

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Patocs A, Zhang L, Xu Y, et al. Breast-cancer stromal cells with *TP53* mutations and nodal metastases. *N Engl J Med* 2007;357:2543-51.

**Supplemental Table S1. CLINICOPATHOLOGICAL FEATURES OF BREAST CANCER PATIENTS**

|  | <b>Sporadic</b><br>n=175 | <b>Hereditary breast cancer</b><br>n=43 | <b>p-value</b>  |
|--|--------------------------|---|-----------------|
| Number of cases                              |                          |   |                 |
| <b>Age (years) (range)</b>                   | 52.3 (25-82)             | 42.6 (23-86)                            | <b>P=0.002*</b> |
| <b>Tumor stage (%, n/d)</b>                  |                          |   |                 |
| 0-I  | 29.8 (42/141)            | 20.5 ( 7/34)                            | P=0.55          |
| II   | 50.3 (71/141)            | 58.8 (20/34)                            |                 |
| III  | 19.8 (28/141)            | 20.5 ( 7/34)                            |                 |
| Non-informative                              | 34/175                   | 9/43                                    |                 |
| <b>Nodal status (%, n/d)</b>                 |                          |   |                 |
| 0  | 47.6 (60/126)            | 52.9 (18/34)                            | P=0.58          |
| >1   | 52.4 (66/126)            | 47.1 (16/34)                            |                 |
| Non-informative                              | 49/175                   | 9/43                                    |                 |
| <b>Estrogen receptor status (%, n/d)</b>     |                          |   |                 |
| Positive                                     | 64.9 (100/154)           | 41.3 (12/29)                            | <b>P=0.017*</b> |
| Negative                                     | 35.0 ( 54/154)           | 58.6 (17/29)                            |                 |
| Non-informative                              | 21/175                   | 14/43                                   |                 |
| <b>Progesterone receptor status (%, n/d)</b> |                          |   |                 |
| Positive                                     | 64.9 (100-154)           | 41.3 (12/29)                            | <b>P=0.017*</b> |
| Negative                                     | 35.0 ( 54/154)           | 58.6 (17/29)                            |                 |
| Non-informative                              | 21/175                   | 14/43                                   |                 |

\*indicates a significance with P value < 0.05.

A binomial model with nested structure was used to compare the distributions of clinicopathological features for patients with germline BRCA1/2 mutations/variants to sporadic breast cancer patients.

(%, n/d) denotes percentage (numerator divided by denominator)

**Supplemental Table S2. PRIMERS USED FOR DGGE AND SEQUENCING OF TP53**

| Sequencing Primers  | 5'- 3'   | TM (°C) |
|---------------------|--|---------|
| P53-4Fseq           | CCTGGTCCTCTGACTGCTCTTTTCACCCA  | 55      |
| P53-4Rseq           | GGCCAGGCATTGAAGTCTCAT  |         |
| P53-5Fseq           | CAACTCTGTCTCCTTCCT   | 55      |
| P53-5Rseq           | TGTCGTCTCTCCAGCCCC   |         |
| P53-6Fseq           | AGAGACGACAGGGCTGGTTG   | 55      |
| P53-6Rseq           | CTTAACCCCTCCTCCCAGAG   |         |
| P53-7Fseq           | CCTCATCTTGGGCCTGTGTT   | 55      |
| P53-7Rseq           | AGTGTGCAGGGTGGCAAGTG   |         |
| P53-8Fseq           | CCTTACTGCCTCTTGCTTCT   | 55      |
| P53-8Rseq           | ATAACTGCACCCTTGGTCTC   |         |
| P53-9Fseq           | GGAGACCAAGGGTGCAGTTATGCCTCAG   | 55      |
| P53-9Rseq           | CCCAATTGCAGGTAAAACAG   |         |
| <b>DGGE PRIMERS</b> | <b>5'- 3'</b>  |         |
| P53-4.1F            | CGTCCCGCTGGTCCTCTGACTGCTCTTT   | 55      |
| P53-4.1R            | CGCCCGCCGCGCCCCGCGCCCGTCCCGCCGCCCC<br>GCCCGCATTCTGGGAGCTTCATCTG            |         |
| P53-4.2F            | AAGCTCCCAGAATGCCAG   | 55      |
| P53-4.2R            | CGCCCGCCGCCGCCCCGCGCGCCCCGCGCCCCGTCC<br>CGCCGCCCCCGCCCGGCAAGAAGCCAGACGGA   |         |
| P53-4.3F            | CGCCCGCCGCCGCCCCGCGCGCCCCGCGCCCCGTCC<br>CGCCGCCCCCGCCCGTCCCTTCCAGAAAACCT   | 55      |
| P53-4.3R            | TGAAGTCTCATGGAAGCC   |         |
| P53-5F              | CGCCCGCCGCCGCCCCGCGCGCCCCGCGCCCCGTCC<br>CGCCGCCCCCGCCCGCAACTCTGTCTCCTTCCT  | 62      |
| P53-5R              | TGTCGTCTCTCCAGCCCC   |         |
| P53-6F              | AGAGACGACAGGGCTGGTTG   | 62      |
| P53-6R              | CGCCCGCCGCGCCCCGCGCCCCGCCCCGCCGCCCC<br>GCCCGAAATAATAAACCTTAACCCCTCCTCCCAGA |         |
| P53-7F              | CGCCCGCCGCGCCCCGCGCCCCGTCCCGCCGCCCC<br>GCCCG- CCTCATCTTGGGCCTGTGTT         | 57      |
| P53-7R              | AGTGTGCAGGGTGGCAAGTG   |         |
| P53-8F              | CGCCCGCCGCGCCCCGCGCCCCGTCCCGCCGCCCC<br>GCCCG-CCTTACTGCCTCTTGCTTCT          | 57      |
| P53-8R              | ATAACTGCACCCTTGGTCTC   |         |
| P53-9F              | GCGCG-GCAGTTATGCCTCAGATTCA   | 55      |
| P53-9R              | CGCCCGCCGCGCCCCGCGCCCCGTCCCGCCGCCCC<br>GCCCG-CCCAATTGCAGGTAAAACAG          |         |

DGGE: denaturant gradient gel electrophoresis

**Supplemental Table S3A. GERMLINE *BRCA1/2* AND SOMATIC *TP53* MUTATIONS IN SAMPLES FROM HEREDITARY BREAST AND OVARIAN CANCER (HBOC) PATIENTS**

| Fam | Sample ID | Germline <i>BRCA</i> mutation |                      | Somatic <i>TP53</i> mutation |                        |
|-----|-----------|-------------------------------|----------------------|------------------------------|------------------------|
|     |           |                               |                      | Epithelium                   | Stroma                 |
| 1   | 1         | <i>BRCA1</i>                  | 4020delAG            | Pro89Ser<br>1612insA         | Pro89Ser<br>Arg273Cys  |
| 2   | 2         | <i>BRCA1</i>                  | IVS4-1G>T            | Pro89Ser                     | -                      |
| 3   | 3         | <i>BRCA1</i>                  | 1135insA             | Pro89Ser                     | -                      |
| 4   | 4         | <i>BRCA1</i>                  | 2530delAG            | Pro89Ser                     | Pro89Ser               |
| 5   | 5         | <i>BRCA1</i>                  | 1240delC             | Pro89Ser<br>Arg273Cys        | -                      |
| 6   | 6         | <i>BRCA1</i>                  | 589delCT             | Pro219Ser                    | -                      |
| 7   | 7         | <i>BRCA1</i>                  | IVS18+3A/C           | -                            | Asp41Asn               |
| 8   | 8         | <i>BRCA1</i>                  | 1389insAG            | -                            | codon209 delGA         |
| 9   | 9         | <i>BRCA1</i>                  | IVS6-1C/T            | Pro89Ser                     | Pro89Ser<br>Asp184Asn  |
| 10  | 10        | <i>BRCA1</i>                  | del ex23-24          | 1733insA                     | -                      |
| 11  | 11        | <i>BRCA1</i>                  | IVS18+3A/C           | Thr170Met                    | -                      |
| 12  | 12        | <i>BRCA1</i>                  | del ex23-24          | -                            | -                      |
| 13  | 13        | <i>BRCA1</i>                  | 157delCT             | -                            | Thr150Ile              |
| 14  | 14        | <i>BRCA1</i>                  | 4229insATCT          | Val157Ile<br>Arg248Glu       | Pro89Ser               |
| 15  | 15        | <i>BRCA1</i>                  | 5385insC             | Arg273Cys                    | -                      |
| 16  | 16        | <i>BRCA1</i>                  | 2552delC             | -                            | -                      |
| 17  | 17        | <i>BRCA1</i>                  | C61G                 | Pro89Ser<br>Ser149Phe        | -                      |
| 18  | 18        | <i>BRCA1</i>                  | IVS5-11T>G           | Arg248Glu                    | -                      |
| 19  | 19        | <i>BRCA1+</i><br><i>BRCA2</i> | A1708E+8234del<br>TT | Ala88Thr<br>Glu144Arg        | -                      |
|     | 20        | <i>BRCA2</i>                  | 6503delTT            | -                            | -                      |
| 20  | 21        | <i>BRCA2</i>                  | 6503delTT            | -                            | Glu198Lys              |
| 21  | 22        | <i>BRCA2</i>                  | 2567delC             | Pro89Ser                     | Pro89Ser<br>Arg273Cys  |
| 22  | 23        | <i>BRCA2</i>                  | Y1894X               | -                            | -                      |
| 23  | 24        | <i>BRCA2</i>                  | 5578delAA            | -                            | -                      |
| 24  | 25        | <i>BRCA2</i>                  | 8234del23            | Pro177Arg<br>Glu221Lys       | -                      |
| 25  | 26        | <i>BRCA2</i>                  | 5804delAAAA          | -                            | Glu198Lys              |
| 26  | 27        | <i>BRCA2</i>                  | 3036delACAA          | -                            | -                      |
| 27  | 28        | <i>BRCA2</i>                  | 8294insTT            | -                            | Pro89Ser               |
| 28  | 29        | <i>BRCA1uv</i>                | S1040N               | Pro89Ser                     | -                      |
| 29  | 30        | <i>BRCA1uv</i>                | S1040N               | -                            | -                      |
| 30  | 31        | <i>BRCA1uv</i>                | N1236K               | -                            | Ser313Asn              |
| 31  | 32        | <i>BRCA1uv</i>                | A1623G               | -                            | -                      |
|     | 33        | <i>BRCA1uv</i>                | S1623G               | -                            | Pro177Ser              |
| 32  | 34        | <i>BRCA1uv</i>                | IVS2-14T>C           | -                            | Asp184Asn              |
| 33  | 35        | <i>BRCA2uv</i>                | I3412V               | -                            | Pro89Ser<br>His179Arg  |
| 34  | 36        | <i>BRCA2uv</i>                | K1057R               | Pro89Ser<br>Thr140Ala        | Ala161Thr<br>Asp186Gly |
| 35  | 37        | <i>BRCA2uv</i>                | A2466V               | -                            | -                      |
| 36  | 38        | <i>BRCA2uv</i>                | IVS8+56T>C           | Ala161Val                    | Arg174Gly              |

|    |    |                |             |                       |           |
|----|----|----------------|-------------|-----------------------|-----------|
| 37 | 39 | <i>BRCA2uv</i> | A2951T      | Thr170Ala Glu180Gly   | Pro152Ser |
| 38 | 40 | <i>BRCA2uv</i> | A2951T      | -                     | Met133Val |
| 39 | 41 | <i>BRCA2uv</i> | IVS21-11A/C | Pro89Ser ivs8 + 1 G/T | Pro89Ser  |
|    | 42 | <i>wt</i>      | -           | Pro89Ser Asp324His    | Pro89Ser  |
| 40 | 43 | <i>wt</i>      | -           | -                     | -         |

**Supplemental Table S3B. SOMATIC MUTATIONS OF TP53 IN EPITHELIAL AND STROMAL DNA IN SPORADIC BREAST CANCER PATIENTS**

| Sample ID | Somatic TP53 mutation |                      |
|-----------|-----------------------|----------------------|
|           | Epithelium            | Stroma               |
| 1         | Del1bp codon 171      | -                    |
| 2         | Pro89Ser              | -                    |
| 3         | delT codon275         | -                    |
| 4         | Arg196X               | -                    |
| 5         | His296Tyr             | -                    |
| 6         | Val173Met             | -                    |
| 7         | Arg214X               | -                    |
| 8         | Gly245Ser             | -                    |
| 9         | Pro152Leu, Arg158Cys  | -                    |
| 10        | Arg213X               | -                    |
| 11        | 393insC               | -                    |
| 12        | Arg273Cys             | -                    |
| 13        | Ile195Thr             | -                    |
| 14        | Arg209Lys             | -                    |
| 15        | His179Asp             | -                    |
| 16        | Cys176Trp             | -                    |
| 17        | Arg282Gly             | -                    |
| 18        | Arg156His, Pro177Ser  | -                    |
| 19        | His178Tyr             | -                    |
| 20        | Val172Ile             | -                    |
| 21        | 532delC               | -                    |
| 22        | Leu137Pro, Val172Ala  | -                    |
| 23        | Asp184Gly             | -                    |
| 24        | Pro98Leu, His168Tyr   | -                    |
| 25        | Gln136Arg             | -                    |
| 26        | Trp146Arg, Pro316Leu  | -                    |
| 27        | -                     | Pro177Leu            |
| 28        | -                     | Glu198Lys            |
| 29        | -                     | His168Tyr            |
| 30        | -                     | Cys182Arg            |
| 31        | -                     | Val157Asp            |
| 32        | -                     | Leu188Pro, Glu198Lys |
| 33        | -                     | Phe270Leu            |
| 34        | -                     | Cys277Gly            |
| 35        | -                     | Arg158Ser            |
| 36        | -                     | Ala159Pro            |
| 37        | -                     | Ala159Pro            |
| 38        | -                     | Arg213X              |
| 39        | -                     | Thr155Ala, Thr155Ile |
| 40        | -                     | Met133Val, His178Arg |
| 41        | -                     | Arg213X              |
| 42        | -                     | Pro151Ser            |
| 43        | -                     | Thr155Ile            |
| 44        | -                     | Val218Ala            |
| 45        | -                     | Thr150Ile            |

|    |                      |                      |
|----|----------------------|----------------------|
| 46 | -                    | Leu145Pro, Arg196X   |
| 47 | -                    | Val173Ala            |
| 48 | -                    | Glu198Lys            |
| 49 | -                    | 532insC              |
| 50 | -                    | Ser183Leu            |
| 51 | -                    | Pro75Leu             |
| 52 | -                    | Pro278Ser            |
| 53 | -                    | Gly325Arg            |
| 54 | -                    | Gly226Ser            |
| 55 | -                    | Thr140Ile, 565delG   |
| 56 | -                    | Asp210Ser            |
| 57 | -                    | Gln167His            |
| 58 | -                    | Gln136X, His214Tyr   |
| 59 | -                    | Glu198Lys, Val218Ala |
| 60 | -                    | Ser149Phe, Pro153Ser |
| 61 | delG codon108        | Pro153Ser, Glu198Lys |
| 62 | 532delC              | Arg174Gly, 599delA   |
| 63 | Arg156Cys, 532delC   | Gln165Arg            |
| 64 | Glu198Lys, Arg273His | His296Leu, His297Tyr |
| 65 | Gln136Arg            | Arg290Gln            |
| 66 | Ala161Val, Pro316Leu | Gly279Glu            |
| 67 | Ala138Thr, Ser149Ala | Thr170Ala, Thr170Met |
| 68 | Asp184Asn            | Gly279Arg            |
| 69 | Ser166Leu, Cys176Ser | Arg175Cys            |
| 70 | Arg213Glu            | Arg213Glu            |
| 71 | Tyr236Cys            | Arg174Gly, Cys176Tyr |
| 72 | Ser183Leu            | Arg280Ser            |
| 73 | Phe134Cys            | Thr155Ser            |
| 74 | Arg181Cys            | Arg273Cys            |

**Supplemental Table S4.** MUTATED *TP53*-ASSOCIATED MARKERS IN BOTH EPITHELIUM AND STROMA OF SPORADIC BREAST CANCER.

| <b>Loci</b> | <b>Marker</b> | <b>LOH frequency<br/>(Epithelium)</b> | <b>P value*</b> | <b>LOH frequency<br/>(Stroma)</b> | <b>P value*</b> | <b>Gene(s)</b>                        |
|-------------|---------------|---------------------------------------|-----------------|-----------------------------------|-----------------|---------------------------------------|
| 2q34        | D2S2944       | 18/29 (0.62)                          | 0.010           | 22/32 (0.69)                      | 0.021           | <i>SPAG16</i>                         |
| 3q27.3      | D3S1262       | 18/28 (0.64)                          | <.001           | 18/24 (0.79)                      | <.001           | <i>TP73L, SST, SENP2,<br/>MAP3K13</i> |
| 5q15        | D5S1462       | 22/27 (0.81)                          | <.001           | 21/29 (0.72)                      | 0.005           | <i>LNPEP, LIX1, RIOK2</i>             |
| 7p12.3      | D7S1818       | 16/19 (0.84)                          | 0.006           | 20/25 (0.80)                      | 0.005           | <i>ABC13</i>                          |
| 15q11.2     | D15S128       | 17/22 (0.77)                          | 0.002           | 14/21 (0.67)                      | 0.009           | <i>SNORD107</i>                       |
| 16p13       | D16S2616      | 18/29 (0.62)                          | 0.014           | 20/30 (0.67)                      | 0.004           | <i>MYLE, SOCS1, TNP2</i>              |
| 18q23       | D18S1390      | 14/22 (0.64)                          | 0.011           | 19/28 (0.68)                      | 0.001           | <i>PARD6G, TXNL4A</i>                 |
| 20p13       | D20S103       | 15/28 (0.54)                          | 0.021           | 17/32 (0.53)                      | 0.005           | <i>CSNK2A1, TCF15,<br/>SCRT2</i>      |

\*Multiple testing adjustment is based on false-positive report probability  $FPRP_{0.01} < 0.5$

**Supplemental Table S5. HOTSPOTS OF LOH/AI ASSOCIATED WITH MUTATED *TP53* IN EITHER EPITHELIUM OR STROMA OF BREAST CANCER.**

| Loci†  | Marker   | LOH frequency (Mutated <i>TP53</i> ) | LOH frequency (Wild-type <i>TP53</i> ) | P value* | Gene(s)   |
|--|----------|--------------------------------------|--|----------|---|
| <b><u>Sporadic Breast cancer Samples</u></b> |          |                                      |  |          |   |
| <b>Epithelium</b>                            |          |                                      |  |          |   |
| 5q35.1                                       | D5S1456  | 21/25 (0.84)                         | 34/82 (0.41)                           | <.001    | <i>STK10, DRD1, FGFR4, MGAT1, MAPK9</i>                 |
| 8q22   | GAAT1A4  | 24/26 (0.92)                         | 46/89 (0.52)                           | <.001    | <i>STK3, COX6C, POLR2K, TIEG, PPM2C, POPI, TP53INP1</i> |
| 16p12  | D16S403  | 18/32 (0.56)                         | 25/103 (0.24)                          | 0.002    | <i>POLR3E, NDUFAB1</i>                                  |
| 22q11.2                                      | D22S345  | 20/29 (0.69)                         | 25/78 (0.32)                           | 0.001    | <i>CABIN</i>  |
| <b>Stroma</b>                                |          |                                      |  |          |   |
| 7q21.3                                       | D7S821   | 21/26 (0.81)                         | 31/75 (0.41)                           | 0.001    | <i>SHFM1, SLC25A13</i>                                  |
| 8q24.13                                      | D8S1179  | 17/21 (0.81)                         | 28/71 (0.39)                           | 0.002    | <i>FBOX032, ANXA13</i>                                  |
| 11p15.5                                      | D11S1984 | 23/32 (0.72)                         | 30/82 (0.37)                           | 0.001    | <i>COX8B, STK29, DUSP8, IGF2, INS, TH, SYT8</i>         |
| 12q21  | D12S1052 | 19/25 (0.76)                         | 21/73 (0.29)                           | <.001    | <i>CAPS2, RAB21, THAP2, PPP1R12A,</i>                   |
| 13q32.3                                      | D13S779  | 15/17 (0.88)                         | 14/51 (0.27)                           | <.001    | <i>FGF14, VGCNLI</i>                                    |
| 18q21.32                                     | D18S1357 | 20/26 (0.77)                         | 26/68 (0.38)                           | 0.002    | <i>BCL2, DCC</i>  |
| <b><u>HBOC samples</u></b>                   |          |                                      |  |          |   |
| <b>Stroma</b>                                |          |                                      |  |          |   |
| 2p25.1                                       | D2S1400  | 14/18 (0.78)                         | 4/17 (0.23)                            | <.001    | <i>E2F6, ROCK2</i>                                      |

LOH: loss of heterozygosity; HBOC: hereditary breast/ovarian cancer

\* Multiple testing adjustment is based on false-positive report probability  $FPRP_{0.01} < 0.5$

† Highest ranked markers;  $P < 0.005$  (Supplemental Tables S6-7).

**Supplemental Table S6:** Mutated *TP53* associated LOH/AI hotspot markers in sporadic breast cancer Epithelium

| Loci              | Marker     | LOH frequency<br>( <i>TP53</i> -mutated) | LOH frequency<br>( <i>TP53</i> -wild type) | <i>P</i> value* | Gene(s)   |
|-------------------|------------|--|--|-----------------|---|
| <b>Epithelium</b> |            |  |  |                 |   |
| 1q23.1            | D1S1653    | 18/27 (0.67)                             | 29/80 (0.36)                               | 0.011           | <i>CD cluster</i>                                       |
| 2p13              | D2S1394    | 19/27 (0.70)                             | 37/98 (0.38)                               | 0.005           | <i>SPR, EMX1, SFXN5</i>                                 |
| 2p25              | D2S1400    | 16/26 (0.62)                             | 26/82 (0.32)                               | 0.012           | <i>E2F6, ROCK2</i>                                      |
| 2p14              | D2S441     | 18/25 (0.72)                             | 37/89 (0.42)                               | 0.013           | <i>PPP3R1, PNO1</i>                                     |
| 4q23              | D4S1647    | 18/26 (0.69)                             | 41/98 (0.42)                               | 0.023           | <i>TSPAN5, BTF3L3, RAPIGDS1</i>                         |
| 5q35.1            | D5S1456    | 21/25 (0.84)                             | 34/82 (0.41)                               | <.001           | <i>STK10, DRD1, FGFR4, MGAT1, MAPK9</i>                 |
| 5q14              | D5S1725    | 18/26 (0.69)                             | 33/83 (0.40)                               | 0.016           | -   |
| 6q24.3            | GATA184A08 | 18/25 (0.72)                             | 33/80 (0.41)                               | 0.014           | -   |
| 8q22              | GAAT1A4    | 24/26 (0.92)                             | 46/89 (0.52)                               | <.001           | <i>STK3, COX6C, POLR2K, TIEG, PPM2C, POPI, TP53INP1</i> |
| 8q24.3            | D8S373     | 15/20 (0.75)                             | 29/76 (0.38)                               | 0.007           | <i>GLI4, LY6H, MAFA</i>                                 |
| 12q12             | D12S1301   | 18/25 (0.72)                             | 37/94 (0.39)                               | 0.007           | <i>IRAK4, PUS7L</i>                                     |
| 12q24             | D12S1045   | 19/34 (0.56)                             | 31/98 (0.32)                               | 0.021           | <i>TMEM132D, FZD10</i>                                  |
| 12q21             | D12S1064   | 19/27 (0.70)                             | 37/88 (0.42)                               | 0.018           | -   |
| 14q32.2           | D14S1426   | 20/28 (0.71)                             | 39/98 (0.41)                               | 0.007           | <i>DEGS2, EVL, YY1</i>                                  |
| 15q22.2           | D15S643    | 20/26 (0.77)                             | 44/95 (0.46)                               | 0.010           | <i>LDHAL6B, FAM81A</i>                                  |
| 15q13.3           | D15S165    | 18/22 (0.82)                             | 23/49 (0.47)                               | 0.012           | <i>KIAA1018, MTMR10, TRPM1</i>                          |
| 16p12             | D16S403    | 18/32 (0.56)                             | 25/103 (0.24)                              | 0.001           | <i>POLR3E, NDUFAB1</i>                                  |
| 17q21.31          | D17S579    | 18/25 (0.72)                             | 33/77 (0.43)                               | 0.014           | <i>DBF4B, CCDC43, ADAM11</i>                            |
| 17q21.32          | D17S2180   | 17/25 (0.68)                             | 36/90 (0.40)                               | 0.024           | <i>HOX cluster</i>                                      |
| 18q22.3           | ATA82B02   | 22/29 (0.76)                             | 40/88 (0.45)                               | 0.008           | -   |
| 18q12.3           | D18S535    | 21/32 (0.66)                             | 34/90 (0.38)                               | 0.012           | -   |
| 20p13             | D20S482    | 20/31 (0.65)                             | 36/96 (0.38)                               | 0.015           | <i>RASSF2, ADRA1D</i>                                   |
| 22q11.2           | D22S345    | 20/29 (0.69)                             | 25/78 (0.32)                               | 0.001           | <i>CABIN</i>  |
| 22q11.2           | D22S1045   | 20/24 (0.83)                             | 36/77 (0.47)                               | 0.003           | <i>SSTR3, COX5BL7, BIK</i>                              |
| Xq25              | GATA165B12 | 18/22 (0.82)                             | 36/82 (0.44)                               | 0.003           | <i>NKAP, NDUFA</i>                                      |

LOH: loss of heterozygosity; HBOC: hereditary breast ovary cancer

\* Multiple testing adjustment is based on false-positive report probability  $FPRP_{0.01} < 0.5$

**Supplemental Table S7.** Mutated *TP53* associated LOH/AI hotspot markers in sporadic breast cancer Stroma

| Loci          | Marker     | LOH frequency<br>( <i>TP53</i> -mutated) | LOH frequency<br>( <i>TP53</i> -wild type) | P value* | Gene(s)   |
|---------------|------------|--|--|----------|---|
| <b>Stroma</b> |            |  |  |          |   |
| 1p34.2        | D1S3721    | 19/25 (0.83)                             | 32/72 (0.44)                               | 0.003    | <i>MED8, CITED4</i>                             |
| 1p21          | D1S1627    | 19/26 (0.73)                             | 30/76 (0.39)                               | 0.006    | -   |
| 1p31          | D1S1596    | 17/28 (0.61)                             | 22/71 (0.31)                               | 0.012    | <i>GBP cluster</i>                              |
| 3p26.3        | D3S3630    | 18/24 (0.75)                             | 28/73 (0.38)                               | 0.003    | <i>CNTN4</i>                                    |
| 3p24.1        | D3S2432    | 19/27 (0.70)                             | 36/92 (0.39)                               | 0.008    | <i>GPD1L</i>                                    |
| 3q24          | D3S1744    | 20/26 (0.77)                             | 34/83 (0.41)                               | 0.002    | <i>CPB1</i>                                     |
| 3q29          | D3S1311    | 16/27 (0.59)                             | 31/94 (0.33)                               | 0.024    | <i>DLG1</i>                                     |
| 3q28          | D3S2418    | 17/29 (0.59)                             | 26/79 (0.33)                               | 0.028    | <i>FGF12</i>                                    |
| 4q35.1        | D4S408     | 13/16 (0.81)                             | 22/55 (0.40)                               | 0.008    | <i>ENPP6</i>                                    |
| 7p21.3        | D7S3047    | 19/25 (0.76)                             | 36/78 (0.46)                               | 0.017    | -   |
| 7q21.3        | D7S821     | 21/26 (0.81)                             | 31/75 (0.41)                               | 0.001    | <i>SHFM1, SLC25A13</i>                          |
| 8q24.13       | D8S1179    | 17/21 (81.0)                             | 28/71 (39.4)                               | 0.002    | <i>FBOX032, ANXA13</i>                          |
| 10p13         | D10S1430   | 16/23 (0.70)                             | 32/81 (0.40)                               | 0.020    | <i>CAMK1D, CCDC3</i>                            |
| 10q23.3       | D10S677    | 21/30 (0.70)                             | 32/87 (0.37)                               | 0.003    | <i>PLCE1, NOC3L</i>                             |
| 10q24.3       | D10S1239   | 15/20 (0.75)                             | 25/67 (0.37)                               | 0.006    | <i>BTRC, POLL</i>                               |
| 11p15.5       | D11S1984   | 23/32 (71.9)                             | 30/82 (36.6)                               | 0.001    | <i>COX8B, STK29, DUSP8, IGF2, INS, TH, SYT8</i> |
| 12p13         | D12S372    | 16/24 (0.67)                             | 24/71 (0.34)                               | 0.009    | <i>TSPAN9, PRMT8</i>                            |
| 12q21         | D12S1052   | 19/25 (76.0)                             | 21/73 (28.8)                               | <.001    | <i>CAPS2, RAB21, THAP2, PPP1R12A</i>            |
| 12q23         | PAH        | 14/18 (0.78)                             | 19/57 (0.33)                               | 0.002    | <i>PAH, ASCL1</i>                               |
| 13q32.3       | D13S779    | 15/17 (88.2)                             | 14/51 (27.4)                               | <.001    | <i>FGF14, VGCNLI</i>                            |
| 13q           | ATA5A09    | 17/24 (0.71)                             | 32/84 (0.38)                               | 0.009    |   |
| 16p           | D16S3401   | 17/26 (0.65)                             | 28/91 (0.31)                               | 0.003    |   |
| 16q24         | D16S413    | 20/25 (0.80)                             | 35/77 (0.45)                               | 0.005    | <i>SLC7A5, CA5A</i>                             |
| 17p13.1       | D17S974    | 9/12 (0.75)                              | 18/62 (0.29)                               | 0.006    | <i>MYH cluster, SCO1</i>                        |
| 17q24.2       | D17S2193   | 17/24 (0.71)                             | 30/74 (0.41)                               | 0.019    | <i>PRKARIA</i>                                  |
| 18p11         | D18S843    | 17/24 (0.71)                             | 28/74 (0.38)                               | 0.009    | <i>RAB12</i>                                    |
| 18q21.32      | D18S1357   | 20/26 (76.9)                             | 26/68 (38.2)                               | 0.001    | <i>BCL2, DCC</i>                                |
| 18q12.1       | D18S877    | 17/23 (0.74)                             | 26/69 (0.38)                               | 0.005    | -   |
| 22q11         | D22S686    | 20/27 (0.74)                             | 14/38 (0.37)                               | 0.006    | <i>IGLV4-3</i>                                  |
| 22q13.31      | D22S532    | 17/25 (0.68)                             | 21/61 (0.34)                               | 0.009    | <i>ATXN10, WNT7B</i>                            |
| 22q           | GATA198B05 | 20/33 (0.61)                             | 36/103 (0.35)                              | 0.016    |   |
| 22q13         | D22S1169   | 20/33 (0.61)                             | 34/95 (0.36)                               | 0.022    | -   |
| Xq25          | DXS1047    | 16/22 (0.73)                             | 35/85 (0.41)                               | 0.016    | <i>UTP14A, RAB33A, ELF4</i>                     |

LOH: loss of heterozygosity; HBOC: hereditary breast ovary cancer

- Multiple testing adjustment is based on false-positive report probability  $FPRP_{0.01} < 0.5$

**Supplemental Table S8. ASSOCIATION BETWEEN SOMATIC *TP53* MUTATION STATUS AND CLINICOPATHOLOGICAL FEATURES (CPF) IN EPITHELIUM AND STROMA OF SPORADIC BREAST CANCER PATIENTS.**

| CPF                          | Level | Epithelium              |                          |                                       | Stroma                  |                          |                                    |
|------------------------------|-------|-------------------------|--------------------------|---------------------------------------|-------------------------|--------------------------|------------------------------------|
|                              |       | Mutated <i>TP53</i> (N) | Wildtype <i>TP53</i> (N) | P value *<br>Odds Ratio (95% CI)<br>‡ | Mutated <i>TP53</i> (N) | Wildtype <i>TP53</i> (N) | P value *<br>Odds ratio (95% CI) ‡ |
| <b>Grade (Tumor Stage)</b>   |       | 0.99                    |                          |                                       | <b>0.08</b>             |                          |                                    |
|                              | 1     | 3                       | 9                        |                                       | 2                       | 10                       |                                    |
|                              | 2     | 19                      | 63                       | 2 vs 1<br>0.91 (0.22, 3.68)           | 29                      | 53                       | 2 vs 1<br>2.74 (0.56, 13.34)       |
|                              | 3     | 18                      | 59                       | 3 vs 1<br>0.92 (0.22, 3.75)           | 16                      | 61                       | 3 vs 1<br>1.31 (0.26, 6.59)        |
| <b>Estrogen_Receptor</b>     |       | 0.29                    |                          |                                       | 0.87                    |                          |                                    |
|                              | 0     | 15                      | 39                       |                                       | 13                      | 41                       |                                    |
|                              | 1     | 20                      | 79                       | 1 vs 0<br>0.66 (0.30, 1.42)           | 25                      | 74                       | 1 vs 0<br>1.07 (0.49, 2.30)        |
| <b>Progesterone_Receptor</b> |       | 0.64                    |                          |                                       | 0.44                    |                          |                                    |
|                              | 0     | 14                      | 40                       |                                       | 12                      | 42                       |                                    |
|                              | 1     | 20                      | 69                       | 1 vs 0<br>0.83 (0.38, 1.82)           | 25                      | 64                       | 1 vs 0<br>1.37 (0.62, 3.02)        |
| <b>HER2_NEU</b>              |       | 0.63                    |                          |                                       | 0.32                    |                          |                                    |
|                              | 0     | 28                      | 89                       | 1 vs 0<br>0.80 (0.31, 2.02)           | 27                      | 90                       | 1 vs 0<br>1.53 (0.66, 3.52)        |
|                              | 1     | 7                       | 28                       |                                       | 11                      | 24                       |                                    |
| <b>pT (Tumor Size)</b>       |       | 0.78 **                 |                          |                                       | 0.99 **                 |                          |                                    |
|                              | 1     | 15                      | 50                       |                                       | 19                      | 46                       |                                    |
|                              | 2     | 13                      | 44                       | 2 vs 1<br>0.99 (0.42, 2.30)           | 16                      | 41                       | 2 vs 1<br>0.95 (0.43, 2.08)        |
|                              | 3     | 3                       | 5                        | 3 vs 1<br>2.00 (0.43, 9.36)           | 2                       | 6                        | 3 vs 1<br>0.81 (0.15, 4.36)        |
|                              | 4     | 2                       | 7                        | 4 vs 1<br>0.95 (0.18, 5.08)           | 2                       | 7                        | 4 vs 1<br>0.69 (0.13, 3.64)        |
| <b>pN (Nodal Status)</b>     |       | 0.21 †                  |                          |                                       | <b>0.003 †</b>          |                          |                                    |
|                              | 0     | 12                      | 47                       |                                       | 18                      | 42                       |                                    |
|                              | 1     | 10                      | 37                       | 1 vs 0<br>1.06 (0.41, 2.72)           | 7                       | 40                       | 1 vs 0<br>0.41 (0.15, 1.08)        |
|                              | 2     | 5                       | 8                        | 2 vs 0<br>2.45 (0.68, 8.85)           | 5                       | 8                        | 2 vs 0<br>1.46 (0.42, 5.07)        |

|   |   |   |                             |   |   |                               |
|---|---|---|-----------------------------|---|---|-------------------------------|
| 3 | 3 | 3 | 3 vs 0<br>3.92 (0.77, 21.9) | 5 | 1 | 3 vs 0<br>11.67 (1.27, 107.1) |
|---|---|---|-----------------------------|---|---|-------------------------------|

\*: Chi-square

†: Fischer exact test

‡: Odds ratio test: baseline is wildtype *TP53* and the first level of each parameter.