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ORIGINAL ARTICLE

New Insights into the Role of Sorcin and Annexin A3 in Breast Cancer Patients

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ABSTRACT

Background Breast cancer is regarded as the second leading cause of cancer-related mortality among women and the most widespread malignancy affecting females globally. Our research seeks to elucidate the function of sorcin and annexin A3 in the detection of breast cancer. **Methods:**This research involved 59 female cases selected from the South Egypt Cancer Institute, Surgery Department, and Assiut University for the period March 2019 to December 2019. They were separated into two groups as follows: Prior to the procedure, Group one involved 48 women with breast cancer, and Group two involved 11 women with benign breast diseases. The control group consisted of 15 female volunteers recruited from staff or colleagues and screened with a thorough history and examination. **Results:** The breast cancer group had significantly higher levels of sorcin relative gene expression and annexin A3 compared to the control and benign groups (p-value < 0.001 for each). Additionally, the benign group showed a statistically significant difference in sorcin relative gene expression compared to the controls. **Conclusion:** In terms of our findings, we concluded that Sorcin gene expression represented significantly higher diagnostic accuracy for breast cancer yielding AUC 0.933 with 93.75% sensitivity and 84.62% specificity compared to ANXA3 level, which represented significant diagnostic accuracy for breast cancer yielding AUC 0.779 with 83.33% sensitivity and 65.33% specificity.

Keywords: Annexin A3, BC, Sorcin.

INTRODUCTION

Breast cancer is considered the 2nd most frequent reason for cancer-related mortality in women and the greatest prevalent female malignancy worldwide [1]. Soluble resistance-associated Sorcin is a PEF calcium-binding protein with a molecular mass of twenty-two kDa that is involved in cell calcium homeostasis regulation. The EF-hand, which is a helix-loop-helix, is a structural motif that is frequently utilized by proteins in order to make calcium binding possible. On the majority of proteins, there is an even number of EF-hands, which are typically bound together both physically and functionally. There are several proteins that

belong to the penta-EF hand (PEF) family. These proteins include sorcin, calpains, peflin, grancalcin, in addition to programmed cell death protein 6 (PDCD6) [2].The expression of ATP-binding Cassette Subfamily B Member 1 with a cyclic adenosine monophosphate response element is increased when sorcin is overexpressed, which results in an increase in resistance to a wide variety of chemotherapeutic drugs. The reversal of drug resistance is achieved by inhibiting expression of sorcin through sorcin-targeting RNA interference. Sorcin is becoming more widely recognized as a valuable MDR indicator and could serve as a therapeutic target for reversing tumor multidrug resistanc [3]. Annexins are a group of intracellular proteins that bind membrane phospholipids in a manner that relies on the concentration of calcium. There are twelve distinct annexins encoded in the human genome, each of which has a distinct expression and distribution through the tissues. Some of these are expressed ubiquitously (A1, A6, A7, A2, & A5), although others are selective (A8, A3, A9, A13, & A10). Several annexins play a critical role in tumor progression[4]. Neoplastic mammary cells are responsible for the secretion and expression of AnxA3, and the suppression of this protein stops cancer cells from migrating from breast cells. The expression of annexin A3 in human breast cancer was found to have a substantial association with both the size of the tumor and the presence of axillary lymph node metastases [5].Thisresearch aimed to investigate the role of annexin A3 and sorcin in breast cancer diagnosis.

METHODS

For the period from March 2019 to December 2019, 59 female cases were selected from the South Egypt Cancer Institute, Surgery Department, and Assiut University. They were separated into two groups in the following manner: Group I involved 48 female cases who had breast cancer prior to the surgery; their ages varied from thirty to 79 years, with a mean ± standard deviation of 52.77±12.99, and Group II included 11 female cases who had benign breast diseases; their ages varied among 19 & 60 years, with a mean ± SD of 39.6±10.6. Controls: The study included 15 apparently healthy-matched female volunteers as controls. They were employed by colleagues or staff and screened using careful history and examination.

Ethical consideration: The Ethics Committee of the Faculty of Medicine at Assiut University accepted the research criteria, and all volunteers provided written informed consent prior to their participation in the research (Code: 17100825). ***The inclusion criteria*** include breast cancer cases who are admitted to the Surgery Department of the South Egypt Cancer Institute at Assiut University prior to surgery. ***Exclusion criteria:*** cases with malignancies located elsewhere in the body, those receiving neoadjuvant chemotherapy, those with chronic cardiac diseases, and those with either renal disease or neurodegenerative disease.

Sample collection and processing: Venous blood samples: We collected five milliliters of blood from the antecubital vein. Every sample was separated into two tubes as follows: For the serum specimen's 2.5 ml, blood wasn't gathered with anticoagulant, stored at room temperature for twenty to thirty minutes, then

centrifuged at three hundred revolutions per minute (r.p.m.) for fifteen minutes at room temperature, separated, and frozen at −20°C till time of analysis. The remaining two-point five milliliters of blood were collected on EDTA tubes and kept frozen at -80 degrees Celsius until genomic RNA extraction and RT-PCR [6].The method used to determine serum annexin A3 (ANXA3) [5], Serum annexin A3 levels (in ng/ml) were assessed by an ELISA kit (Cloud Clone Corporation, USA, Catalog No. E-02676Hu) regarding the manufacturer's instructions.

Assay procedure: All samples and reagents were cooled to ambient temperature (eighteen to twenty-five °C). Prior to the assay, we centrifuged the samples once more after thawing, and prior to pipetting, we thoroughly mixed the reagents by gently swirling. Foaming was prevented. Duplicate analyses were conducted for all standards. Next, we added 50 l of the standard to the well. We diluted the testing sample well with 40 µl of sample diluent after adding 10 µl of the testing sample. The blank well didn't require any additions. We covered each well with an adhesive strip, added one hundred µl of HRP-conjugate reagent, and incubated it at thirty-seven degrees Celsius for sixty minutes. For a total of five cleanses, we repeated the process four times, aspirating each well and washing it. We used a spray bottle, manifold dispenser, or auto washer to fill each well with four hundred microliters of Wash Solution. At each stage, a satisfactory presentation necessitates the complete eradication of liquid. Following the final wash, we removed any remaining cleanse solution by decanting or aspirating. After inverting the plate, we wiped it with clean paper towels. We added 50 µl of chromogen solution A and fifty microliters of chromogen solution B to every well. We then combined them and incubated them at 37 degrees Celsius for fifteen minutes. In each well, we added fifty microliters of Stop Solution. The color of the wells was changed from blue to yellow. We gently tap the plate to ensure that the wells were thoroughly mixed if the color change wasn't uniform or the color in the wells was green. Within fifteen minutes, we utilized a microtiter plate reader to determine the optical density (O.D.) at four hundred and fifty nanometers. The law of OD calculation: A = log10 100 / %T(5) , Reverse transcription-PCR (RT-qPCR) of sorcin[3],RNA Extraction ,Direct-zolTM RNA Miniprep (Zymo Research, USA, Catalog No. R2050) is used.

Reagents:TRIzol Reagent®, prewash buffer, wash buffer, RNase-free water, DNase-I, and digestion buffer.

Procedure: We lysed a 200 l whole blood sample in 700 l TRIzol Reagent® and homogenized it; then, we centrifuged the homogenized tissue to remove particulate detritus and then transferred the supernatant to an RNase-free tube. We added an equal volume of ethanol (ninety-five to one hundred percent) to a sample that had been lysed in TRIzol Reagent® or a similar product and mixed the mixture thoroughly. After transferring the mixture to a Zymo-SpinTM column in a collection vessel, we centrifuged it. We discarded the flow-through and transferred the column to a novel collection tube [3].

Recommended: DNase I treatment: we centrifuged the column after adding four hundred µl of RNA Wash Buffer and mixed

five microliters of DNase I and seventy-five microliters of DNA digestion buffer in an RNase-free tube. We incorporated the mixture directly into the column matrix. For a duration of fifteen minutes, incubated at ambient temperature (twenty to thirty degrees Celsius). We added four hundred µl of Direct-zol™ RNA prewash to the column and centrifuged. The flow through was discarded, and the process was repeated. To ensure that the wash buffer was completely removed, we added seven hundred microliters of RNA wash buffer to the column and centrifuged for two minutes and transferred the column to a sterile, one-point, five-milliliters microcentrifuge tube. To elute RNA, fifty microliters of elution buffer had been added to the membrane's central region. The mixture was incubated at room temperature for 1 minute and then centrifuged for thirty seconds. The nanodrop spectrophotometer (SPECTROstar® Nano Microplate and Cuvette Spectrophometer, BMG LABTECH, Germany) was employed to ascertain the total RNA concentrations. The RNA was maintained at negative eighty degrees Celsius until the reverse transcription process.

STATISTICAL ANALYSIS: The data was analyzed using the computer program SPSS "Ver. 20" from Chicago, United States of America. The information is presented as the mean, standard deviation, and percentage. The MedCalc program was employed to detect the termination point, sensitivity, and specificity. The variables have been subjected to the Shapiro-Wilk W test to determine their normal distribution prior to analysis. To determine variances among the tested groups, the student t-test was employed for normally distributed information, and the Mann-Whitney U test has been employed for skewed information. Significant variances were defined as $p \leq 0.05$. The significance of categorical variables was determined using the Chi-Square test ($\chi 2$). In order to compare the means of the three groups, the one-way ANOVA was implemented. Correlations among categories were determined using Pearson correlation.

RESULTS

Our findings indicated that the breast cancer group's age was significantly higher than that of the benign breast illness group. The number of deliveries and breast-feeding duration in the breast cancer disease group were significantly higher than those in the benign breast diseases and control groups (Table 1).This study found a big variation among the breast cancer group and the control and benign groups in the levels of sorcin relative gene expression and annexin A3 (p-value < 0.001 for each). Table 2 shows a statistically significant difference in sorcin relative gene expression between the benign group and the controls.The current study also found a strong link between the levels of sorcin and annexin A3 and the clinical and pathological features of breast cancer that were looked at. These included TNM stage, distant metastasis, and progesterone receptor (only in annexin A3). They showed no association with grade, tumor size, pathological tumor type, menopausal status, estrogen receptor, HER2\ neu, BMI, and molecular types (Table 3).Table 4 showed that sorcin sensitivity, specificity, and area under the ROC curve were 93.75, 84.62, and 0.933, respectively, and AnnexinA3 sensitivity, specificity, and area under the

ROC curve were 83.33, 65.33, and 0.779, respectively.

There was a strong link ($p<0.001$) between sorcin gene expression, serum annexin A3, and white blood cell count in the BC group. A significant positive association has been observed among cumulative years of lactation, number of deliveries, and age at first delivery. A significant negative association was observed among cumulative years of lactation and diastolic blood pressure (Table 5).

Table (1): The general characteristics of cases and controls. (Mean±SD)

	Control (n=15)	Benign (n=11)	Carcinoma (n=48)	P. value
	Mean±SD	Mean±SD	Mean±SD	
Age at diagnosis	43.6±7.11	39.6±10.6	52.77±12.99	0.001**
			P1: 0.003**	
		P3: 0.213	P2: 0.05	
Age at menarche (years)	13.6±1.18	14.09±2.21	13.85±1.49	0.726
			P1: 0.651	
		P3: 0.430	P2: 0.583	
Age at marriage (years)	18.27±1.62	19.56±4.19	18.9±4.65	0.799
			P1: 0.671	
		P3: 0.505	P2: 0.663	
Number of deliveries	1.87±1.64	1.73±1.68	4.35±2.33	<0.001***
			P1: <0.001***	
		P3: 0.869	P2: <0.001***	
Age at 1st Childbirth (years)	15.73±10.28	15.09±10.38	18.44±7.37	0.354
			P1: 0.242	
		P3: 0.849	P2: 0.285	
Breast feeding duration in years	2.87±2.42	3.18±2.64	5.98±3.42	0.001**
			P1: 0.009**	
		P3: 0.801	P2: <0.001***	
Body mass index (kg /m2)	30.68±3.73	30.88±9.21	31.76±9.28	0.888
			P1:0.756	
		P3: 0.952	P2: 0.666	

* Statistically significant variance ($p<0.05$), **Statistically significant variance ($p<0.01$), ***Statistically significant variance ($p<0.001$), P1: Comparison among Carcinoma& benign, P2: Comparison among Carcinoma& control, P3: Comparison among benign & control.

Table (2): The relative gene expression of sorcin & the level of annexin A3 in different groups.

Parameters	Control (n=15)	Benign (n=11)	Carcinoma (n=48)	P. value
	Mean±SD	Mean±SD	Mean±SD	
Sorcin gene expression	1.66±1.59	31.19±24	143.3±94	**<0.001*** **
			P1:**0.001****	
		P3: **0.001****	P2: **<0.001*** **	
Annexin A3 (ng/ml)	11.73±4.54	13.05±2.3	15.91±2.53	**<0.001*** **
			P1:**0.001****	
		P3: 0.387	P2: **<0.001*** **	

** Statistically significant variance (p<0.01), ***Statistically significant variance (p<0.001), P1: Comparison among carcinoma& benign, P2: Comparison between carcinoma& control, P3: Comparison between benign & control

Table (3): Association of sorcin expression pattern and annexin A3 level with the examined clinicopathological characteristics in BC.

Variables	Number of patients	AnnexinA3	Sorcin
		Mean±SD	Mean±SD
Grade			
-II	**35**	16.11±2.35	134.3±91
-III	**13**	15.39±3.03	167.9±99
P. value		0.397	0.276
TNM stage			
-I + II	**18**	14.57±2.1	77.96±58
-III + VI	**30**	16.72±2.5	182.56±90
P. value		**0.003****	**<0.001*** **
Tumor size			
≤2	**15**	15.55±1.56	130.7±73
>2	**33**	16.07±2.88	149.12±102
P. value		0.512	0.536
Pathological tumor type			
IDC	**46**	16.0±2.56	143.6±96
Ductal carcinoma insitu	**2**	14.03±0.53	137.2±18.73
P. value		0.286	0.926
Distant metastasis			
M0	**42**	15.5±2.25	123.9±79.9
M1	**6**	18.62±2.9	279.5±72.8
P. value		**0.004****	**<0.001*** **
Menopausal status			
-Premenopausal	**23**	14.9±2.2	134.8±79.6
-Postmenopausal	**25**	16.2±2.2	112.9±80
P. value		0.089	0.382
Estrogen receptor			
-Positive	**30**	16.05±2.3	127.5±96
-Negative	**18**	15.7±3.02	169.8±86.8

Variables	Number of patients	AnnexinA3	Sorcin
		Mean±SD	Mean±SD
P. value		0.642	0.132
Progesterone receptor			
-Positive	**25**	16.65±2.4	130.8±103
-Negative	**23**	15.11±2.46	156.9±82
P. value		**0.033***	0.342
HER_2\ neu			
-Positive	**23**	16.28±1.68	148.16±94
-Negative	**25**	15.33±3.10	138.9±95
P. value		0.10	0.742
Body mass index (BMI)			
- <30	**20**	15.44±1.8	175.2±85.7
- ≥30	**28**	16.25±2.9	120.6±94
P. value		0.275	0.056
Molecular type			
-Luminal A	13	15.7±3.0	111.2±95
-Luminal B	20	16.5±1.7	152.4±97
-Triple Negative	12	14.93±3.25	169.1±89
-HER2 enriched	3	16.58±1.01	119.3±74
P. value		0.435	0.356

* Statistically significant variance ($p<0.05$), ** Statistically significant variance ($p<0.01$), *** Statistically significant variance ($p<0.001$).

Table (4): Sensitivity, specificity and area under ROC curve of sorcin and annexin A3 in BC patients.

	Sensitivity	Specificity	AUC	PPV	NPV	Accuracy
Sorcin	93.75	84.62	0.933	91.8	0.074	89.185
AnnexinA3	83.33	65.33	0.779	81.6	0.25	74.33

AUC; area under ROC curve: PPV: positive predictive value: NPV; negative predictive value

Table (5): Correlation coefficients (r) of numerous clinical data and parameters in breast cancer cases.

Carcinoma group	Age	Age at menarche (years)	Age at marriage (years)	Number of deliveries	Age at first delivery (years)	Cumulative years of lactation	Body mass index	Sorcin	AnnexinA3
Age at menarche (years)	.082								
Age at marriage (years)	-.200	.343*							
Number of deliveries	.046	-.261	-.221						
Age at first delivery (years)	-.163	-.060	.337*	.267					

Carcinoma group	Age	Age at menarche (years)	Age at marriage (years)	Number of deliveries	Age at first delivery (years)	Cumulative years of lactation	Body mass index	Sorcin	AnnexinA3
Cumulative years of lactation	.021	-.056	-.182	.739**	.293*				
Body weight	-.030	-.012	-.004	-.037	.077	-.127			
Body height	-.013	.119	.189	-.035	.062	.087			
Body Mass Index	.018	-.098	-.169	.004	-.023	-.154			
Sorcin	-.122	-.025	-.272	.031	-.006	.171	-.150		
AnnexinA3	.049	.219	.085	-.095	.137	-.197	.126	.407**	
Systolic blood pressure	.451**	.103	-.280	-.223	-.180	-.217	.187	-.074	.134
Diastolic blood pressure	.280	-.133	-.175	-.277	-.108	-.315-*	.075	-.012	.072
White blood count	-.390-**	-.113	-.274	.033	.157	-.035	.064	.335*	.081
Hemoglobin	-.097	.071	-.007	.150	.124	.153	.044	-.107	-.008
Urea	.258	.170	.004	-.085	-.107	-.089	-.206	.019	-.170
Creatinine	.045	.122	-.114	.016	.008	.027	-.048	-.099	.159
ALT	-.061	.138	.027	.061	.153	.101	.046	-.013	-.109
AST	-.050	.154	.135	.105	.206	.117	.052	-.155	-.120
Random blood glucose	.211	.185	-.152	.171	-.016	.219	-.095	.103	.148

* Statistically significant correlation ($p<0.05$), ** Statistically significant correlation ($p<0.01$)

DISCUSSION

Advancing to hyperplasia, ductal carcinoma in situ (DCIS), invasive malignancy, and culminating in metastatic carcinoma. Despite substantial study aimed at elucidating the molecular alterations associated with carcinogenesis, the processes driving the onset of breast cancer remain unclear[1].The human genome encodes twelve distinct annexins, differing in expression and distribution across organs. Certain receptors are universally expressed (A1, A2, A5, A6, & A7), whilst others exhibit selective expression (A3, A8, A9, A10, & A13). The differential expression of ANXA3 significantly contributes to carcinogenesis, treatment resistance, as well as metastasis [5].The age of the breast cancer cohort is significantly higher than that of the benign breast illness group. The breast cancer disease group exhibited a considerably higher number of deliveries and a longer duration of breast-feeding than the benign breast diseases and control groups. These findings are consistent with those of Kelsey et al [7] as well as Anastasiadi et al [8].

In this trail, the mean levels of BMI were slightly higher in the breast cancer group contrasted with the benign breast disease group and controls.Also, our findings were consistent with those of Sparano et al [9] and Nair [10], who found that hormonal changes,

such as inflammation, local estrogen release, and high serum estrogen levels, may be ways that obesity leads to cancer. Another theory posits that overweight and obese women may have a higher insulin resistance, resulting in a higher production of insulin that is believed to stimulate the development of breast cancer cells.There was a statistically significant variance in the mean sorcin relative gene expression and annexin A3 between the BC group and the control and benign groups, with a p-value of less than 0.001 for each. Additionally, the benign group's sorcin relative gene expression differs significantly from the controls.Sorcin gene expression demonstrated notable diagnostic accuracy for BC, resulting in an area under the curve of 0.933, 93.75 percent sensitivity, and 84.62 percent specificity. These findings were consistent with those of He et al [11] and Zhou et al. [12] who identified that upregulation of sorcin in malignant cells was associated with late stages, histological grade, and tumor size. Furthermore, they observed that the excessive expression of sorcin significantly induced cancer cell production, migration, and invasion, while the knockdown of the sorcin gene reduced proliferation, migration, and invasion. These results highlight the significance of sorcin in the development and progression of cancer.The current investigation demonstrated a significant relationship among the levels of sorcin and annexin A3 and the clinicopathological characteristics examined in BC, specifically in relation to TNM stage, distant metastasis, and progesterone receptor (specifically in annexin A3). They showed no association with grade, tumor size, pathological tumor type, menopausal status, estrogen receptor, HER2\ neu, BMI, and molecular types.

These findings align with those of Hu et al. [13], who identified a correlation among sorcin expression levels as well as neoadjuvant chemotherapy (NAC) outcomes in breast cancer individuals. The remission rate was considerably higher in cases with lower levels of sorcin expression contrasted with those with higher levels of sorcin expression. The idea was that the amount of sorcin expressed in breast cancer could be used to predict how well the paclitaxel /epirubicin combination would work in neoadjuvant chemotherapy. The hypothesis was that the expression of sorcin would decrease as a result of the management. It was hypothesised that the level of sorcin expression in breast cancer could be used to predict the effectiveness of the paclitaxel/ epirubicin regimen in NAC.The ANXA3 level represented significant diagnostic accuracy for BC yielding area under the curve 0.779 with 83.33% sensitivity & 65.33% specificity. In support of our findings, Du et al. [14] demonstrated that ANXA3 is substantially upregulated in breast tumor tissues obtained from clinical biopsies. The suppression of breast cancer cell invasion with promotion of multiplication both in vitro and in vivo have been observed because of ANXA3 knockdown, which was facilitated by the IκBα-mediated EMT as well as the transition of distinct states of the breast cancer surveillance consortium. Furthermore, they demonstrated that ANXA3 suppression facilitated the uptake of doxorubicin, & inhibiting ANXA3 in conjunction with doxorubicin might effectively prevent tumor growth and metastasis.In the BC group, there was a strong positive link (p value less than 0.001) between sorcin gene expression, serum annexin A3, and white blood cell count. Significant positive associations have been observed among cumulative years of lactation, number of deliveries, and age at first delivery. A significant negative connection was identified among total years of lactation as well as diastolic blood pressure.

CONCLUSION:

Regarding our results, we concluded that Sorcin gene expression represented significant higher diagnostic accuracy for breast cancer yielding area under the curve 0.933 with 93.75% sensitivity & 84.62%

specificity compared to the ANXA3 level, which represented significant diagnostic accuracy for breast cancer yielding area under the curve 0.779 with 83.33% sensitivity & 65.33% specificity.

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REFERENCES

1. **Huerta-Nuñez L, Gutierrez-Iglesias G, Martinez-Cuazitl A, Mata-Miranda M, Alvarez-Jiménez V, Sánchez-Monroy V, et al.** A biosensor capable of identifying low quantities of breast cancer cells by electrical impedance spectroscopy. Sci Rep.2019;9(1):6419.
2. **Colotti G, Poser E, Fiorillo A, Genovese I, Chiarini V, Ilari AJM.** Sorcin, a calcium binding protein involved Zn the multidrug resistance mechanisms in cancer cells.Molecules. 2014;19(9):13976-89.
3. **Kawai M, Liu N, Hattori T, Kataoka YH, Takigawa M, Kubota S, Yamamoto T, Ohura K**. Sorcin expression in the epiphyseal growth plates of mice. Journal of Hard Tissue Biology. 2016;25(1):57-62.
4. **Wu X, Wang Y, Bian Y, Ren Y, Xu X, Zhou F, et al.** A critical review on plant annexin: Structure, function, and mechanism. Plant Physiol Biochem. 2022; 190:81-9.
5. **Zhou T, Li Y, Yang L, Tang T, Zhang L, Shi JJBri**. Annexin A3 as a prognostic biomarker for breast cancer: A retrospective study. Biomed Res Int..2017;2017(1):2603685.
6. **Gong Z, Sun P, Chu H, Zhu H, Sun D, Chen J.** Overexpression of sorcin in multidrug-resistant human breast cancer. Oncology letters. 2014 Dec 1;8(6):2393-8.
7. **Kelsey JL, Gammon MD, John EM.** Reproductive factors and breast cancer. Epidemiologic reviews. 1993;15(1):36.
8. **Anastasiadi Z, Lianos GD, Ignatiadou E, Harissis HV,** Mitsis M. Breast cancer in young women: an overview. Updates in surgery. 2017;69(3):313-7.
9. **Sparano JA, Wang M, Zhao F, Stearns V, Martino S, Ligibel JA, et al.** Obesity at diagnosis is associated with inferior outcomes in hormone receptor‐positive operable breast cancer. Cancer. 2012;118(23):5937-46.
10. **Nair NS**. Bigger is not better! The risk of obesity and risk of breast cancer incidence and recurrence in the Indian subcontinent. South Asian journal of cancer. 2013;2(3):119.
11. **He Q, Zhang G, Hou D, Leng A, Xu M, Peng J, et al**. Overexpression of sorcin results in multidrug resistance in gastric cancer cells with up-regulation of P-gp. Oncology reports. 2011;25(1):237-43.
12. **Zhou X, Wu X, Chen BJCm**, research. Sorcin: a novel potential target in therapies of cancers. Cancer Manag Res. 2019:7327-36.
13. **Hu Y, Li S, Yang M, Yan C, Fan D, Zhou Y, et al**. Sorcin silencing inhibits epithelial-to-mesenchymal transition and suppresses breast cancer metastasis in vivo. Breast cancer research and treatment. 2014;143(2):287-99.
14. **Du R, Liu B, Zhou L, Wang D, He X, Xu X, et al.** Downregulation of annexin A3 inhibits tumor metastasis and decreases drug resistance in breast cancer. Cell Death Dis. 2018;9(2):126.

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