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# MicroRNA-21 EXPRESSION IN PROSTATE CANCER: A SYSTEMATIC REVIEW

**Maria Ulfa[1]*, Krisna Murti[1], Irsan Saleh[2], Debby Handayati[3]**
[1]Departement of Anatomical Pathology, Faculty of Medicine, Universitas Sriwijaya, Jalan Dokter Muhammad Ali, Sekip Jaya, Kemuning, Palembang, Sumatera Selatan 30114, Indonesia
[2]Department of Biomedical science of Doctoral Program, Faculty of Medicine, Universitas Sriwijaya, Jalan Dokter Muhammad Ali, Sekip Jaya, Kemuning, Palembang, Sumatera Selatan 30114, Indonesia
[3]Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Jalan Dokter Muhammad Ali, Sekip Jaya, Kemuning, Palembang, Sumatera Selatan 30114, Indonesia
*mariaulfa@fk.unsri.ac.id

**ABSTRACT**
Prostate cancer is the second most prevalent and fourth largest cause of death for men globally. Meanwhile, in Indonesia, prostate cancer ranks and is the fourth leading cause of death. Molecular studies continue to be conducted to understand the molecular heterogeneity, both genetic and epigenetic, that affects the progression of prostate cancer, one of which is the role of microRNA. This study aims to analyze the expression profile of microRNA-21 associated with the development and aggressiveness of prostate cancer. Comprehensive search into three databases; PubMed, Cochrane Library, and Science Direct was performed by authors. The study that best met the inclusion criteria was chosen from among duplicates. The QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool was used to assess the risk of bias before the relevant data were retrieved for analysis. There were eleven studies that included a variety of sample sources, sample size and methods. Although a number of the studies had unclear standard reporting, the research overall quality was acceptable. For the results, Prostate cancer samples showed a significantly higher expression level of miR-21 than controls in ten of the studies, and was linked to cancer aggressiveness. In one study, the expression of miR-21 did not significantly increase, despite the use of extracellular vesicle isolation samples.

Keywords: expression; microRNA-21; prostate cancer

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## INTRODUCTION

Prostate cancer (PCa) is one type of cancer that commonly found in men. If this cancer is diagnosed at an early stage, the patient's prognosis is good, whereas if diagnosed at an advanced stage, the prognosis becomes poor (Amin MB et al.,2022; Ferlay J et al.,2024). Research on the molecular heterogeneity, that influences the development of prostate cancer is still ongoing. One such study is the role of microRNA (Abudoubari et al.,2023; Doldi V et al.,2021). MicroRNA (miRNA/miR) is a small non-coding RNA involved in the regulation of up to 60% of protein-coding genes. miRNA are involved in carcinogenesis, which includes the processes of differentiation, proliferation, apoptosis, epithelial-mesenchymal transition (EMT), and tumor angiogenesis (Sidarova EA et al.,2023;Velky JE & Ricke WA 2020). The involvement of miRNA in prostate cancer was first reported by Porkka et al, whose study results showed dysregulation of 51 miRNAs in patient samples, both upregulation and downregulation. Some miRNAs that showed changes are located in the genome associated with prostate cancer (Porkka KP et al.,2007). miR-21 is one of the miRNAs involved in the carcinogenesis of prostate cancer. Upregulation of miR-21 is consistently found in prostate cancer associated with metastasis, so the aggressiveness and recurrence of prostate cancer correlate with high expression of miR-21. Additionally, the increased expression of miR-21 promotes the spread of prostate cancer, particularly to the bones (Rafikova G et al.,2023; Bilal

M et al.,2022). miR-21 is involved in the development of prostate cancer through various molecular mechanisms. As an oncogene (oncomiR), miR-21 plays a role in promoting the growth, proliferation, invasion, and resistance of prostate cancer by targeting various tumor suppressor genes such as TGFβR2, PTEN, PDCD4, and RECK. The main target of miR-21 is the PDCD4 gene, the suppression of PDCD4 allows the proliferation and migration of cancer cells. miR-21 also suppresses PTEN expression, and the reduction of PTEN decreases AR degradation, thereby enhancing AR activity and creating a positive feedback loop that supports cancer growth.Targeting PTEN will activate the PI3K/Akt pathway, which supports the proliferation and migration of prostate cancer cells (Shukla KK et al.,2023; Sanchez DB et al.,2020). Additionally, miR-21 affects the hypoxia and ROS pathways, induced by hypoxic conditions in prostate cancer, which will increase the expression of miR-21 and suppress the expression of RHOB, a tumor suppressor gene, thereby facilitating the development of prostate cancer. ROS triggers the Akt pathway, which increases the expression of miR-21, enhancing the invasive capabilities of prostate cancer cells that support cancer invasion and aggressiveness (Bilal M et al.,2022; Thorson P&Humphrey PA 2000).

## METHOD

### Literature Search & Strategy

A comprehensive search of three databases; PubMed, Cochrane Library, and ScienceDirect was independently performed by all authors to identify any relevant miRNA expression profiling studies published in English, spanning from 2015 to 2025. The search terms used in the title and abstract were: (“microRNA-21” OR “miR-21“ OR “miRNA-21” OR "MIRN-21") and (“Prostate cancer” OR “Prostate Neoplasm”). Detailed search strategies are provided in the Table 1. Any disagreements between investigators were discussed and resolved through consensus by the corresponding authors (MU).

Table 1.
Summary of Search Strategy

| No. | Database | Keywords & Operators | Hits |
|---|---|---|---|
| 1 | Cochrane | (Prostate Cancer) AND (MicroRNA-21) | 2 |
| 2 | Science Direct | ("Prostate Cancer" OR "Prostate Neoplasm") AND ("microRNA-21" OR "miRNA-21" OR "miR-21) | 969 |
| 4 | PubMed | ("Prostate Cancer "OR "Prostatic Neoplasms") AND ("MIRN21" OR "microRNA-21" OR miR-21") | 23 |

### Literature Selection

The inclusion criteria for studies were: 1) subject comprised of prostate cancer patients; 2) miRNA samples derived from blood, plasma, serum, urine, seminal fluid, tissue and FFPE; 3) dysregulated miRNAs with specified sample sizes; 4) miRNA expression levels measured by qPCR, RT-PCR, microarray assay or others; 5) studies published in English. Exclusion criteria were: 1) cell-line experimental studies; 2) non-clinical study-based publications; 3) patients with multiple primary tumours; 4) studies with insufficient data for analysis. When duplicated studies from the same research were encountered, the study that best fit the inclusion criteria was selected. Two investigators (MU and KM) independently reviewed the studies for eligibility, with any discrepancies resolved by a third reviewer (IS or DH) through consensus.

### Data Collection & Quality Assessment

Data from all eligible studies were extracted independently, including information on the first author, year of publication, sample source, miRNA detection methods, number of specimens, normalisation standards, and the lists of miR-21 expression. The quality of the included articles was evaluated using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool, which consists of eight key checklists. Both investigators performed the quality

assessment independently, and any discrepancies were resolved through discussion until decision was reached.

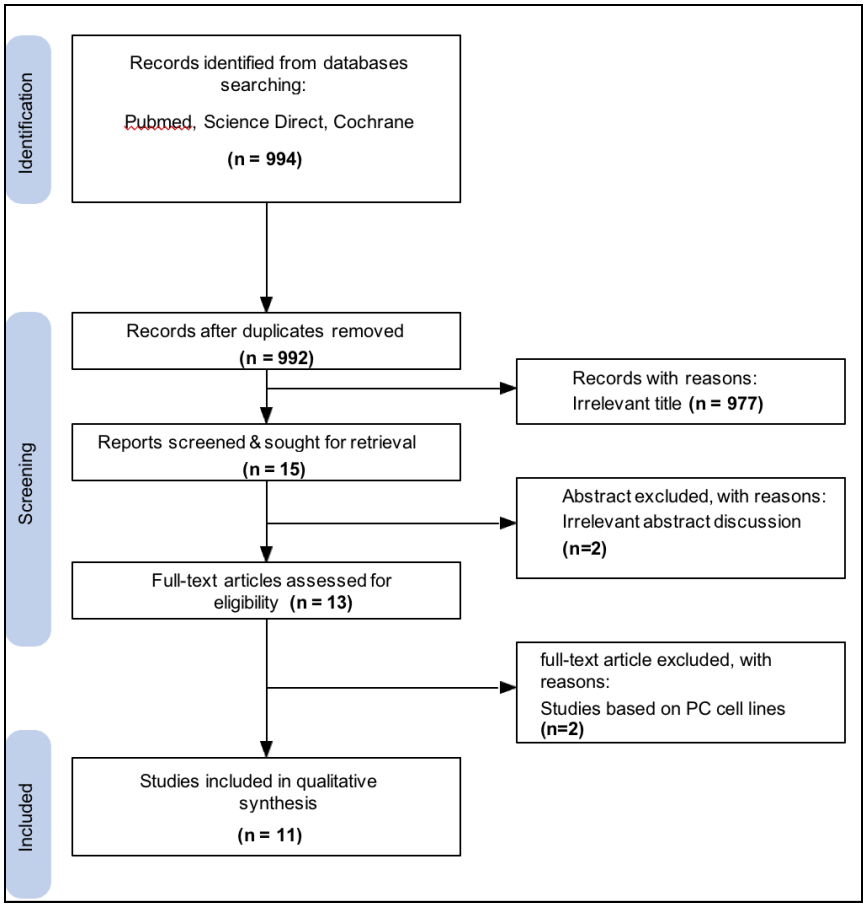


Fig 1. Search Strategy using PRISMA flowchart

## RESULT

The study retrieval process using PRISMA flowchart is summarized in Figure 1**.** There were 994 records in all in the search result, which were first found by searching Science Direct, the Cochrane Library, and PubMed. Two duplicate entries were eliminated, leaving 992 studies. Titles and abstracts were used to screen records, and 977 records were deemed irrelevant. Full-text readings of the remaining 15 articles were sought. Two articles were eliminated after the abstract screening process because they did not meet the inclusion requirements. The eligibility of thirteen full-text articles was then evaluated. According to a further examination, two more articles were disqualified for using prostate cancer cell lines in their research. In the end, 11 research that focused on the levels of miR-21 expression in prostate cancer patient samples were included into the qualitative synthesis (summarized in the Table 2). A variety of sample sources, including serum, plasma, exosomal, PBMC, urine, tissue, and FFPE, were used in the 11 research, which were published between 2015 and 2025. Prostate cancer patients in the included studies range in number from 15 to 149, and the size of the control groups varies as well. RT-PCR served as the main technique for evaluating miRNA expression in each study. Remarkably, several normalizing criteria were documented; yet, certain studies did not provide a standard. The expression level of miR-21 on prostate cancer samples was determined by each study. The majority of the studies showed an increase (upregulated) in miR-21 expression.

Table 2.
Summary of Study Characteristics

| Study | Sample source | Method | Sample size | | Normalization standards | miR-21expression in PCa |
|---|---|---|---|---|---|---|
| | | | Case | Control | | |
| Pang S et al. (2024) | Urine | silver nanoparticle sensor and qRT-PCR | 30 (PCa) | 8 (3 BPH, 5 healthy person) | Not Reported | Upregulated |
| Shukla K et al. (2023) | Tissue, plasma | qRT-PCR | 45 (localised PCa) 45 (metastatic PCa) | 45 (BPH) | RNU6 | Upregulated |
| Gunawan R et al. (2023) | Urine | qRT-PCR | 20 (PCa) | 20 (BPH) | Hsa-miR-16-5p | Upregulated |
| Jokovic S et al. (2022) | Plasma, exosomal | qRT-PCR | 34 (PCa) | 34 (BPH) | hsa-miR-1228 | Upregulated in exosomal |
| Kim J et al. (2021) | Plasma | qRT-PCR | 38 (PCa) | 8 (BPH) | Not Reported | not significantly altered |
| Zedan A et al. (2019) | Plasma | RT-PCR | 149 (Local or locally advanced PCa) | - | miR-17 | Upregulated |
| Kumar B et al. (2018) | Tissue | RT-ddPCR | 15 (Primary PCa) | 15 (normal prostate) | RNU6B | Upregulated |
| Forzycki et al. (2018) | Serum | RT-PCR | 20 (PCa) | 6 (healthy person) | RNU6 and SNORD44 | Upregulated |
| Stuopelyte K et al. (2016) | Tissue, urine | qRT-PCR | 143 (PCa) | 12 (BPH) | Not Reported | Upregulated |
| Yang B et al. (2016) | PBMC | RT-PCR | 92 (PCa) | 85 (BPH) 97 (healthy person) | miR-16 | Upregulated |
| Mohamad M et al. (2016) | FFPE | qRT-PCR | 16 (PCa) | 20 (BPH) | GAPDH | Upregulated |

PBMC: Peripheral blood mononuclear cell ; PCa:prostate cancer ; BPH: benign prostate hyperplasia ; FFPE: formalin-fixed parafin embedded

**Study Quality**

The QUADAS-2 tool was used to evaluate the quality of the included studies, as explained in the methods section. The majority of the studies satisfied the crucial requirements for patient selection, index testing, flow, and timing, however their quality varied. Due to inconsistent explanations of sample normalization techniques, certain research pose an unknown risk with regard to reporting reference standards. However, the included studies' overall quality is deemed suitable for qualitative synthesis. Discussions among the researchers helped to settle all disagreements.

**miR-21 Expression Analysis**

Ten out of the eleven studies showed an increase in miR-21 expression, whereas the other one did not. Six studies compared the expression of miR-21 in PCa samples with that in BPH samples, two compared them with normal prostates or healthy person, and two compared them with both. Whereas one study assessed the expression of miR-21 in local or locally advanced PCa. Two studies that report different miR-21 expression results in two different types of samples. Jokovic S et al reported that the expression levels of miR-21 in exosomes were significantly higher in aggressive cancer, but no significant difference was found in plasma miR-21 levels between PCa and BPH (Jokovic s et al.,2022). Furthermore, Stuopelyte K et al reported that miR-21 expression is upregulated in PCa tissues and blood, but lower in urine samples (Stuopelyte K et al.,2016). The only study that reported different results was Kim J et

al, who reported that the expression of miR-21 did not significantly increase in extracellular vesicles (Kim J et al.,2021).

## DISCUSSION

miRNAs are generally located in genomic lesions associated with cancer or within fragile chromosomes that exhibit DNA amplification, deletion, or translocation during tumor development (Doldi V et al.,2021; Ge Qi et al.,2023). About 20-40% of miRNAs are located near CpG islands, confirming the possibility of epigenetic silencing, especially in urological diseases (Doldi V et al.,2021). Recent research showed that miRNA encapsulated in extracellular vesicles modulates both the local and distant tumor microenvironment, allowing prostate cancer cells and tumor microenvironment cells to communicate with each other, which contributes to the development of the tumor microenvironment (Ge Qi et al.,2023).

Biochemical progression (increasing PSA levels) and metastatic progression (metastasis to bones and other organs) are the hallmarks of castration-resistant prostate cancer (CRPC), a kind of prostate cancer that is resistant to androgen deprivation therapy (ADT). Because the change to this state is associated with a bad prognosis, subsequent studies have concentrated on the molecular mechanisms underlying this process. miR-21 contributes to hormonal resistance by supporting oncogenic pathways that maintain cancer cell proliferation even after androgen-based therapy has been administered and also promotes oncogenic pathways that sustain cancer cell proliferation even after androgen-based therapy has been provided, it plays a role in hormonal resistance (Gan L et al.,2024; Umbas R et al.,2011).

miR-21 promotes androgen reseptor activity even under low androgen circumstances, it can increase resistance to ADT (Eringyte L et al.,2020). Previous study demonstrated that direct transcriptional regulation is indicated by androgen-induced AR binding to the miR-21 promoter. Furthermore, it has been demonstrated that increased expression of miR-21 enhances in vivo prostate tumor growth and is sufficient for androgen-dependent tumors to overcome castration-mediated growth cessation, which is consistent with the CRPC phenotype. Inhibition of miR-21 also decreases the proliferation of androgen-induced prostate cancer cells. Therefore, castration resistance can be conferred simply by increased expression of miR-21 (Porkka KP et al.,2007).

Upregulation of miR-21 expression is associated with a more aggressive phenotype of prostate cancer. Suppression of PTEN and PDCD4 in PCa, which results in excessive expression of miR-21, leading to the CRPC phenotype (Kojima S et al.,2017). Recent studies show that the overexpression of miR-21 causes aberrant TGFβ signaling, EMT, increased aggressiveness, and metastasis in prostate cancer (Kirandep et al.,2016). Specifically, miR-21 targets the PDCD4 gene, which inhibits osteoclast differentiation, promotes osteoclastogenesis, and accelerates bone damage, making miR-21 one of the commonly found pro-metastatic miRNAs in metastatic bone prostate cancer (Taheri M et al.,2021).

Based on the results of this systematic review, upregulation of miR-21 expression was reported in 10 studies. Jokovic S et al showed patients with PCa whose PSA was greater than 20 ng/mL and with aggressive prostate cancer had significantly higher levels of exosomal miR-21. However, there was no significantly difference in the levels of miR-21 between PCa and BPH in the plasma samples. This suggests that exosomal miR-21 might be a more accurate diagnostic for aggressive prostate cancer than circulating plasma miR-21 (Jokovic S et al.,2022). Shukla K et al found that miR-21 expression was considerably upregulated in both localized and metastatic prostate cancer, and that it was correlated with greater levels of prostate CSC markers including CD44+/CD24- and CD44+/CD133+. Prostate cancer stem cells (PCSCs), which are connected to tumor development, treatment resistance, and metastasis, proliferate when miR-21 is present. Higher levels of prostate CSC markers are

correlated with increased miR-21 expression, suggesting that miR-21 plays a role in preserving stemness and tumor development in PCa with bone metastases (Shukla K et al 2023). Mohamad M et al also showed upregulated expression of miR-21. Vinculin (VCL), a crucial tumor suppressor involved in cell adhesion and migration, was discovered to be negatively regulated by miR-21. The downexpression of VCL causes the tumor's motility and invasion to increase, which facilitates the patient PCa's spread (Mohamad M et al.,2016).

The results of a study by Forzycki et al, that measured the expression of miR-21, miR-141, and miR-375 indicate that combining these three miRNAs increased the detection accuracy of PCa. This combination provided higher predictive value (93%), making it more effective than a single miRNA (Porzycki et al.,2018). Yang B et al**.** reported a clear differentiation between PCa and non-cancerous controls by expressing miR-21 using PCa samples from peripheral blood mononuclear cells (PBMCs). Key clinical characteristics such advanced stages, high Gleason score, PCa with bone metastases, and tumor recurrence were all highly connected with miR-21 expression. As an oncogene, miR-21 suppresses tumor suppressor genes such PDCD4, PTEN, and SMAD7, which lowers apoptosis and increases tumor cell survival. Thus, the aggressiveness of cancer is linked to the overexpression of miR-21 (Yang B. et al.,2016). Tumor progression and recurrence are aggressive PCa indicators. According to Kumar et al, PCa patients who had higher expression of miR-21 also had a worse prognosis following radical prostatectomy and were considerably more likely to experience biochemical recurrence. In addition, this study showed that miR-21 is expressed in both the stromal and epithelial compartments of prostate tissue. In contrast to the epithelium, the stroma showed greater expression of miR-21 (Kumar B et al.,2018). Pang ST et al evaluated the expression of miR-21 in urine samples using a silver nanoparticle-based biosensor that confirmed by RT-PCR, showing significantly increased expression, which then decreases post-surgery. This study introduces a highly sensitive biosensor that offers a promising alternative to PSA testing, improving early detection and treatment monitoring of PCa (Pang ST et al.,2024).

Zedan AH et al examined the expression levels of circulating miRNA in patients with localized/locally advanced prostate cancer following radical prostatectomy and radiation therapy. They evaluated the expression of four miRNAs (miR-21, miR-93, miR-125b, and miR-221) and found that there was a weak correlation between the plasma levels of miR-21 with tumor stage (cT), but no significant correlation with PSA, Gleason score, or risk profile. miR-21 did not significantly change after intervention, suggesting that it may not be permanently impacted by radikal or radiotherapy prostatectomies. In contrast, miR-93 and miR-221 significantly decreased after treatment (Zedan AH et al.,2019). Stuopelyte K et al found that miR-21 levels were lower in urine from PCa patients compared to BPH patients, which contrasts with findings in prostate tissue and blood where miR-21 is typically overexpressed. Different processes of miRNA production in urine versus blood circulation may be the cause of this disparity. It has been proposed that in cases of aggressive PCa, miR-21 may be excreted differently or may be selectively maintained in cancer cells (Stuopelyte K et al.,2016). Unlike Gunawan RR et al, who also assessed miR-21 expression through urine samples, it was found that miR-21 is significantly overexpressed in prostate cancer (PCa) patients compared to benign prostatic hyperplasia (BPH) patients, supporting its potential as a non-invasive biomarker (Gunawan RR et al.,2023). The only differing result reported by Kim J et al, there was no discernible variation in the expression levels of miR-21 between PCa and BPH patients when it was examined in extracellular vesicles (EVs) that were separated from plasma. Accordingly, miR-21 levels in EVs could not be a strong indicator of prostate cancer when analyzed in isolation (Kim et al.,2021)

## CONCLUSION

According to the results of this systematic review study, miR-21 expression was frequently upregulated in prostate cancer patients, and was linked to cancer aggressiveness. Large-scale

research is still required to determine whether this miRNA could be a useful biomarker for prostate cancer patients' diagnosis and prognosis.

## REFERENCES


Abudoubari, S., Ke, B., Mei, Y., Maimaitiyiming, A., An, H., & Tao, N. (2023). Preliminary study in miRNA in prostate cancer. *World Journal of Surgical Oncology*, 21,270. https://doi.org/10.1186/s12957-023-03151-1

Amin, MB., Kench, JG., Rubin, MA., Srigley, JR., & Tsuzuki, T. (2022). *WHO Classification of Tumours Urinary and Male Genital Tumours* (5th ed.). IARC

Bilal, M., Javaid, A., Amjad, F., Youssif, TA., & Afzal, S. (2022). An overview of prostate cancer (PCa) diagnosis: Potential Role of miRNAs. *Translational Oncology*, 26,101542. doi: 10.1016/j.tranon.2022.101542

Doldi,V., Bezawy, RE., & Zaffaroni, N. (2021). MicroRNAs as Epigenetic Determinants of Treatment Response and Potential Therapeutic Targets in Prostate Cancer. *Cancer*,13, 2380. https://doi.org/10.3390/cancers13102380

Eringyte, L., Losada, JN., Powell, SM., Bevan, CL., & Fletcher CE. (2020). Coordinated AR and microRNA regulation in prostate cancer. *Asian Journal of Urology*,7(3),233-250. doi: 10.1016/j.ajur.2020.06.003

Ferlay, J., Ervik, M., Lam, F., Laversanne, M., Colombet, M., Mery, L., Pineros, M., Znaor, A., Soerjomataram, I., & Bray, F.(2024). *Global Cancer Observatory*. http: //gco.iarc.who.int

Gan, L., Zheng, L., Zou, J., Luo, P., Chen, T., Zou, J., Li, W., Chen, Qi., Cheng, L., Zhang, F.,& Qian, B. (2024). MicroRNA-21 in urologic cancers: from molecular mechanism to clinical implications. *Front. Cell Dev. Biol*, 12, 1437951. doi: 10.3389/fcell.2024.1437951

Ge, Qi., Li, J., Yang, F., Tian, X., Zhang, M., Hao, Z., Liang, C., & Meng, J. (2023). Molecular classifications of prostate cancer: basis for individualized risk stratification and precision therapy. *Ann Med*, 8, 55(2),2279235. doi: 10.1080/07853890.2023.2279235

Gunawan, RR., Indwiani, A., & Danarto, HR. (2023). miRNA-21 as High Potential Prostate Cancer Biomarker in Prostate Cancer Patients in Indonesia. *Asian Pac J Cancer Prev*, 24 (3), 1095-1099. doi:10.31557/APJCP.2023.24.3.1095

Jokovic, SM., Dobrijevic, Z., Kotarac, N., Filipovic, L., Popovic, M., Korac, A., Ivan.,Vukovic, I., Pavicevic, DS., & Goran, Brajuskovic. (2022). MiR-375 and miR-21 as Potential Biomarkers of Prostate Cancer: Comparison of Matching Samples of Plasma and Exosomes. *Genes*, 13, 2320. https://doi.org/10.3390/genes13122320

Kim, J., Cho, S., Park, Y., Lee, J., & Park, J. (2021). Evaluation of micro-RNA in extracellular vesicles from blood of patients with prostate cancer. *PLoS ONE*, 16(12), e0262017. https://doi.org/10.1371/ journal.pone.0262017

Kirandeep., Sekhon, K., Bucay, N., Majid, S., Dahiya, R., & Saini, S. (2016). MicroRNAs and Epithelial-mesenchymal transition in prostate cancer. *Oncotarget*, 7(41), 67597-67611. https://doi.org/10.18632/oncotarget.11708

Kojima, S., Goto, Y., & Naya, Y. (2017). The roles of microRNAs in the progression of castration-resistent prostate cancer. *Journal of Human Genetics*, 62,25-31. doi:10.1038/jhg.2016.69

Kumar, B., Rosenberg, AZ., Choi, SM,. Talbot, KF., De, M., Nonn, L., Brennen, WN., Marchionni, L., Halushka, MK., & Lupold, SE. (2018). Cell-type specific expression of oncogenic and tumor suppressive microRNAs in the human prostate and prostate cancer. *Scientific Reports*, 8,7189. doi:10.1038/s41598-018-25320-z

Mohamad, M., Wahab, NA., Yunus, R., Murad, NA., Zainuddin, Z., Sundaram, M., & Mokhtar, NM. (2016). Roles of MicroRNA-21 and MicroRNA-29a in Regulating Cell Adhesion Related Genes in Bone Metastasis Secondary to Prostate Cancer. *Asian Pac J Cancer Prev*, 17 (7), 3437-3445

Pang, ST., Chiou, YE., Lim, J., Zhang, YC., Zeng, WZ., Ong, TA., & Weng, WH. (2024). Urinary MicroRNA-21 for Prostate Cancer Detection Using a Silver Nanoparticle Sensor: A Promising Diagnostic Tool. *Biosensors*,14,599. https:// doi.org/10.3390/bios14120599

Porkka, KP., Pfeiffer, MJ., Waltering, KK., Vassella, RL., Tammela, TL.,& Visakorpi, T. (2007). MicroRNA expression profiling in prostate cancer. *Cancer Res*, 67 (13), 6131-6135. doi: 10.1158/0008-5472.CAN-07-0533

Porzycki, P., Ciszkowicz, E., Semik, M., & Tyrka, M. (2018). Combination of three miRNA (miR-141, miR-21, and miR-375) as potential diagnostic tool for prostate cancer recognition. *International Urology and Nephrology*, 50, 1619–1626. https://doi.org/10.1007/s11255-018-1938-2

Rafikova, G., Gilyazova, I., Enikeeva, K., Pavlov, V., & Kzhyshkowska, J. (2023). Prostate Cancer: Genetics, Epigenetics, and the Need of Immunological Biomarkers. *Int J Mol Sci*, 24,12797. doi: 10.3390/ijms241612797

Sanchez, DB., Canon, CA., Torres, AP., Velazquez, IA., Barrios, RG., Espinosa, LC., Manriquez, RM., Hernandez, CC., Ontiveros, VF., Gomez, RM., & Herrera, LA. (2020). The Promising Role of miR-21 as a Cancer Biomarker and Its Importance in RNA-Based Therapeutics. *Molecular Therapy:Nucleic Acids*, 20, 409-420. doi: 10.1016/j.omtn.2020.03.003

Shukla, KK., Choudhary, GR., Sankanagoudar, S., Misra, S., Vishnoi, JR., Pareek, P., Pilla, KK., Pandey, SN., & Sharma, P. (2023). Deregulation of miR-10b and miR-21 Correlate with Cancer Stem Cells Expansion through the Apoptotic Pathway in Prostate Cancer. *Asian Pac J Cancer Prev*, 24 (6), 2105-2119. doi:10.31557/APJCP.2023.24.6.2105

Sidarova, EA., Zhernov, YV., Antsupova, MA., Khadzhieva, KR., Izmailova, AA., Kraskevich, DA., Belova, EF., Simanovsky, AA., Shcherbakov, DV., Zabroda, NN., & Mitrokhin, OV. (2023). The Role of Different Types of microRNA in the Pathogenesis of Breast and Prostate Cancer. *Int J Mol Sci*, 24,1980. https://doi.org/10.3390/ijms24031980

Stuopelyte, K., Daniunaite, K., Jankevicius, F.,& Jarmalaite, S. (2016). Detection of miRNAs in urine of prostate cancer patients. *Medicina*, 52, 116-124

Taheri, M., Khoshbakht, T., Jamali, E., Kallenbach, J., Fard, SG., & Baniahmad, A. (2021). Interaction between Non-Coding RNAs and Androgen Receptor with an Especial Focus on Prostate Cancer. *Cells*, 10, 3198. https://doi.org/10.3390/cells10113198

Thorson, P.,& Humphrey, PA. (2000). Minimal adenocarcinoma in prostate needle biopsy tissue. *Am J Clin Pathol*, 114 (6), 896-909. doi: 10.1309/kvpx-c1em-142l-1m6w

Umbas, R., Hardjowijoto, S., Mochtar, CA., Safriadi, F., Djatisoesanto, W., Soedarso, MA., Danarto., & Sihombing, AT. (2011). *Panduan Penanganan Kanker Prostat*. Ikatan Ahli Urologi Indonesia

Vellky, JE., & Ricke, WA. (2020). Development and prevalence of castration-resistent prostate cancer subtypes. *Neoplasia*, 22, 566-575

Yang, B., Liu, Z., Ning, H., Zhang, K., Pan, D., Ding, K., Huang, W., Kang, XL., Wang, Y,.& Chen, X. (2016). MicroRNA-21 in peripheral blood mononuclear cells as a novel biomarker in the diagnosis and prognosis of prostate cancer. *Cancer Biomarkers*, 17, 223–230. doi:10.3233/CBM-160634

Zedan, AH., Madsen, JS., Hansen, TF., Assenholt, J.,& Osther, JS. (2019). Circulating miRNAs in localized/locally advanced prostate cancer patients after radical prostatectomy and radiotherapy. *The Prostate*, 79, 425-432. doi: 10.1002/pros.23748