Supplementary Table S1. Clinicopathologic characteristics of pre-invasive carcinomas

Characteristic	No. (n=176)
Age at diagnosis, years	
Mean ± standard deviation	48.3 ± 10.0
Follow-up, years	
Mean ± standard deviation	6.7 ± 3.0
Extent, cm	
Mean ± standard deviation	3.2 ± 2.1
Histological subtype	
DCIS	175 (99.4)
Mixed DCIS and LCIS	1 (0.6)
Nuclear grade	
Low	11 (6.3)
Intermediate	98 (55.7)
High	67 (38.1)
Comedo-type necrosis	
Absent	133 (75.6)
Present	43 (24.4)
Estrogen receptor	
Positive	154 (87.5)
Negative	22 (12.5)
Progesterone receptor	
Positive	134 (76.1)
Negative	83 (23.9)
HER2 status	
Negative	151 (85.8)
Positive	25 (14.2)
Ki67 index	
Low (<10%)	165 (93.8)
High (≥10%)	11 (6.3)
P53 overexpression	
Absent	155 (88.1)
Present	21 (11.9)
Subtype	
Luminal A	127 (72.2)
Luminal B	28 (15.9)
HER2+	8 (4.5)
Triple negative	13 (7.4)
Adjuvant radiation therapy	
Not received	71 (40.3)
Received	105 (59.7)
Adjuvant hormonal therapy	
Not received	105 (59.7)
Received	71 (40.3)

Unless specified, number in parenthesis indicates percentage.

DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ

Supplementary Table S2. Clinicopathologic characteristics of invasive carcinomas

Characteristic	No. (n=524)
Age at diagnosis, years	
Mean ± standard deviation	51.2 ± 11.8
Follow up, years	
Mean ± standard deviation	9.4 ± 4.0
T stage	
T1	246 (47.0)
T2	251 (47.9)
T3	19 (3.6)
T4	8 (1.5)
N stage	
N0	300 (57.3)
N1	137 (26.1)
N2	50 (9.5)
N3	37 (7.1)
Histologic subtype	
Invasive carcinoma of no special type	456 (87.0)
Invasive lobular carcinoma	20 (3.8)
Mucinous carcinoma	15 (2.9)
Metaplastic carcinoma	14 (2.7)
Others	19 (3.6)
Histologic grade	
Low	94 (17.9)
Intermediate	166 (31.7)
High	264 (50.4)
Lymphovascular invasion	
Absent	296 (56.5)
Present	228 (43.5)
Estrogen receptor	
Positive	353 (67.4)
Negative	171 (32.6)
Progesterone receptor	
Positive	278 (53.1)
Negative	246 (46.9)
HER2 status	
Negative	404 (77.1)
Positive	120 (22.9)
Ki67 index	
Low (<20%)	301 (57.4)
High (≥20%)	223 (42.6)
P53 overexpression	
Absent	386 (73.7)
Present	138 (26.3)
Subtype	
Luminal A	225 (42.9)
Luminal B	139 (26.5)
HER2+	64 (12.2)
Triple negative	96 (18.3)
Neo-adjuvant chemotherapy	
Not received	491 (93.7)
Received	33 (6.3)
Adjuvant chemotherapy*	
Not received	87 (16.6)
Received	431 (85.3)
Adjuvant HER2-targeted therapy*	
Not received	460 (87.8)
Received	58 (11.1)
Adjuvant radiation therapy*	
Not received	204 (38.9)
Received	314 (59.9)
Adjuvant hormonal therapy*	
Not received	159 (30.3)
Received	359 (68.5)

Unless specified, number in parenthesis indicate percentage.

*Information on adjuvant therapy could not be assessed in 6 cases due to follow-up loss.

Supplementary Table S3. Relationship between S100A8 expression in tumor cells and immune cells and clinicopathological features of pre-invasive carcinoma

Clinicopathological feature	S100A8+ TC		p value	S100A8+ IC		p value
	Negative	Positive		Negative	Positive	
Extent			0.012			0.238
<3.2cm	61 (50.0)	38 (70.4)		49 (52.1)	50 (61.0)	
≥3.2cm	61 (50.0)	16 (29.6)		45 (47.9)	32 (39.0)	
Nuclear grade			0.004			0.594
Low	10 (8.2)	1 (1.9)		7 (7.4)	4 (4.9)	
Intermediate	75 (61.5)	23 (42.6)		54 (57.4)	44 (53.7)	
High	37 (30.3)	30 (55.6)		33 (35.1)	34 (41.5)	
Comedo-type necrosis			0.027			0.081
Absent	98 (80.3)	35 (64.8)		76 (80.9)	57 (69.5)	
Present	24 (19.7)	19 (35.2)		18 (19.1)	25 (30.5)	
ER			<0.001			0.030
Positive	119 (97.5)	35 (64.8)		87 (92.6)	67 (81.7)	
Negative	3 (2.5)	19 (35.2)		7 (7.4)	15 (18.7)	
PR			<0.001			0.389
Positive	110 (90.2)	24 (44.4)		74 (78.7)	60 (73.2)	
Negative	12 (9.8)	30 (55.6)		20 (21.3)	22 (26.8)	
HER2 status			0.001			0.147
Negative	112 (91.8)	39 (72.2)		84 (89.4)	67 (81.7)	
Positive	10 (8.2)	15 (27.8)		10 (10.6)	15 (18.3)	
Ki67 index			0.036			0.087
Low (<10%)	111 (91.0)	43 (79.6)		86 (91.5)	68 (82.9)	
High (≥10%)	11 (9.0)	11 (20.4)		8 (8.5)	14 (17.1)	
P53 overexpression			0.005			0.134
Absent	113 (92.6)	42 (77.8)		86 (91.5)	69 (84.1)	
Present	9 (7.4)	12 (22.2)		8 (8.5)	13 (15.9)	
Subtype			<0.001			0.215
Luminal A	101 (82.8)	26 (48.1)		73 (77.7)	54 (65.9)	
Luminal B	18 (14.8)	10 (18.5)		14 (14.9)	14 (17.1)	
HER2+	1 (0.8)	7 (13.0)		3 (3.2)	5 (6.1)	
Triple negative	2 (1.6)	11 (20.4)		4 (4.3)	9 (11.0)	

P values are calculated by Chi-square or Fisher's exact test. Number in parenthesis indicates percentage.

TC, tumor cell; IC, immune cell; ER, estrogen receptor; PR, progesterone receptor

Supplementary Table S4. Relationship between S100A8 expression in tumor cells and immune cells and clinicopathological features of invasive carcinoma

Clinicopatholgical features	S100A8+ TC		p value	S100A8+ IC		p value
	Negative	Positive		Negative	Positive	
T stage			0.689			0.064
T1	166 (47.6)	80 (45.7)		142 (50.7)	104 (42.6)	
T2-T4	183 (52.4)	95 (54.3)		138 (49.3)	140 (57.4)	
N stage			0.880			0.068
N0	199 (57.0)	101 (57.7)		150 (53.6)	150 (61.5)	
N1-N3	150 (43.0)	74 (42.3)		130 (46.4)	94 (38.5)	
Histologic grade			<0.001			<0.001
Low	85 (24.4)	9 (5.1)		72 (25.7)	22 (9.0)	
Intermediate	136 (39.0)	30 (17.1)		124 (44.3)	42 (17.2)	
High	128 (36.7)	136 (77.7)		84 (30.0)	180 (73.8)	
LVI			0.557			0.393
Absent	194 (55.6)	102 (58.3)		163 (58.2)	133 (54.5)	
Present	155 (44.4)	73 (41.7)		117 (41.8)	111 (45.5)	
ER			<0.001			<0.001
Positive	287 (82.2)	66 (37.7)		236 (84.3)	117 (48.0)	
Negative	62 (17.8)	109 (62.3)		44 (15.7)	127 (52.0)	
PR			<0.001			<0.001
Positive	227 (65.0)	51 (29.1)		187 (66.8)	91 (37.3)	
Negative	122 (35.0)	124 (70.9)		93 (33.2)	153 (62.7)	
HER2 status			<0.001			<0.001
Negative	56 (16.0)	64 (36.6)		42 (15.0)	78 (32.0)	
Positive	293 (84.0)	111 (63.4)		238 (85.0)	166 (68.0)	
Ki67 index			<0.001			<0.001
Low	248 (71.1)	53 (30.3)		214 (76.4)	87 (35.7)	
High	101 (28.9)	122 (69.7)		66 (23.6)	157 (64.3)	
P53 overexpression			<0.001			<0.001
Absent	286 (81.9)	100 (57.1)		232 (82.9)	154 (63.1)	
Present	63 (18.1)	75 (42.9)		48 (17.1)	90 (36.9)	
Subtype			<0.001			<0.001
Luminal A	195 (55.9)	30 (17.1)		169(60.4)	56 (23.0)	
Luminal B	96 (27.5)	43 (24.6)		71 (25.4)	68 (27.9)	
HER2+	19 (5.4)	45 (25.7)		16 (5.7)	48 (19.7)	
Triple negative	39 (11.2)	57 (33.4)		24 (8.6)	72 (29.5)	

P values are calculated by Chi-square or Fisher's exact test. Number in parenthesis indicates percentage.

TC, tumor cell; IC, immune cell; LVI, lymphovascular invasion; ER, estrogen receptor; PR, progesterone receptor

Supplementary Table S5. Correlations between S100A8+ immune cells, infiltration of CD4+, CD8+, and FOXP3+ tumor infiltrating lymphocytes and PD-L1+ immune cells in pre-invasive and invasive carcinoma

Disease group	Correlation between markers	S100A8+ IC	CD4+ TIL	CD8+ TIL	FOXP3+ TIL	PD-L1+ IC
Pre-invasive carcinoma	S100A8+ IC	-	0.281 (<0.001)	0.249 (0.001)	0.209 (0.006)	0.248 (0.001)
	CD4+ TIL	0.281 (<0.001)	-	0.610 (<0.001)	0.463 (<0.001)	0.391 (<0.001)
	CD8+ TIL	0.249 (0.001)	0.610 (<0.001)	-	0.458 (<0.001)	0.344 (<0.001)
	FOXP3+ TIL	0.209 (0.006)	0.463 (<0.001)	0.458 (<0.001)	-	0.434 (<0.001)
	PD-L1+ IC	0.248 (0.001)	0.391 (<0.001)	0.344 (<0.001)	0.434 (<0.001)	-
Invasive carcinoma	S100A8+ IC	-	0.263 (<0.001)	0.474 (<0.001)	0.482 (<0.001)	0.525 (<0.001)
	CD4+ TIL	0.263 (<0.001)	-	0.487 (<0.001)	0.306 (<0.001)	0.336 (<0.001)
	CD8+ TIL	0.474 (<0.001)	0.487 (<0.001)	-	0.588 (<0.001)	0.616 (<0.001)
	FOXP3+ TIL	0.482 (<0.001)	0.306 (<0.001)	0.588 (<0.001)	-	0.565 (<0.001)
	PD-L1+ IC	0.525 (<0.001)	0.336 (<0.001)	0.616 (<0.001)	0.565 (<0.001)	-

Data are presented as rho correlation coefficients calculated by Spearman's rank correlation test and p values in parentheses.

TIL, tumor-infiltrating lymphocyte; IC, immune cell