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                             | 134 (76.1)  |
| Negative                             | 83 (23.9)   |
| Progesterone receptor                |             |
| Positive                             | 154 (87.5)  |
| Negative                             | 22 (12.5)   |
| 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 |  | S100A8+ IC |  |
|-----------------------------|------------|----------------|------------|----------------|
|                             | Negative | Positive |  p value | Negative | Positive |  p value |
| Extent                      |          |          |          |          |          |          |
| <3.2 cm                     | 61 (50.0) | 38 (70.4) | 0.012 | 49 (52.1) | 50 (61.0) | 0.238 |
| ≥3.2 cm                     | 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

| Clinicopathological features | S100A8+ TC |       |        | S100A8+ IC |       |        |
|-----------------------------|------------|-------|-------|------------|-------|-------|
|                             | Negative   | Positive | p value | Negative   | Positive | p value |
| T stage                     |            |         |        |            |         |        |
| T1                          | 166 (47.6) | 80 (45.7) | 0.689  | 142 (50.7) | 104 (42.6) | 0.064 |
| T2-T4                       | 183 (52.4) | 95 (54.3) | 0.880  | 138 (49.3) | 140 (57.4) | 0.068 |
| N stage                     |            |         |        |            |         |        |
| N0                          | 199 (57.0) | 101 (57.7) | <0.001 | 150 (53.6) | 150 (61.5) | <0.001 |
| N1-N3                       | 150 (43.0) | 74 (42.3) | 0.557  | 130 (46.4) | 94 (38.5) | 0.393 |
| Histologic grade            |            |         |        |            |         |        |
| Low                         | 85 (24.4)  | 9 (5.1)  | <0.001 | 72 (25.7)  | 22 (9.0)  | <0.001 |
| 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                         |            |         |        |            |         |        |
| 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                          |            |         |        |            |         |        |
| Positive                    | 287 (82.2) | 66 (37.7)  | <0.001 | 236 (84.3) | 117 (48.0) | <0.001 |
| Negative                    | 62 (17.8)  | 109 (62.3) |         | 44 (15.7)  | 127 (52.0) |         |
| PR                          |            |         |        |            |         |        |
| Positive                    | 227 (65.0) | 51 (29.1)  | <0.001 | 187 (66.8) | 91 (37.3)  | <0.001 |
| Negative                    | 122 (35.0) | 124 (70.9) |         | 93 (33.2)  | 153 (62.7) |         |
| HER2 status                 |            |         |        |            |         |        |
| Negative                    | 56 (16.0)  | 64 (36.6)  | <0.001 | 42 (15.0)  | 78 (32.0)  | <0.001 |
| Positive                    | 293 (84.0) | 111 (63.4) |         | 238 (85.0) | 166 (68.0) |         |
| Ki67 index                  |            |         |        |            |         |        |
| Low                         | 248 (71.1) | 53 (30.3)  | <0.001 | 214 (76.4) | 87 (35.7)  | <0.001 |
| High                        | 101 (28.9) | 122 (69.7) |         | 66 (23.6)  | 157 (64.3) |         |
| P53 overexpression          |            |         |        |            |         |        |
| Absent                      | 286 (81.9) | 100 (57.1) | <0.001 | 232 (82.9) | 154 (63.1) | <0.001 |
| Present                     | 63 (18.1)  | 75 (42.9)  |         | 48 (17.1)  | 90 (36.9)  |         |
| Subtype                     |            |         |        |            |         |        |
| Luminal A                   | 195 (55.9) | 30 (17.1)  | <0.001 | 169 (60.4) | 56 (23.0)  | <0.001 |
| 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           |                             | -          | 0.281 (<0.001) | 0.249 (0.001) | 0.209 (0.006) | 0.248 (0.001) |
| S100A8+ IC          |                             |            |          |          |            |           |
| 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           |                             | -          | 0.263 (<0.001) | 0.474 (<0.001) | 0.482 (<0.001) | 0.525 (<0.001) |
| S100A8+ IC          |                             |            |          |          |            |           |
| 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