were measured 48 h after transfection using the Dual Luciferase Reporter Assay Kit (Promega), following the manufacturer's instructions. Luciferase activity values were normalized to Renilla activity as relative activity.

Statistical analysis

All data were acquired from three independent experiments. Statistical analysis was performed using SPSS 19.0 (IBM, NY, USA) and results are expressed as means ± SD. Differences between two groups and multiple groups were assessed using Student's t-test and one-way ANOVA, respectively. In cases of comparing two groups across multiple time points, the post-hoc Bonferroni test was applied after ANOVA. P values < 0.05 were considered significant.

Results

The elevated expression of RCOR1 in tissues and its promotional effect on the development of prostate cancer (PCa) cells

To investigate the biological functions of RCOR1 in PCa cell lines, we utilized RT-qPCR, Western blotting, colony formation, and Transwell assays to analyze proliferation and migration. Initially, we assessed the endogenous mRNA and protein levels of RCOR1 in PCa cell lines. As illustrated in **Figure 1A-C**, the expression of RCOR1 was significantly upregulated in PCa cell lines DU145, PC3, and LNCap compared to normal prostate epithelial cells. Additionally, we constructed an overexpressing plasmid carrying the RCOR1 gene and confirmed its expression in DU145 cells (**Figure 1D**). Two genetic knockdown siRNA fragments against RCOR1 were designed and synthesized, with siRCOR1 #2 demonstrating a more effective silencing effect than #1 and the negative control (**Figure 1E**). Therefore, siRCOR1 #2 was selected for subsequent knockdown experiments. According to the CCK-8 assay, overexpression of RCOR1 promoted the cell growth of DU145 and LNCap cells, while knockdown of RCOR1 resulted in decreased cell growth (**Figure 1F**, **1G**). The same trend was observed in the colony forma-

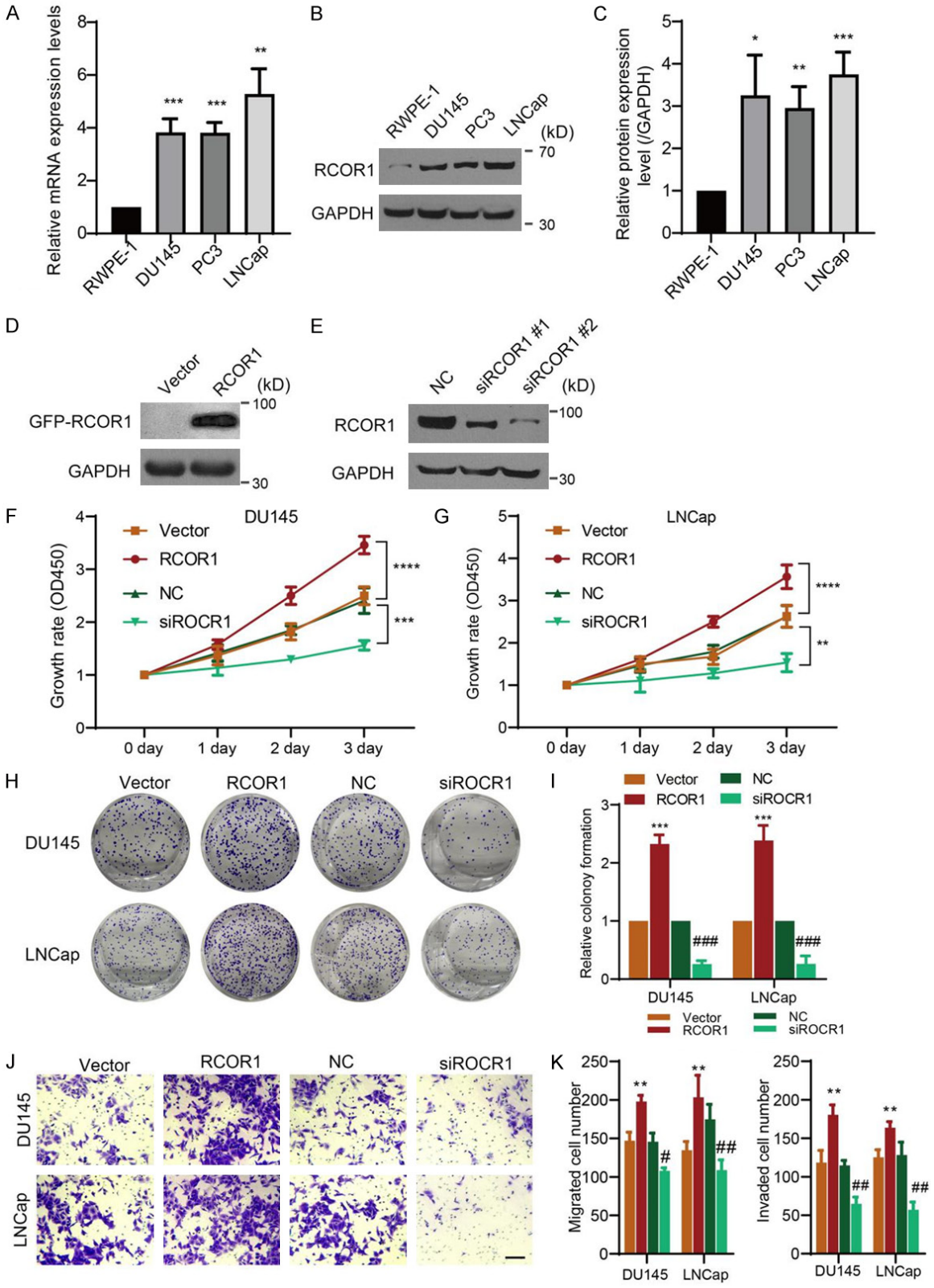

Figure 1. RCOR1 regulates the development of PCa cells. A. mRNA levels of REST Corepressor 1 (RCOR1) in Prostate cancer (PCa) cell lines were validated using qRT-PCR; B-E. Expression levels of RCOR1 in PCa cells and transfection efficiency were confirmed by Western blotting; F, G. Cell proliferation of PCa cell lines after transfection with NC mimics and RCOR1 was assessed using CCK-8 assay; H, I. Proliferative capacity of PCa cell lines after transfection with NC mimics and RCOR1 mimics was evaluated through colony formation assays (magnification: 40 ×); J, K. Migration of PCa cell lines after transfection with NC mimics and RCOR1 mimics was determined using Transwell assays (scale bar, 20 μm); Data presented as mean ± standard deviation, *P < 0.05, **P < 0.01.

tion assay (**Figure 1H**, **1I**) and Transwell assays (**Figure 1J**, **1K**). These data indicate that RCOR1 is overexpressed in PCa cells and that it promotes the proliferation, colony formation, and migration of PCa cells.

RCOR1 is a downstream target of miR-23b-3p

To explore the upstream regulator of RCOR1, we screened the 3'UTR of RCOR1. As depicted in **Figure 2A**, **2B**, bioinformatics analysis revealed that the wildtype region of the 3'UTR of RCOR1 exhibited a matched sequence to miR-23b-3p (**Figure 2A**), and this sequence conservation was observed across different vertebrate species (**Figure 2B**), indicating a potential regulatory relationship between miR-23b-3p and RCOR1. To confirm this, we constructed a luciferase reporter system with WT or MUT (mutant; **Figure 2B**) plasmids containing the 3'UTR region of RCOR1. MiR-23b-3p mimic or inhibitor fragments were synthesized, with mimic NC and inhibitor NC serving as controls. As illustrated in **Figure 2C**, overexpression of miR-23b-3p mimic upregulated the expression level, while the inhibitor suppressed it. Subsequently, PCa cells were transfected with or without miR-23b-3p mimics, along with RCOR1 WT or MUT luciferase reporter plasmids. **Figure 2D** demonstrates that overexpression of miR-23-3p mimic significantly suppressed the luciferase activity of WT RCOR1, but not the MUT one. Furthermore, the endogenous mRNA (**Figure 2E**) and protein (**Figure 2F**, **2G**) levels of RCOR1 were also significantly upregulated by the transfection of miR-23b-3p mimic, but suppressed by the inhibitor, in both DU145 and LNCap cells. These findings suggest that RCOR1 is directly regulated by miR-23b-3p in PCa cells.

miR-23b-3p negatively regulates RCOR1 to inhibit malignant progression of PCa cells

To further elucidate the biological role of RCOR1 regulated by miR-23b-3p in PCa cell lines, counteractive experiments were conducted. As depicted in **Figure 3A**, **3B**, PCa cells transfected with miR-23b-3p mimic exhibited suppressed cell growth compared to the mimic NC group in the CCK-8 assay. However, co-transfection of RCOR1 significantly reversed this inhibitory effect, restoring the growth rate to mimic NC levels (**Figure 3A**, **3B**). The colony formation assay (**Figure 3C**, **3D**) and migration and invasion assays (**Figure 3E-H**) demonstrated a similar trend, where the suppressed colony formation, migration, and invasion ability by miR-23b-3p could be counteracted by the overexpression of RCOR1. These findings suggest that miR-23b-3p regulates the malignant progression of PCa cells by modulating RCOR1.

Discussion

RCOR, as a constituent component of the silencing transcription factor REST, has been demonstrated to play a role in neurodevelopment and various neuronal biological processes [12]. Additionally, RCOR is believed to function in various diseases. For instance, it exerts an influence on the terminal differentiation of osteoarthritis (OA) cartilage cells [13] and affects the differentiation of normal bone marrow red cell lineages and other biological processes [14]. Furthermore, the mutant GF60 variant of RCOR1 has been isolated in Drosophila follicular epithelium and activates the Notch signaling pathway [15]. In recent years, an increasing number of studies suggest that RCOR may play a role in the tumorigenesis process. For example, in the tumorigenesis of estrogen receptor-positive breast cancer, RCOR drives development and induces resistance to endocrine therapy by switching the recruitment site of complexes [16]. Research has demonstrated that RCOR also plays a role in tumor immunity. Knocking down RCOR1 in Foxp3+ Tregs can activate the function of Tregs, and IL-2 and IFN-γ in peripheral lymphoid tissues simultaneously increase, promoting anti-tumor immunity [17]. In our study, both mRNA and protein expression levels of RCOR1 in PCa cell lines are significantly elevated. Overexpression of RCOR1 promotes the proliferation of PCa cell lines and significantly enhances the migration of PCa cell lines.

Numerous studies indicate that RCOR is a target of microRNAs such as miR-22 [18], miR-124 [19], miR-9 [20], miR-432 [21], playing critical roles in many biological processes. MiR-27 cluster is part of a polycistronic cluster of miRNAs, including miR-23 and miR-24. MiR-23a-27a-24 is intergenic, having its own promoter on chromosome 19, while miR-23b-27b-24 is intronic, located on chromosome 9. The miR-23-27-24 cluster in humans occupies two

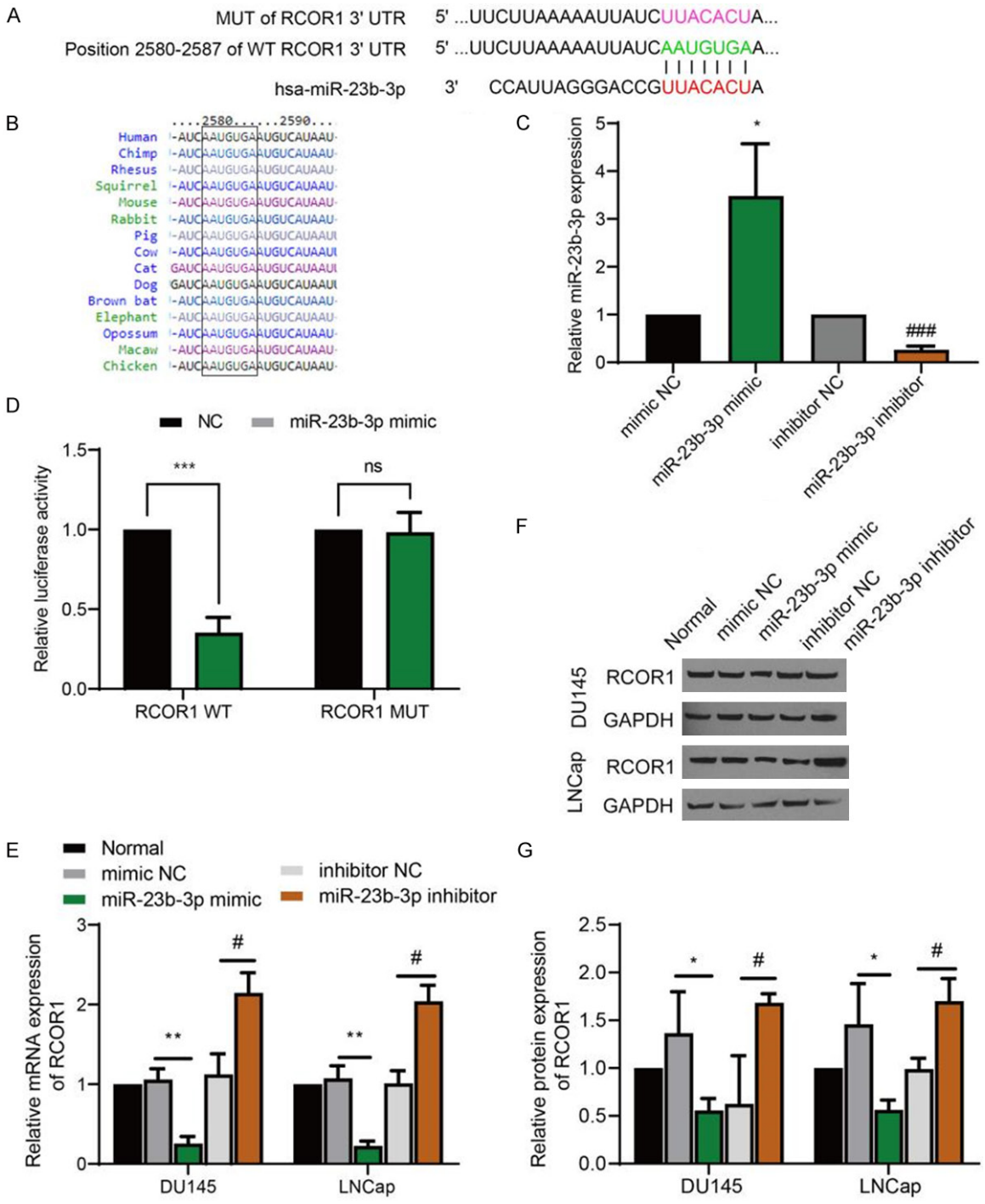

Figure 2. RCOR1 is a direct downstream target of miR-23b-3p in PCa cells. A, B. Dual luciferase reporter gene assays indicated that miR-23b-3p directly targets RCOR1; C, D. miR-23b-3p expression exhibited a significant negative correlation with RCOR1 expression in PCa tissues; F, G. Protein blotting confirmed expression levels of RCOR1 in PCa cell lines transfected with NC mimics and miR-23b-3p mimics; E, F. qRT-PCR validated RCOR1 expression levels in PCa cell lines transfected with NC mimics and miR-23b-3p mimics; Data presented as mean ± standard deviation, *P < 0.05, **P < 0.01.

genomic loci: miR-23a-27a-24-2 cluster is intergenic and generates mature miR-23a, miR-27a, and miR-24, whereas miR-23b-27b-24-1 cluster is intronic and generates mature miR-23b, miR-27b, and miR-24 [22]. This cluster is highly conserved in vertebrates and fish, although not as

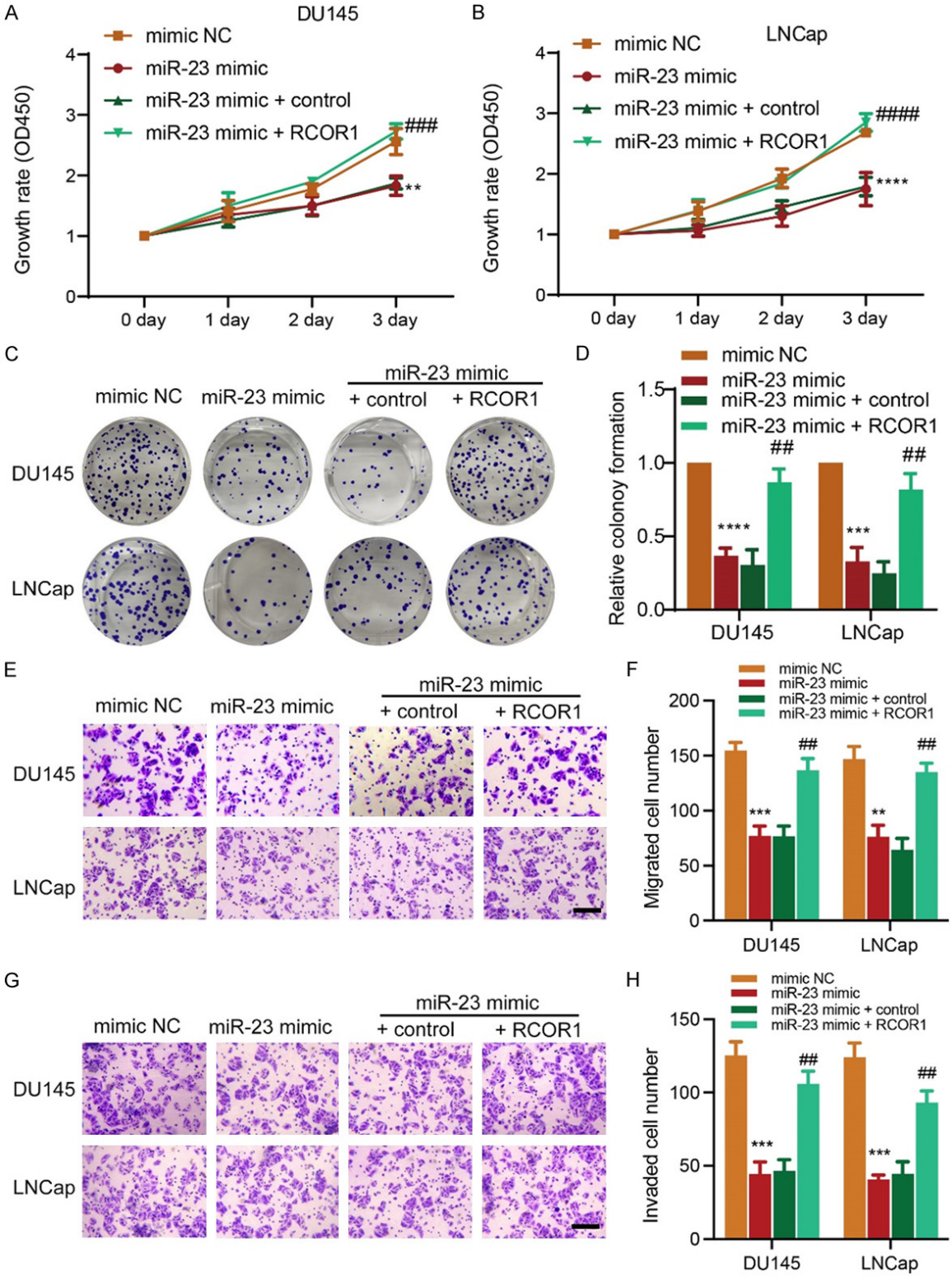

Figure 3. miR-23b-3p/RCOR1 axis regulates the development of PCa cells. A, B. Cell proliferation of PCa cell lines co-transfected with miR-23b-3p and RCOR1 was assessed using CCK-8 assay; C, D. Proliferative capacity of PCa cell lines co-transfected with miR-23b-3p and RCOR1 was evaluated through colony formation assays (magnification: 40 ×); E-H. Transwell assays detected cell migration of PCa cell lines co-transfected with miR-23b-3p and RCOR1 (scale bar, 20 μm); Data presented as mean ± standard deviation, *P < 0.05, **P < 0.01.

tightly clustered [23, 24]. Members of this cluster have been described to have functions in several organs/developmental systems, including cancer [25], the central nervous system [26], and vascular organs [27]. In recent years, increasing evidence suggests that microRNAs (miRNAs) play a significant role in tumor progression, including prostate cancer [28]. However, there is still much to be elucidated regarding the functional mechanisms of miRNAs in cancer pathogenesis.

MiR-23b-3p exhibits a close association with various functional specificities in different cancers in a cell-type-dependent manner. For example, the downregulation of miR-23b-3p can act as a tumor suppressor by targeting downstream protein expression. In gastric cancer, the downregulation of miR-23b-3p inhibits the growth and invasion of gastric cancer cells by targeting Notch 2 and suppressing its expression [29]. In bladder cancer, miR-23b-3p serves as a tumor suppressor by targeting Zeb1 [30]. In cervical cancer cells, miR-23b-3p reduces proliferation, migration, and invasion of cervical cancer cell lines by reducing c-Met expression [31]. However, miR-23b-3p is also associated with poor prognosis and acts as a cancer promoter in many tumors. For example, in osteosarcoma, miR-23b-3p inhibits PGC1α and promotes osteosarcoma proliferation by reprogramming metabolism [32]. MiR-23b-3p promotes osteosarcoma through the VEPH1/phosphoinositide 3-kinase/protein kinase B (PI3K/AKT) pathway targeting VE-PTP expressed in the ventricular area [33]. In breast cancer cells, miR-23b-3p negatively regulates Nischarin (an intracellular protein) to modulate tumor cell migration behavior [34]. In renal cell carcinoma cells, upregulation of miR-23b-3p promotes migration by targeting phosphatase and tensin homolog (PTEN) [28]. MiR-23b-3p acts as an anti-apoptotic factor in gastric cancer cells by directly targeting programmed cell death 4 (a cell apoptosis-regulating protein) [35]. Therefore, different miRNAs may have varying roles in different aspects of cancer, and understanding the specific functions of miR-23b-3p in prostate cancer (PCa) is an important question to address.

The role of RCOR1 during PCa development remains obscure. In the current study, we observed that RCOR1 was upregulated in PCa cells. Overexpression of RCOR1 promoted, while genetic knockdown of RCOR1 suppressed the growth, colony formation, migration, and invasion of both DU145 and LNCap cells. Bioinformatics analysis and luciferase reporter gene assays confirmed that RCOR1 was directly targeted by miR-23b-3p. MiR-23b-3p regulated the development of PCa cells by modulating RCOR1. Although these observations should be further confirmed in clinical data samples of PCa and in animal *in vivo* models, our data suggest the new miR-23b-3p/RCOR1 axis regulates the development of PCa cells, providing new evidence to elucidate the mechanism of PCa progression.

Acknowledgements

This work was supported by Medical Scientific Research Foundation of Guangdong Province of China (No. B2021402) and Science and Technology Project of Huizhou City (No. 2021WC0106410).

Disclosure of conflict of interest

None.

Address correspondence to: Chenli Liu, Department of Urology, Huizhou Central People's Hospital, No. 41 Eling North Road, Huizhou 516000, Guangdong, China. E-mail: lcl725@yeah.net

References

[1] Xia C, Dong X, Li H, Cao M, Sun D, He S, Yang F, Yan X, Zhang S, Li N and Chen W. Cancer statistics in China and United States, 2022: profiles, trends, and determinants. Chin Med J (Engl) 2022; 135: 584-590.

[2] Siegel RL, Miller KD, Fuchs HE and Jemal A. Cancer statistics, 2021. CA Cancer J Clin 2021; 71: 7-33.

[3] Achard V, Putora PM, Omlin A, Zilli T and Fischer S. Metastatic prostate cancer: treatment options. Oncology 2022; 100: 48-59.

[4] Ma L and Weinberg RA. Micromanagers of malignancy: role of microRNAs in regulating metastasis. Trends Genet 2008; 24: 448-456.

[5] Nicoloso MS, Spizzo R, Shimizu M, Rossi S and Calin GA. MicroRNAs--the micro steering wheel of tumour metastases. Nat Rev Cancer 2009; 9: 293-302.

[6] Turai PI, Herold Z, Nyiro G, Borka K, Micsik T, Toke J, Szucs N, Toth M, Patocs A and Igaz P. Tissue miRNA combinations for the differential diagnosis of adrenocortical carcinoma and ad-

enoma established by artificial intelligence. Cancers (Basel) 2022; 14: 895.
[7] Zheng R, Pan Y, Liu X, Liu F, Li A, Zheng D and Luo Y. Comprehensive analysis of REST corepressors (RCORs) in pan-cancer. Front Cell Dev Biol 2023; 11: 1162344.
[8] Maimaiti A, Xingliang L and Shi L. In vitro and in vivo anti-lung cancer activity of emodin: a RNA-seq transcriptome analysis. Curr Med Chem 2022; 2: 34.
[9] Xiang Z, Zhou S, Liang S, Zhang G and Tan Y. RCOR1 directly binds to MED28 and weakens its inducing effect on cancer stem cell-like activity of oral cavity squamous cell carcinoma cells. J Oral Pathol Med 2020; 49: 741-750.
[10] Yucebas M, Yilmaz Susluer S, Onur Caglar H, Balci T, Dogan Sigva ZO, Akalin T, Oktar N, Dalbasti T, Biray Avci C and Gunduz C. Expression profiling of RE1-silencing transcription factor (REST), REST corepressor 1 (RCOR1), and Synapsin 1 (SYN1) genes in human gliomas. J BUON 2016; 21: 964-972.
[11] Mazumdar S, Arendt LM, Phillips S, Sedic M, Kuperwasser C and Gill G. CoREST1 promotes tumor formation and tumor stroma interactions in a mouse model of breast cancer. PLoS One 2015; 10: e0121281.
[12] Maksour S, Ooi L and Dottori M. More than a corepressor: the role of CoREST proteins in neurodevelopment. eNeuro 2020; 7: ENEURO.0337-19.2020.
[13] Xiao J, Li T, Wu Z, Shi Z, Chen J, Lam SK, Zhao Z, Yang L and Qiu G. REST corepressor (CoREST) repression induces phenotypic gene regulation in advanced osteoarthritic chondrocytes. J Orthop Res 2010; 28: 1569-1575.
[14] Yao H, Goldman DC, Fan G, Mandel G and Fleming WH. The corepressor Rcor1 is essential for normal myeloerythroid lineage differentiation. Stem Cells 2015; 33: 3304-3314.
[15] Domanitskaya E and Schuepbach T. CoREST acts as a positive regulator of Notch signaling in the follicle cells of Drosophila melanogaster. J Cell Sci 2012; 125: 399-410.
[16] Garcia-Martinez L, Adams AM, Chan HL, Nakata Y, Weich N, Stransky S, Zhang Z, Alshalalfa M, Sarria L, Mahal BA, Kesmodel SB, Celia-Terrassa T, Liu Z, Minucci S, Bilbao D, Sidoli S, Verdun RE and Morey L. Endocrine resistance and breast cancer plasticity are controlled by CoREST. Nat Struct Mol Biol 2022; 29: 1122-1135.
[17] Xiong Y, Wang L, Di Giorgio E, Akimova T, Beier UH, Han R, Trevisanut M, Kalin JH, Cole PA and Hancock WW. Inhibiting the coregulator CoREST impairs Foxp3(+) Treg function and promotes antitumor immunity. J Clin Invest 2020; 130: 1830-1842.
[18] Volvert ML, Prevot PP, Close P, Laguesse S, Pirotte S, Hemphill J, Rogister F, Kruzy N, Sacheli R, Moonen G, Deiters A, Merkenschlager M, Chariot A, Malgrange B, Godin JD and Nguyen L. MicroRNA targeting of CoREST controls polarization of migrating cortical neurons. Cell Rep 2014; 7: 1168-1183.
[19] Baudet ML, Zivraj KH, Abreu-Goodger C, Muldal A, Armisen J, Blenkiron C, Goldstein LD, Miska EA and Holt CE. miR-124 acts through CoREST to control onset of Sema3A sensitivity in navigating retinal growth cones. Nat Neurosci 2011; 15: 29-38.
[20] Packer AN, Xing Y, Harper SQ, Jones L and Davidson BL. The bifunctional microRNA miR-9/miR-9* regulates REST and CoREST and is downregulated in Huntington's disease. J Neurosci 2008; 28: 14341-14346.
[21] Das E and Bhattacharyya NP. MicroRNA-432 contributes to dopamine cocktail and retinoic acid induced differentiation of human neuroblastoma cells by targeting NESTIN and RCOR1 genes. FEBS Lett 2014; 588: 1706-1714.
[22] Chhabra R, Dubey R and Saini N. Cooperative and individualistic functions of the microRNAs in the miR-23a~27a~24-2 cluster and its implication in human diseases. Mol Cancer 2010; 9: 232.
[23] Liang T, Yu J, Liu C and Guo L. An exploration of evolution, maturation, expression and function relationships in mir-23 approximately 27 approximately 24 cluster. PLoS One 2014; 9: e106223.
[24] Wienholds E, Kloosterman WP, Miska E, Alvarez-Saavedra E, Berezikov E, de Bruijn E, Horvitz HR, Kauppinen S and Plasterk RH. MicroRNA expression in zebrafish embryonic development. Science 2005; 309: 310-311.
[25] Acunzo M, Romano G, Palmieri D, Lagana A, Garofalo M, Balatti V, Drusco A, Chiariello M, Nana-Sinkam P and Croce CM. Cross-talk between MET and EGFR in non-small cell lung cancer involves miR-27a and Sprouty2. Proc Natl Acad Sci U S A 2013; 110: 8573-8578.
[26] Lin ST, Huang Y, Zhang L, Heng MY, Ptacek LJ and Fu YH. MicroRNA-23a promotes myelination in the central nervous system. Proc Natl Acad Sci U S A 2013; 110: 17468-17473.
[27] Chhabra R, Adlakha YK, Hariharan M, Scaria V and Saini N. Upregulation of miR-23a-27a-24-2 cluster induces caspase-dependent and -independent apoptosis in human embryonic kidney cells. PLoS One 2009; 4: e5848.
[28] Majid S, Dar AA, Saini S, Arora S, Shahryari V, Zaman MS, Chang I, Yamamura S, Tanaka Y, Deng G and Dahiya R. miR-23b represses proto-oncogene src kinase and functions as methylation-silenced tumor suppressor with diagnostic and prognostic significance in prostate cancer. Cancer Res 2012; 72: 6435-6446.
[29] Huang TT, Ping YH, Wang AM, Ke CC, Fang WL, Huang KH, Lee HC, Chi CW and Yeh TS. The

reciprocal regulation loop of Notch2 pathway and miR-23b in controlling gastric carcinogenesis. Oncotarget 2015; 6: 18012-18026.
[30] Majid S, Dar AA, Saini S, Deng G, Chang I, Greene K, Tanaka Y, Dahiya R and Yamamura S. MicroRNA-23b functions as a tumor suppressor by regulating Zeb1 in bladder cancer. PLoS One 2013; 8: e67686.
[31] Campos-Viguri GE, Peralta-Zaragoza O, Jimenez-Wences H, Longinos-Gonzalez AE, Castanon-Sanchez CA, Ramirez-Carrillo M, Camarillo CL, Castaneda-Saucedo E, Jimenez-Lopez MA, Martinez-Carrillo DN and Fernandez-Tilapa G. MiR-23b-3p reduces the proliferation, migration and invasion of cervical cancer cell lines via the reduction of c-Met expression. Sci Rep 2020; 10: 3256.
[32] Zhu R, Li X and Ma Y. miR-23b-3p suppressing PGC1alpha promotes proliferation through reprogramming metabolism in osteosarcoma. Cell Death Dis 2019; 10: 381.
[33] Fan L, Cao X and Lei Y. MicroRNA miR-23b-3p promotes osteosarcoma by targeting ventricular zone expressed PH domain-containing 1 (VEPH1)/phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) pathway. Bioengineered 2021; 12: 12568-12582.
[34] Jin L, Wessely O, Marcusson EG, Ivan C, Calin GA and Alahari SK. Prooncogenic factors miR-23b and miR-27b are regulated by Her2/Neu, EGF, and TNF-alpha in breast cancer. Cancer Res 2013; 73: 2884-2896.
[35] Huang Z, Zhang N, Ma W, Dai X and Liu J. MiR-337-3p promotes chondrocytes proliferation and inhibits apoptosis by regulating PTEN/AKT axis in osteoarthritis. Biomed Pharmacother 2017; 95: 1194-1200.