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miRNA-1226: As a Potential Diagnostic Marker in FFPE Tissue of Breast Cancer

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ABSTRACT

Backgrounds: Researchers have just commenced the exploration of miRNAs as a prospective new class of biomarkers. This study investigates the potential of miR-1226 as a significant prognostic factor for BC. **Methods:** The miR-1226 expression was detected in 30 pairs of FFPE tissues using qRT-PCR. The clinicopathological characteristics of patients regarding miR-1226 expression, together with fold change analysis using the $2^{-\Delta\Delta CT}$ method, were further investigated. All statistical analyses were performed with GraphPad and MedCalc. **Results:** We found that the miR-1226 level in BC FFPE tissues is slightly increased compared to control tissues. Also, we examined the relationship associated with clinicopathological features and miR-1226 expression levels of BC patients. This investigation revealed no significant association between miR-1226 expression levels and the clinical progression. Age, lymph node involvement, and Ki-67 expression had no significant correlation with outcome status. No significant relationships were observed between tumor-related factors such as grade and size. The hormone receptor status, PR status, and HER-2 status did not exhibit a significant correlation with outcome stratification. The trend regarding PR status may necessitate additional examination for its prognostic significance. Moreover, the p-value, AUC, and Std. Error, sensitivity, and specificity are ($p < 0.006$, 0.684,0.0723, 83.3, and 60, respectively), which signifies a moderate capacity of the test to differentiate between tumors and controls. The results of fold change analysis employing the $2^{-\Delta\Delta CT}$ method indicated a (1)-fold elevation in miR-1226 expression in tumors relative to controls. **Conclusions:** We demonstrated that a slight elevation of miR-1226 expression correlates with the progression of BC, and this indicates that miR-1226 may possess an oncogenic function in BC tumorigenesis and progression.

1. Introduction

Among females, breast cancer (BC) occurs more frequently than any other malignant tumor, with more than 2.3 million people diagnosed worldwide in 2023 (Siegel et al., 2023). Current research indicates that the death rate of breast cancer has risen in recent years, implying that the monitoring and treatment of tumor stage and progression in breast cancer patients remain insufficient (Houghton and Hankinson, 2021). Notwithstanding significant advancements in the early diagnosis of BC and the increasing accessibility of therapies, including surgical resection (Moore-Palhares et al., 2024), radiotherapy (Kaidar-Person et al., 2024), endocrine therapy (Ma et al., 2024), and immunotherapy (Michaels et al., 2024), patient's prognosis remains unfavorable due to the elevated incidence of distant metastases associated with BC. Consequently, there is an imperative demand for safer, more straightforward, and more precise methodologies for the prompt evaluation of tumor progression in breast cancer patients.

MicroRNAs, which are noncoding RNAs with a single strand and a short length (about 22 nucleotides), attach to the 3′UTR of target genes and either block translation or degrade them (Mahmoud et al., 2021, Hussen et al., 2023c). Cancerous tissues have microRNA expression levels that differ greatly from neighboring normal tissues, suggesting that these molecules may serve as diagnostic biomarkers. Evidence indicates that miRNAs exert diverse cellular regulatory effects, with certain miRNAs acting as oncogenes or tumor suppressor genes (Svoronos et al., 2016, Otmani and Lewalle, 2021). Extensive research have underscored the prognostic significance of miRNA-1226 in many malignancies, including pancreatic ductal adenocarcinoma (Wang et al., 2021), hepatocellular carcinoma(Chen et al., 2019), non-small cell lung cancer (Lin and Li, 2022), and nasopharyngeal carcinoma (Zhang et al., 2024). These results indicate that miRNA-1226 may function as a possible prognostic biomarker and underscore the pressing necessity for additional research to elucidate the molecular pathways influenced by this microRNA.

In this study, for the first time, we provided important clinical evidence that miR-1226 expression was upregulated in neoplastic tissue relative to neighboring non-neoplastic tissue in BC and linked to unfavorable outcomes in BC patients. Additionally, the results of fold change analysis employing the $2^{-\Delta\Delta CT}$ method indicated a (1.305)-fold elevation in the miR-1226 expression level of tumors relative to controls. This suggests that miR-1226 may have an oncogenic role in carcinogenesis, potentially promoting BC development.

2. Materials and methods

2.1. Sampling

Expressions of miR-1226 were quantified in 30 FFPE tissue samples of tumors and the non-tumorous tissues surrounding them. Tissues were obtained from the Par Hospital-Erbil, Kurdistan Region, Iraq. Patient consent and specimen acquisition were both handled in accordance with the standards set out by Par Hospital's protocol. Patients with BC were diagnosed and categorized using the TNM approach developed by the American Joint Committee on Cancer (AJCC). The clinical characteristics of the individuals covered are presented in (Table 1). The clinicopathological parameters and their relation with miR-1226 expression level, categorized as either low or high expression, are shown in (Table 2).

Table 2: Clinicopathological parameters and in relation to the expression level of miR-1226 among 30 cases, categorized as either low or high expression.

miR-1226 Expression Level					
Parameters	**Subclasses**	**Cases**	**Low**	**High**	**P-value**
Age (years)	≥50	26	24	2	0.360
	<50	4	3	1	
Tumor grade	I	2	1	1	0.636
	II	20	14	6	
	III	6	5	1	
	N/A	2	2	0	
Tumor size (mm)	≥15	28	20	8	0.377
	<15	2	2	0	
ER status	Negative	9	7	2	0.719
	Positive	21	15	6	
PR status	Negative	11	6	5	0.077
	Positive	19	16	3	
Her-2 status	Negative	22	15	7	0.290

	Positive	8	7	1	
Lymph Node	Negative	9	8	1	0.894
	Positive	21	19	2	
Ki67	Negative	19	17	2	0.887
	Positive	9	8	1	
	N/A	2	2	0	

2.2. RNA isolation and reverse transcription

Total RNA was isolated from 30 FFPE tissue pairs of tumoral samples and their control tissues utilizing the miRNeasy FFPE kit (Qiagen, catalog no 217504) and reverse transcribed into cDNA utilizing the miScript II RT Kit (cat. nos. 218161).

2.3. Real-time quantitative PCR

Two-step qRT-PCR was conducted following the manufacturer's instructions using the miScript SYBR Green PCR kit (Qiagen, catalog no. 218073), incorporating the miScript universal primer and the miR-1226-specific forward primer supplied by Immunogen CENTER. The primers for miR-1226 and the endogenous control U6 are shown in (Table 3). The U6 RNA was chosen as an endogenous reference to determine the relative amount of miR-1226 expression in tumor tissues in comparison to control tissues using the $2^{-\Delta\Delta Ct}$ approach, where [ΔCT = CT (a target miRNA) – CT (a reference gene)].

Table 3: Nucleotide sequences of primers.

miRNA & HKGs	Sequence of the primers
MiR-1226	Forward: AACAAGGTGAGGGCATGCAG Reverse: GTGCAGGGTCGGAGGT
U6	Forward: GTGCTGCTTGGGCAGCA Reverse: GAAATATGGAACGGTTC

Table 1. Clinical and demographic features of the enrolled patients.

No	Age	Size (mm)	Grade	Stage	ER	PR	Her-2	Lymph Node	Ki67
1	40	30	III	IIIA	+	-	-	+	+
2	56	26	II	IIB	+	-	-	+	-
3	55	35	II	IIB	+	-	-	+	-
4	57	24	II	IIIA	+	+	-	+	-
5	58	28	II	IIB	-	-	+	+	N/A
6	60	30	I	IIA	-	-	-	-	-
7	57	22	II	IIIA	+	+	-	+	-
8	77	30	II	IIA	+	+	-	-	-
9	58	6	II	IA	-	-	-	-	+
10	61	15 & 5	II	IIIA	+	+	+	+	N/A
11	53	40	N/A	N/A	-	-	+	-	-
12	60	27	II	IIA	+	+	-	-	-
13	62	32	II	IIA	+	+	-	-	-
14	59	25	II	IIIA	+	+	-	+	-
15	52	40	N/A	N/A	+	+	-	+	-
16	68	25	III	IIIA	-	-	+	+	+

17	66	15	II	IA	+	+	-	-	+
18	67	28	II	IIB	+	+	-	+	-
19	49	24	II	IIIC	+	+	-	+	-
20	52	70	III	IIIA	+	+	+	+	+
21	49	25	II	IIA	+	+	-	-	-
22	45	21	III	IIA	+	+	-	-	+
23	51	55	II	IIIA	-	-	+	+	+
24	54	18	I	IIA	+	+	-	+	-
25	70	24	II	IIA	+	+	-	+	-
26	56	45	II	IIIC	+	+	-	+	-
27	72	27	II	IIIA	+	+	-	+	-
28	69	17	III	IIIA	-	-	+	+	+
29	59	30	II	IIA	-	+	-	+	-
30	71	30	III	IIB	-	-	+	+	+

2.4. Statistical analyses

All statistical analyses were conducted utilizing GraphPad Prism version 8.4.3 (686) and MedCalc version 23.1.7. The Wilcoxon test was utilized to compare miRNA expression levels between the FFPE tissue of breast cancer patients and that of breast cancer controls. The Chi-square test (χ^2 test or X^2 test) was utilized to analyze the relationship between miR-1226 expression and clinicopathological characteristics. The ROC curve analysis was employed to assess the diagnostic significance of miR-1226.

3. Results

3.1. Clinical and pathological characteristics of BC patients and the expression of miR-1226

To examine the association between the overexpression of miR-1226 and the clinical development of BC, we assessed the correlation between miR-1226 expression levels and the clinicopathological characteristics of BC patients. As shown in (Table 2) and (Figure 1), Age stratification did not show a statistically significant correlation with the outcome (p = 0.360). Lymph node involvement (p = 0.894) demonstrated no significant relationship. Proliferation marker Ki-67 expression, categorized into three levels, yielded no significant association with outcome status (p = 0.887).

Tumor-related variables, including tumor grade and tumor size, were also evaluated. Neither parameter showed significant associations with the p-value of 0.636 and 0.377, respectively. Hormone receptor status analyses revealed no significant effect of ER status, with p-value = 0.719. PR status demonstrated a non-significant trend towards association, p-value = 0.077, with PR-negative tumors exhibiting a higher proportion of cases classified as High, suggesting potential clinical relevance that merits further investigation in larger cohorts. Finally, HER-2 status did not significantly correlate with outcome stratification, with a p-value of 0.290.

These data collectively suggest that, in this population, none of the assessed clinicopathological variables were significantly correlated with the dichotomized outcome measure. The nearly significant trend noted for PR status may necessitate more investigations with enhanced statistical power to elucidate its predictive value.

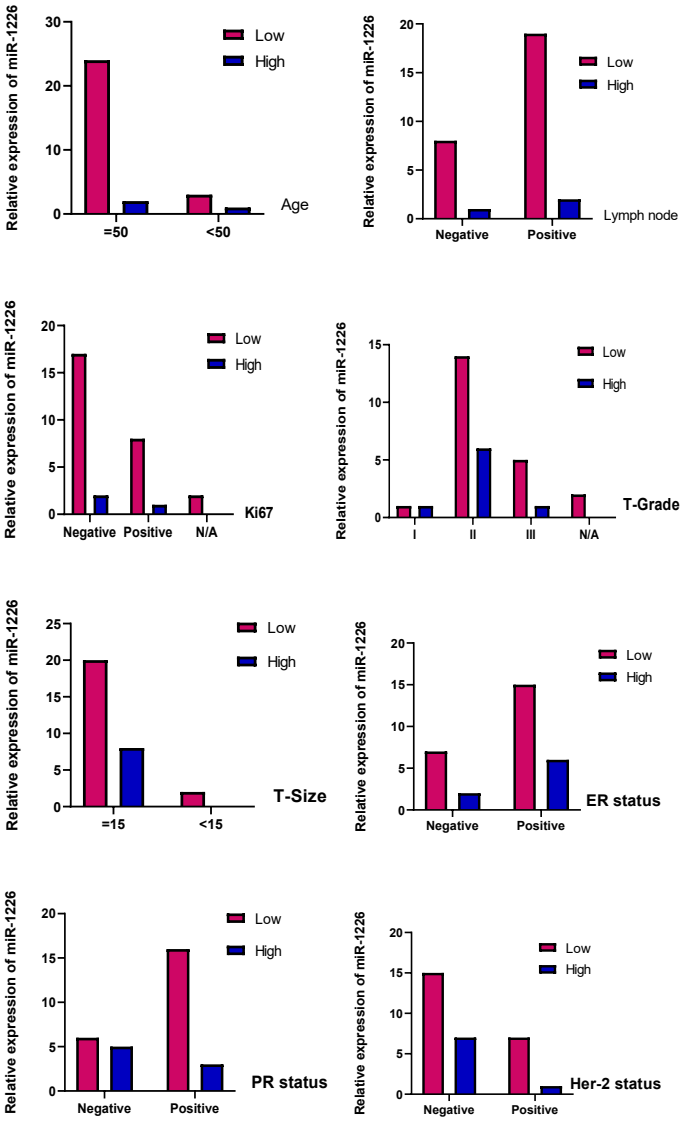

Figure 2 Shows the correlation between miR-1226 expression and BC clinical parameters.

3.2.Correlation and expression of miR-1226 and HKGs in FFPE tissues of BC

The expression levels of miR-1226 were compared between tumor and control samples using the Wilcoxon matched-pairs signed rank test. A significant difference was observed between the groups, with an exact two-tailed P-value of 0.008. The median expression level of miR-1226 in tumor samples was 35.04, compared to 33.11 in control samples, yielding a median difference of –1.930 (Figure 2). These findings indicate that miR-1226 expression is significantly altered in tumor tissues relative to controls.

In addition, the expression of HKGs was also compared between tumor and control groups using the Wilcoxon matched-pairs signed rank test. The analysis yielded an exact two-tailed P-value of 0.123, indicating no statistically significant difference (P > 0.05). The median expression level of HKGs in tumor samples was 37.10, compared to 34.95 in control samples, with a median difference of –2.150 (Figure 3). These findings suggest that HKG expression does not differ significantly between tumor and control tissues.

Furthermore, the ROC curve analysis was performed to evaluate the diagnostic performance of miR-1226 expression in distinguishing between tumor and control groups. The AUC was (0.6844), with a standard error of (0.07162) and a 95% confidence interval ranging from (0.5441 to 0.8248). The P-value from the ROC analysis was (0.014), signifying that miR-1226 possesses a statistically significant discriminatory capacity (Figure 4).

Overall, these findings demonstrate that miR-1226 is markedly elevated in tumor tissues relative to controls and may serve as a possible diagnostic biomarker, as evidenced by the ROC curve analysis. The disparities in housekeeping gene expression further corroborate the observed patterns' regularity.

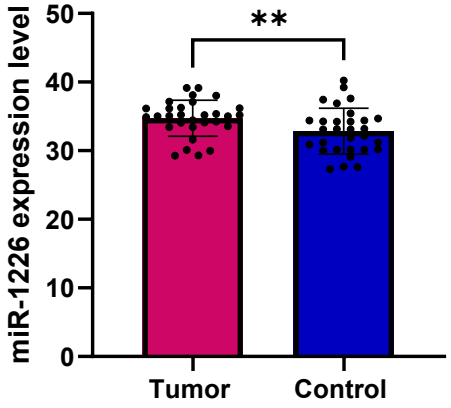

Figure 2. Relative expression level of miR-1226 in 30 FFPE tissue pairings of tumor samples and their control tissues. (**: p-value = 0.008).

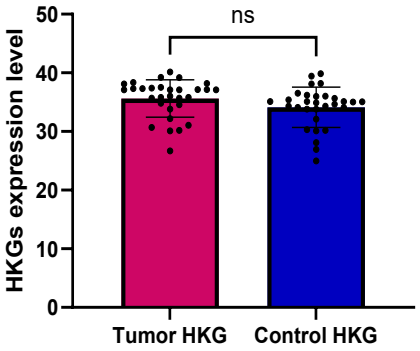

Figure 3. Relative expression level of miR-1226 HKGs in 30 FFPE tissue pairs of tumoral samples and their control tissues. (ns: p-value = 0.123).

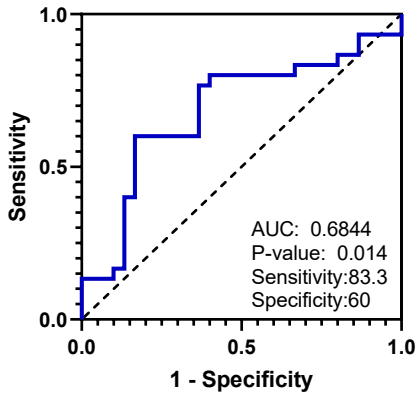

Figure 4. The ROC curve of miR-1226 expression for the differentiation of BC tissues from Control tissues. AUC indicates the area under the ROC curve.

3.3.Folding expression of miR-1226 utilizing 2-ΔΔCT method for qRT-PCR data analysis

The relative expression level of miR-1226 was evaluated using the 2- ΔΔCT method, a widely used qPCR approach for analyzing gene expression differences. This method involves normalizing the cycle threshold (CT) values of the target gene to a reference HKGs within each sample to account for sample-to-sample variation in RNA quantity or quality.

For the target sample, the ΔCT was calculated by subtracting the CT of the reference gene from the CT of miR-1226, resulting in a ΔCT of -0.891 (34.729 – 35.62). Similarly, the ΔCT for the control group was -1.275, obtained by subtracting the reference gene CT (34.116) from the control CT value (32.841).

The difference between these two ΔCT values, known as ΔΔCT, was calculated to be 0.384 (-0.891 – (-1.275)). This ΔΔCT value was then used to determine the relative fold change in expression of miR-1226, using the formula 2 (-ΔΔCT). The resulting fold expression was 1, indicating that miR-1226 is expressed approximately 1.3 times higher in the target sample compared to the control, suggesting a slight upregulation of this miRNA.

Table 5: Shows the results of folding expression of miR-1226 utilizing $2^{-\Delta\Delta CT}$ method for qRT-PCR data analysis.

Equations	
ΔCT target miR-1226	ΔCT = CT (a target miR-1226) – CT (a reference gene) ΔCT (target) = 34.729- 35.62= -0.891
ΔCT control	ΔCT = CT (Control) – CT (control-reference gene) ΔCT (Control) = 32.841- 34.116= -1.275
ΔΔCT	ΔΔCT = ΔCT (a target miR1226) – ΔCT (Control) ΔΔCT = -0.891– (-1.275) = 0.384
Folding Expression	Folding Expression = $2^{-\Delta\Delta CT}$ = $2^{-(0.384)}$ = 1.305

4.Discussion

Altered miRNA expression levels have been identified in numerous cancerous tissues, and the unbalanced microRNAs are recognized as a significant factor in the onset and progression of various malignancies (Hussen et al., 2023b). One of the most dangerous cancers in women is breast cancer, significantly impacting human health and perhaps leading to fatality (Hussen et al., 2023a). It is proposed to be a heterogeneous neoplasm characterized by diverse variations in the expression of miRNA and mRNA profiles (Nurzadeh et al., 2021). A significant amount of research on the aberrant expression levels of several miRNAs and their functions in breast cancer has been recorded. For instance, in patients with BC, miR-21 is overexpressed while miR-125b is under expressed (Najjary et al., 2020, Wang et al., 2012). Similarly, Zhang et al. revealed that serum exosomal miR-1246 and miR-155 were up-regulated in BC patients (Zhang et al., 2020). Moreover, the overexpression of miR-96 has been demonstrated to enhance the migration of breast cancer cells by downregulating Smad7 expression. The data suggest that miR-96 may function as a predictive biomarker for breast cancer (Zhang et al., 2025). Furthermore, research has demonstrated that miR-21 (Yadav et

al., 2016), and miR-133a (Elshimy et al., 2017), despite being involved in tumour progression, do not exhibit consistent age-dependent expression patterns in BC patients. Likewise, miR-155, another key oncomiR involved in immune regulation and cancer progression, has been reported to exhibit dysregulation in BC tissues regardless of the patient's age (Sharma et al., 2022). Similarly, higher levels of miRNAs 187–3p and 143–3p, and lower levels of 205–5p were associated with shorter survival times. miRNA 205, an onco-suppressor, was previously reported to reduce invasion and was associated with better prognosis (Van Schooneveld et al., 2015, Natarajan et al., 2019). These miRNAs are widely expressed across different age groups, reinforcing the idea that specific oncogenic or tumor-suppressor miRNAs operate independently of the patient's age (Chauhan et al., 2025). However, recent research has shown that miRNAs could be optimal candidates for the creation of therapeutic targets and innovative biomarkers.

This study found that no significant correlation between miR-1226 expression levels and the clinical development of BC. Age, lymph node involvement, and Ki-67 expression were not significantly associated with outcome status. Tumor-related variables like grade and size showed no significant associations. Hormone receptor status, PR status, and HER-2 status did not significantly correlate with outcome stratification. The trend for PR status may require further investigation for its predictive value.

Moreover, the study found a significant difference in miR-1226 expression between tumor and control samples using the Wilcoxon test. The median expression was higher in tumor samples (35.04), than in control samples (33.11). The median expression of HKGs was also higher in tumor samples (37.10) compared to control samples (34.95). The ROC curve analysis showed a significant discriminatory capacity for miR-1226, suggesting it may serve as a diagnostic biomarker. The observed patterns in housekeeping gene expression further support the regularity of these findings.

The $2^{-\Delta\Delta CT}$ method was used to evaluate miR-1226's relative expression level. The target sample had a ΔCT of -0.891, while the control group had a ΔCT of -1.275. The difference between these values was 0.384, indicating a relative fold change in miR-1226 expression. The resulting fold expression was 1, indicating a slight upregulation of miRNA.

However, our study has several limitations due to small sample sizes for FFPE tissues, lack of research on miR-1226's diagnostic performance for different ethnic groups, and significant heterogeneity in BC detection due to patients with different TNM stages. Additional study is required to assess the efficacy of miR-1226 as a biomarker for early BC detection.

Conclusion

In conclusion, the deregulation of miRNAs is pivotal in the genesis and progression of BC. This study demonstrated a slight upregulation of miR-1226 in breast cancer tissues compared to controls, with potential diagnostic value indicated by ROC curve analysis. However, no significant correlations were found between miR-1226 expression and clinical parameters such as tumor grade, size, hormone receptor status, or patient outcomes. Despite promising findings, limitations including small sample size, ethnic variability, and disease heterogeneity highlight the need for further research to validate miR-1226 and other miRNAs as reliable biomarkers for breast cancer diagnosis and prognosis.

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Authors' contributions: I contributed to the study's conception and design. I collected the data, wrote the first draft of the manuscript, designed and drew tables, and illustrated the figures.

Data Availability Statement: Applicable.

Research

CHAUHAN, S., MATHUR, R. & JHA, A. K. 2025. The Impact of microRNA SNPs on Breast Cancer: Potential Biomarkers for Disease Detection. *Mol Biotechnol,* 67**,** 845-861.

CHEN, X., TAN, W., LI, W., LI, W., ZHU, S., ZHONG, J., SHANG, C. & CHEN, Y. 2019. miR-1226-3p promotes sorafenib sensitivity of hepatocellular carcinoma via

downregulation of DUSP4 expression. *Journal of Cancer,* 10**,** 2745.

ELSHIMY, R., EL-MAHDY, H. A., MANSOUR, O. A., BADR, M. & ALI, A. M. 2017. MiR-133a and MiR-155 as potential minimally invasive biomarkers in breast cancer. *Cancer Biology,* 7**,** 96-105.

HOUGHTON, S. C. & HANKINSON, S. E. 2021. Cancer progress and priorities: breast cancer. *Cancer epidemiology, biomarkers & prevention,* 30**,** 822-844.

HUSSEN, B. M., ABDULLAH, K. H., ABDULLAH, S. R., MAJEED, N. M., MOHAMADTAHR, S., RASUL, M. F., DONG, P., TAHERI, M. & SAMSAMI, M. 2023a. New insights of miRNA molecular mechanisms in breast cancer brain metastasis and therapeutic targets. *Non-coding RNA Research,* 8**,** 645-660.

HUSSEN, B. M., ABDULLAH, S. R., RASUL, M. F., JAWHAR, Z. H., FARAJ, G. S. H., KIANI, A. & TAHERI, M. 2023b. MiRNA-93: a novel signature in human disorders and drug resistance. *Cell Communication and Signaling,* 21**,** 79.

HUSSEN, B. M., RASUL, M. F., ABDULLAH, S. R., HIDAYAT, H. J., FARAJ, G. S. H., ALI, F. A., SALIHI, A., BANIAHMAD, A., GHAFOURI-FARD, S. & RAHMAN, M. 2023c. Targeting miRNA by CRISPR/Cas in cancer: advantages and challenges. *Military Medical Research,* 10**,** 32.

KAIDAR-PERSON, O., MEATTINI, I., BOERSMA, L. J., BECHERINI, C., CORTES, J., CURIGLIANO, G., DE AZAMBUJA, E., HARBECK, N., RUGO, H. S. & DEL MASTRO, L. 2024. Essential requirements for reporting radiation therapy in breast cancer clinical trials: An international multi-disciplinary consensus endorsed by the European Society for Radiotherapy and Oncology (ESTRO). *Radiotherapy and Oncology,* 195**,** 110060.

LIN, F. & LI, R. 2022. MiR-1226, mediated by ASCL1, suppresses the progression of non-small cell lung cancer by targeting FGF2. *Bulletin du Cancer,* 109**,** 424-435.

MA, Y., LU, Z., QIU, J., LUO, H., TANG, L., LI, Y. & LI, P. 2024. Symptom experience in endocrine therapy for breast cancer patients: A qualitative systematic review and meta-synthesis. *Asia-Pacific Journal of Oncology Nursing,* 11**,** 100364.

MAHMOUD, M. M., SANAD, E. F. & HAMDY, N. M. 2021. MicroRNAs' role in the environment-related non-communicable diseases and link to multidrug resistance, regulation, or alteration. *Environmental Science and Pollution Research,* 28**,** 36984-37000.

MICHAELS, E., CHEN, N. & NANDA, R. 2024. The Role of Immunotherapy in Triple-Negative Breast Cancer (TNBC). *Clinical Breast Cancer*.

MOORE-PALHARES, D., CHEN, H., KHAN, B. M., MCCANN, C., BOSNIC, S., HAHN, E., SOLIMAN, H., CZARNOTA, G., KARAM, I. & RAKOVITCH, E. 2024. Locoregional ablative radiation therapy for patients with breast cancer unsuitable for surgical resection. *Practical Radiation Oncology,* 14**,** 316-327.

NAJJARY, S., MOHAMMADZADEH, R., MOKHTARZADEH, A., MOHAMMADI, A., KOJABAD, A. B. & BARADARAN, B. 2020. Role of miR-21 as an authentic oncogene in mediating drug resistance in breast cancer. *Gene,* 738**,** 144453.

NATARAJAN, L., PU, M., DAVIES, S. R., VICKERY, T. L., NELSON, S. H., PITTMAN, E., PARKER, B. A., ELLIS, M. J., FLATT, S. W., MARDIS, E. R., MARINAC, C. R., PIERCE, J. P. & MESSER, K. 2019. miRNAs and Long-term Breast Cancer Survival: Evidence from the WHEL Study. *Cancer Epidemiol Biomarkers Prev,* 28**,** 1525-1533.

NURZADEH, M., NAEMI, M. & SHEIKH HASANI, S. 2021. A comprehensive review on oncogenic miRNAs in breast cancer. *Journal of Genetics,* 100**,** 1-21.

OTMANI, K. & LEWALLE, P. 2021. Tumor suppressor miRNA in cancer cells and the tumor microenvironment: mechanism of deregulation and clinical implications. *Frontiers in oncology,* 11**,** 708765.

SHARMA, S., OPYRCHAL, M. & LU, X. 2022. Harnessing tumorous flaws for immune supremacy: is miRNA-155 the weak link in breast cancer progression? *J Clin Invest,* 132.

SIEGEL, R. L., MILLER, K. D., WAGLE, N. S. & JEMAL, A. 2023. Cancer statistics, 2023. *CA: a cancer journal for clinicians,* 73**,** 17-48.

SVORONOS, A. A., ENGELMAN, D. M. & SLACK, F. J. 2016. OncomiR or tumor suppressor? The duplicity of microRNAs in cancer. *Cancer research,* 76**,** 3666-3670.

VAN SCHOONEVELD, E., WILDIERS, H., VERGOTE, I., VERMEULEN, P. B., DIRIX, L. Y. & VAN LAERE, S. J. 2015. Dysregulation of microRNAs in breast cancer and their potential role as prognostic and predictive biomarkers in patient management. *Breast Cancer Res,* 17**,** 21.

WANG, C., WANG, J., CUI, W., LIU, Y., ZHOU, H., WANG, Y., CHEN, X., CHEN, X. & WANG, Z. 2021. Serum exosomal miRNA-1226 as potential biomarker of pancreatic ductal adenocarcinoma. *OncoTargets and therapy***,** 1441-1451.

WANG, H., TAN, G., DONG, L., CHENG, L., LI, K., WANG, Z. & LUO, H. 2012. Circulating MiR-125b as a marker predicting chemoresistance in breast cancer. *PloS one,* 7**,** e34210.

YADAV, P., MIRZA, M., NANDI, K., JAIN, S., KAZA, R., KHURANA, N., RAY, P. & SAXENA, A. 2016. Serum microRNA-21 expression as a prognostic and therapeutic biomarker for breast cancer patients. *Tumor Biology,* 37**,** 15275-15282.

ZHANG, X., CONG, L., YU, R., YU, Q., HOU, X. & ZHOU, Y. 2025. MicroRNA-96 promotes the proliferation and migration of breast cancer cells by inhibiting Smad7 expression. *Oncology Letters,* 29**,** 151.

ZHANG, X., LIU, J., JI, M., QI, G. & QIAO, R. 2024. Long noncoding RNA GUSBP11 knockdown alleviates nasopharyngeal carcinoma via regulating miR-1226-3p/TM9SF4 Axis. *Cancer Biotherapy & Radiopharmaceuticals,* 39**,** 133-143.

ZHANG, Z., ZHANG, L., YU, G., SUN, Z., WANG, T., TIAN, X., DUAN, X. & ZHANG, C. 2020. Exosomal miR-1246 and miR-155 as predictive and prognostic biomarkers for trastuzumab-based therapy resistance in HER2-positive breast cancer. *Cancer chemotherapy and pharmacology,* 86**,** 761-772.