

Figure S1. Schematic representation of the study design. Study 1, exosomal miRNA profiles were compared between the patients with pCR (n=12) and non-pCR (n=12). Study 2, exosomal miRNA profiles were compared between the non-pCR patients with breast cancer recurrence (n=8) and no recurrence (n=8). miRNA/miR, microRNA; pCR, pathological complete response; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; TN, triple negative.

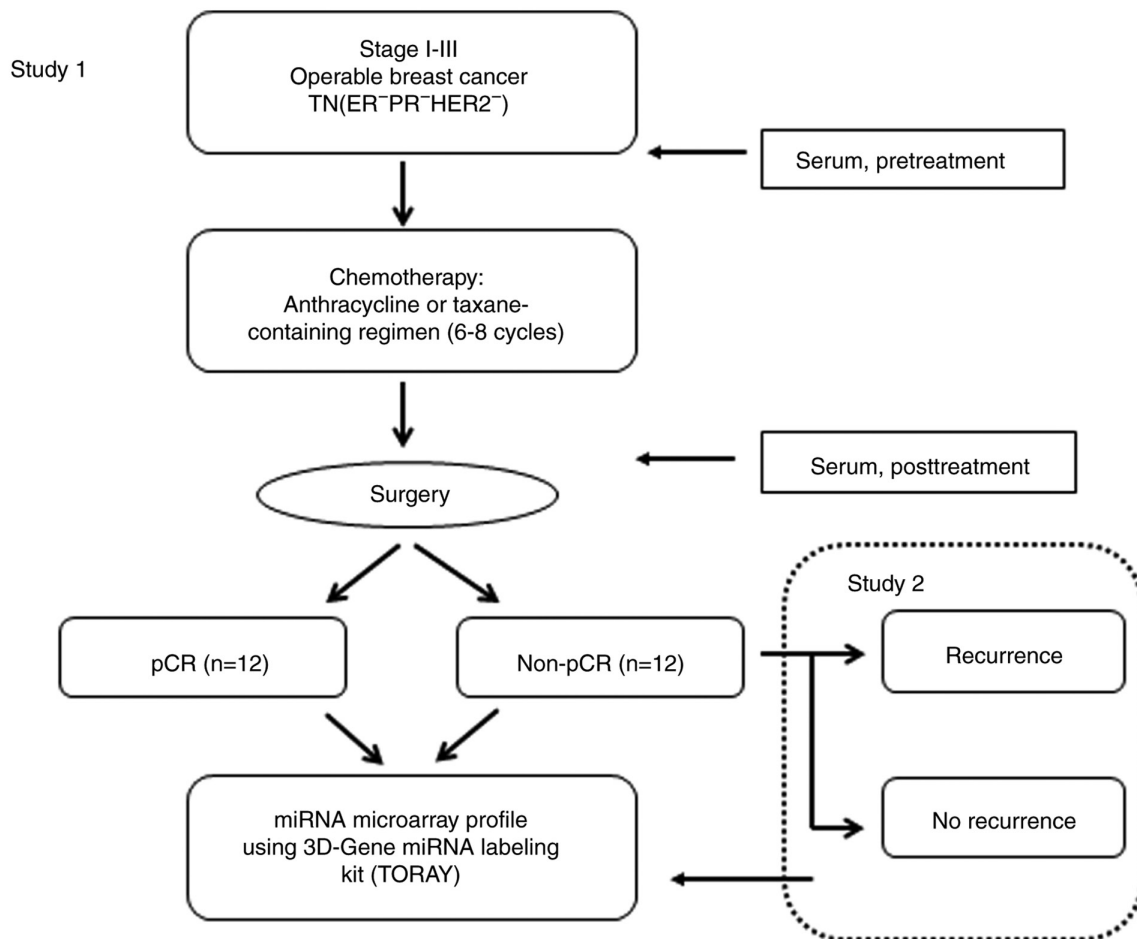


Figure S2. ROC curve analysis of the combined signature four miRNAs predicting pathological complete response. The four miRNAs included miR-4448, miR-2392, miR-2467-3p and miR-4800-3p. AUC, 0.7652. ROS, receiver operating characteristics; miRNA/miR, microRNA; AUC, area under the curve.

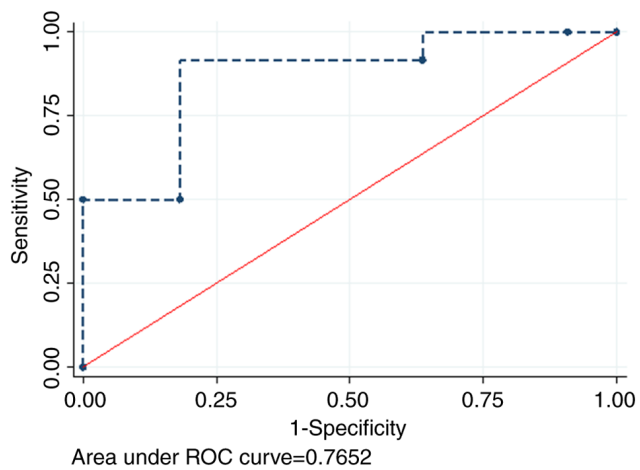


Table SI. Clinical characteristics before chemotherapy in patients with non-pCR.

Clinical characteristics	Patients with breast cancer recurrence (n=8)	Patients without breast cancer recurrence (n=8)	P-value
Median age at diagnosis, median (range)	52 (35-74)	62 (37-68)	0.29
Menopausal status, n (%)			0.25
Premenopausal	3 (37)	1 (13)	
Postmenopausal	5 (63)	7 (87)	
Tumor size, cm, median (range)	4.2 (1.5-10.0)	2.4 (1.7-7.8)	0.61
Nodal status, n (%)			0.28
Negative	1 (13)	4 (50)	
Positive	7 (87)	4 (50)	
Clinical T			0.55
T1	2 (25)	3 (38)	
T2	2 (25)	4 (50)	
T3	1 (13)	0 (0)	
T4	3 (38)	1 (12)	
Stage			0.67
1	1 (13)	2 (25)	
2	3 (38)	4 (50)	
3	4 (50)	2 (25)	
Nuclear grade			0.58
1,2	2 (25)	3 (38)	
3	6 (75)	5 (62)	
Ki67 labeling index, %, median (range)	88 (20-100)	60 (30-78)	0.06
NAC, n (%)			1.00
FEC followed by DOC	5 (63)	5 (63)	
PAC followed by FEC	2 (25)	3 (38)	
FEC	1 (13)	0 (0)	
Median follow-up period, month, median (range)	36 (17-57)	81 (65-121)	

miRNA/miR, microRNA; pCR, pathological complete response; NAC, neo-adjuvant chemotherapy; FEC, 5-fluorouracil, epirubicin and cyclophosphamide; DOC, docetaxel; PAC, paclitaxel.

Table SII. Differentially expressed exosomal miRNAs related to the patients with recurrence (>2-fold-change).

A, Upregulated miRNAs		
Mature ID	Fold-change	P-value
hsa-miR-195-5p	4.43	0.020
hsa-miR-31-5p	4.40	0.002
hsa-let-7f-5p	3.51	0.020
hsa-miR-5584-5p	3.32	0.002
hsa-miR-130a-3p	3.20	0.030
hsa-miR-4421	2.95	0.002
hsa-miR-16-5p	2.81	0.040
hsa-miR-106b-5p	2.77	0.030
hsa-let-7g-5p	2.73	0.040
hsa-miR-3120-3p	2.71	0.008
hsa-miR-378b	2.38	0.040
hsa-miR-515-3p	2.35	0.020
hsa-miR-525-3p	2.24	0.020
hsa-miR-7515	2.08	0.020
hsa-miR-409-5p	2.07	0.020

B, Downregulated miRNAs		
Mature ID	Fold-change	P-values
hsa-miR-548ab	0.23	<0.001
hsa-miR-6751-3p	0.24	<0.001
hsa-miR-4732-3p	0.26	0.004
hsa-miR-6857-3p	0.30	0.003
hsa-miR-487a-5p	0.30	0.020
hsa-miR-769-3p	0.30	0.030
hsa-miR-133a-3p	0.32	0.004
hsa-miR-6783-3p	0.33	0.040
hsa-miR-3943	0.35	0.030
hsa-miR-3617-3p	0.36	0.040
hsa-miR-887-5p	0.36	0.040
hsa-miR-3190-5p	0.37	0.020
hsa-miR-5685	0.37	0.040
hsa-miR-5004-5p	0.37	0.047
hsa-miR-92a-2-5p	0.37	0.004
hsa-miR-1287-5p	0.38	0.030
hsa-miR-466	0.38	0.040
hsa-miR-4708-5p	0.38	0.047
hsa-miR-340-3p	0.38	0.008
hsa-miR-6701	0.38	0.040
hsa-miR-4761-3p	0.39	0.010
hsa-miR-4290	0.43	0.020
hsa-miR-7848-3p	0.45	0.040
hsa-miR-566	0.46	0.030
hsa-miR-4446-5p	0.47	0.030
hsa-miR-4730	0.48	0.002
hsa-miR-34b-3p	0.48	0.030
hsa-miR-5196-3p	0.49	0.040

Only the miRNAs with statistically significant P-values are shown.
miRNA/miR, microRNA.

Table III. Top 20 KEGG pathways among the 43 miRNAs related to the patients with non-pCR and breast cancer recurrence.

KEGG pathway	P-value	Number of genes	Number of miRNAs
'Pathways in cancer'	<0.0001	205	16
'Epstein-Barr virus infection'	0.0006	108	16
'Focal adhesion'	0.0080	104	16
'Proteoglycans in cancer'	<0.0001	118	15
'Protein processing in endoplasmic reticulum'	<0.0001	110	15
'Viral carcinogenesis'	<0.0001	117	15
'Cell cycle'	<0.0001	80	15
'Hippo signaling pathway'	<0.0001	81	15
'Oocyte meiosis'	<0.0001	64	15
'Ubiquitin mediated proteolysis'	<0.0001	80	15
'MAPK signaling pathway'	0.0206	118	15
'Renal cell carcinoma'	<0.0001	44	14
'RNA transport'	<0.0001	93	14
'Bacterial invasion of epithelial cells'	0.0002	46	14
'mTOR signaling pathway'	0.0002	40	14
'Sphingolipid signaling pathway'	0.0003	67	14
'Endocytosis'	0.0004	109	14
'HIF-1 signaling pathway'	0.0050	59	14
'Spliceosome'	0.0119	68	14
'Transcriptional misregulation in cancer'	0.0206	86	14

KEGG, Kyoto Encyclopedia of Genes and Genomes; miRNA/miR, microRNA; pCR, pathological complete response.

Table SIV. Target genes regulated by two miRNAs observed in the patients with non-pCR (Recurrence vs. no recurrence).

Target genes	miRNAs
<i>APP</i>	hsa-miR-130a-3p, hsa-miR-106b-5p
<i>ARL2</i>	hsa-miR-195-5p, hsa-miR-16-5p
<i>ARPC5</i>	hsa-miR-133a-3p, has-miR-31-5p
<i>BCL2L1</i>	has-miR-let-7g-5p, hsa-miR-133a-3p
<i>BIRC5</i>	hsa-miR-195-5p, hsa-miR-16-5p
<i>BMI1</i>	hsa-miR-16-5p, has-miR-let-7g-5p
<i>CCND3</i>	hsa-miR-195-5p, hsa-miR-16-5p
<i>CCNE1</i>	hsa-miR-195-5p, hsa-miR-16-5p
<i>CDC42</i>	hsa-miR-195-5p, hsa-miR-133a-3p
<i>CDK4</i>	hsa-miR-195-5p, hsa-miR-34b-3p
<i>CDKN1A</i>	hsa-miR-515-3p, hsa-miR-106b-5p
<i>CHUK</i>	hsa-miR-195-5p, hsa-16-5p
<i>DICER1</i>	hsa-miR-130a-3p, hsa-miR-195-5p
<i>E2F3</i>	hsa-miR-106b-5p, hsa-miR-195-5p
<i>EGFR</i>	hsa-miR-16-5p, hsa-miR-133a-3p
<i>GALNT7</i>	hsa-miR-34b-3p, hsa-miR-16-5p
<i>HMGA2</i>	hsa-miR-16-5p, has-miR-let-7g-5p
<i>IGF1R</i>	hsa-miR-16-5p, hsa-miR-133a-3p
<i>IL13</i>	has-miR-let-7g-5p, has-miR-let-7f-5p
<i>KRAS</i>	hsa-miR-16-5p, has-miR-let-7g-5p
<i>MYB</i>	hsa-miR-195-5p, hsa-miR-16-5p
<i>MYC</i>	has-miR-let-7g-5p, hsa-miR-34b-3p
<i>RAF1</i>	hsa-miR-195-5p, hsa-miR-16-5p
<i>RET</i>	hsa-miR-195-5p, has-miR-31-5p
<i>PURA</i>	hsa-miR-106b-5p, hsa-miR-16-5p
<i>RUNX3</i>	hsa-miR-130a-3p, hsa-miR-106b-5p
<i>YY1</i>	hsa-miR-34b-3p, has-miR-31-5p

miRNA/miR, microRNA; pCR, pathological complete response.