



|                       |    |    |    |    |    |    |    |    |   |   |   |
|-----------------------|----|----|----|----|----|----|----|----|---|---|---|
| Normal-8              | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 1  | 0 | 0 | 0 |
| Normal-9              | 0  | 1  | 0  | 0  | 1  | 0  | 0  | 0  | 0 | 0 | 0 |
| Normal-10             | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0 | 0 | 0 |
| <hr/>                 |    |    |    |    |    |    |    |    |   |   |   |
| Breast Cancer Tissues |    |    |    |    |    |    |    |    |   |   |   |
| <hr/>                 |    |    |    |    |    |    |    |    |   |   |   |
| Tumor-1               | 0  | 1  | 0  | 4  | 2  | 5  | 4  | 3  | 0 | 0 | 0 |
| Tumor-2               | 5  | 7  | 2  | 3  | 2  | 2  | 3  | 4  | 0 | 0 | 1 |
| Tumor-3               | 5  | 11 | 15 | 10 | 10 | 10 | 6  | 0  | 0 | 0 | 0 |
| Tumor-4               | 33 | 60 | 53 | 35 | 31 | 27 | 23 | 11 | 0 | 0 | 0 |
| Tumor-5               | 1  | 1  | 1  | 1  | 2  | 5  | 3  | 1  | 0 | 0 | 0 |
| Tumor-6               | 2  | 5  | 8  | 0  | 6  | 2  | 0  | 0  | 0 | 1 | 0 |
| Tumor-7               | 5  | 8  | 4  | 6  | 12 | 8  | 5  | 0  | 0 | 0 | 1 |
| Tumor-8               | 2  | 4  | 3  | 13 | 15 | 19 | 7  | 6  | 2 | 1 | 0 |
| Tumor-9               | 1  | 7  | 7  | 7  | 8  | 3  | 0  | 2  | 0 | 0 | 0 |
| Tumor-10              | 5  | 23 | 32 | 11 | 15 | 18 | 13 | 12 | 9 | 7 | 6 |
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|          |    |     |    |    |    |    |    |    |    |    |    |
|----------|----|-----|----|----|----|----|----|----|----|----|----|
| Tumor-11 | 18 | 105 | 86 | 42 | 60 | 45 | 37 | 40 | 39 | 25 | 11 |
| Tumor-12 | 0  | 1   | 0  | 1  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| Tumor-13 | 2  | 0   | 0  | 0  | 0  | 0  | 0  | 2  | 0  | 0  | 0  |
| Tumor-14 | 2  | 1   | 2  | 3  | 0  | 1  | 1  | 0  | 0  | 0  | 0  |
| Tumor-15 | 0  | 0   | 1  | 1  | 0  | 1  | 0  | 1  | 0  | 0  | 0  |
| Tumor-16 | 4  | 11  | 5  | 14 | 3  | 2  | 5  | 4  | 5  | 7  | 2  |
| Tumor-17 | 0  | 1   | 0  | 1  | 1  | 1  | 2  | 1  | 3  | 2  | 0  |
| Tumor-18 | 1  | 3   | 3  | 2  | 6  | 2  | 2  | 2  | 0  | 0  | 1  |
| Tumor-19 | 0  | 0   | 0  | 2  | 1  | 4  | 1  | 0  | 0  | 0  | 0  |
| Tumor-20 | 0  | 0   | 1  | 0  | 0  | 0  | 2  | 0  | 0  | 0  | 0  |
| Tumor-21 | 0  | 0   | 1  | 1  | 3  | 0  | 3  | 1  | 1  | 0  | 0  |
| Tumor-22 | 0  | 0   | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| Tumor-23 | 1  | 0   | 0  | 4  | 4  | 4  | 3  | 2  | 1  | 0  | 1  |
| Tumor-24 | 0  | 8   | 0  | 10 | 3  | 3  | 0  | 2  | 0  | 0  | 0  |
| Tumor-25 | 0  | 0   | 0  | 0  | 3  | 0  | 1  | 0  | 1  | 0  | 0  |

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|          |    |    |    |   |    |   |   |   |   |   |   |
|----------|----|----|----|---|----|---|---|---|---|---|---|
| Tumor-26 | 0  | 0  | 1  | 1 | 4  | 5 | 6 | 1 | 0 | 1 | 0 |
| Tumor-27 | 5  | 3  | 2  | 5 | 1  | 2 | 3 | 2 | 1 | 2 | 1 |
| Tumor-28 | 1  | 0  | 0  | 0 | 1  | 1 | 0 | 0 | 0 | 0 | 0 |
| Tumor-29 | 0  | 1  | 0  | 0 | 7  | 0 | 1 | 0 | 0 | 0 | 0 |
| Tumor-30 | 5  | 22 | 21 | 7 | 11 | 7 | 8 | 2 | 2 | 1 | 1 |
| Tumor-31 | 2  | 0  | 0  | 1 | 1  | 1 | 0 | 1 | 0 | 0 | 0 |
| Tumor-32 | 1  | 1  | 1  | 1 | 2  | 0 | 1 | 1 | 1 | 0 | 0 |
| Tumor-33 | 2  | 5  | 12 | 4 | 5  | 6 | 5 | 4 | 0 | 0 | 0 |
| Tumor-34 | 10 | 5  | 5  | 5 | 3  | 0 | 0 | 1 | 0 | 0 | 0 |
| Tumor-35 | 12 | 16 | 7  | 5 | 8  | 5 | 9 | 4 | 5 | 2 | 2 |
| Tumor-36 | 2  | 0  | 3  | 2 | 0  | 0 | 0 | 1 | 0 | 0 | 0 |
| Tumor-37 | 4  | 7  | 12 | 9 | 3  | 3 | 0 | 0 | 0 | 0 | 0 |
| Tumor-38 | 0  | 1  | 0  | 1 | 1  | 2 | 1 | 0 | 0 | 0 | 1 |
| Tumor-39 | 0  | 0  | 1  | 2 | 0  | 0 | 0 | 0 | 0 | 0 | 0 |
| Tumor-40 | 0  | 0  | 0  | 5 | 1  | 3 | 2 | 0 | 0 | 0 | 0 |

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|----------|---|----|----|----|----|----|----|----|---|---|---|
| Tumor-41 | 0 | 1  | 10 | 2  | 8  | 9  | 6  | 2  | 4 | 1 | 5 |
| Tumor-42 | 4 | 10 | 14 | 5  | 23 | 13 | 17 | 11 | 6 | 7 | 4 |
| Tumor-43 | 1 | 4  | 1  | 1  | 2  | 7  | 1  | 1  | 0 | 0 | 0 |
| Tumor-44 | 0 | 1  | 0  | 0  | 0  | 0  | 1  | 0  | 0 | 1 | 0 |
| Tumor-45 | 0 | 0  | 3  | 1  | 0  | 1  | 4  | 0  | 1 | 0 | 0 |
| Tumor-46 | 1 | 7  | 10 | 16 | 18 | 5  | 14 | 7  | 4 | 4 | 6 |
| Tumor-47 | 0 | 1  | 7  | 0  | 0  | 0  | 3  | 6  | 0 | 0 | 0 |
| Tumor-48 | 5 | 11 | 11 | 4  | 0  | 0  | 0  | 0  | 0 | 0 | 0 |
| Tumor-49 | 1 | 0  | 0  | 0  | 0  | 2  | 1  | 0  | 0 | 0 | 0 |
| Tumor-50 | 1 | 0  | 2  | 1  | 0  | 4  | 2  | 0  | 0 | 0 | 0 |
| Tumor-51 | 0 | 3  | 3  | 1  | 5  | 4  | 2  | 3  | 1 | 0 | 0 |
| Tumor-52 | 1 | 0  | 2  | 0  | 0  | 1  | 0  | 0  | 0 | 0 | 0 |
| Tumor-53 | 0 | 0  | 2  | 0  | 3  | 0  | 0  | 0  | 0 | 0 | 0 |
| Tumor-54 | 0 | 0  | 2  | 0  | 0  | 0  | 0  | 0  | 0 | 0 | 0 |
| Tumor-55 | 0 | 0  | 0  | 0  | 1  | 0  | 0  | 0  | 1 | 0 | 0 |

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|----------|---|----|----|---|----|----|----|----|----|---|---|
| Tumor-56 | 1 | 11 | 7  | 9 | 5  | 3  | 3  | 11 | 10 | 7 | 4 |
| Tumor-57 | 1 | 2  | 1  | 0 | 0  | 4  | 0  | 1  | 0  | 0 | 0 |
| Tumor-58 | 1 | 1  | 5  | 5 | 7  | 6  | 2  | 3  | 0  | 0 | 0 |
| Tumor-59 | 5 | 12 | 16 | 8 | 2  | 10 | 10 | 0  | 0  | 2 | 1 |
| Tumor-60 | 0 | 0  | 1  | 0 | 1  | 0  | 0  | 0  | 0  | 0 | 0 |
| Tumor-61 | 8 | 7  | 7  | 5 | 7  | 9  | 1  | 1  | 5  | 0 | 2 |
| Tumor-62 | 0 | 1  | 2  | 0 | 0  | 1  | 4  | 0  | 0  | 0 | 0 |
| Tumor-63 | 0 | 9  | 3  | 2 | 2  | 1  | 0  | 0  | 0  | 0 | 0 |
| Tumor-64 | 2 | 0  | 0  | 0 | 0  | 1  | 0  | 0  | 0  | 0 | 0 |
| Tumor-65 | 0 | 2  | 1  | 0 | 11 | 7  | 3  | 8  | 0  | 0 | 6 |
| Tumor-66 | 4 | 20 | 25 | 7 | 3  | 6  | 7  | 4  | 3  | 1 | 3 |
| Tumor-67 | 2 | 2  | 1  | 0 | 2  | 1  | 0  | 0  | 0  | 2 | 0 |
| Tumor-68 | 0 | 3  | 4  | 0 | 1  | 2  | 0  | 1  | 0  | 0 | 0 |
| Tumor-69 | 3 | 5  | 12 | 2 | 5  | 7  | 9  | 3  | 1  | 1 | 0 |
| Tumor-70 | 0 | 2  | 1  | 0 | 5  | 5  | 2  | 1  | 0  | 0 | 0 |

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|--------------------------|----|----|----|---|----|----|---|---|---|---|---|
| Tumor-71                 | 9  | 8  | 9  | 5 | 7  | 8  | 5 | 2 | 3 | 0 | 0 |
| Tumor-72                 | 1  | 1  | 2  | 0 | 0  | 2  | 0 | 3 | 0 | 0 | 0 |
| Tumor-73                 | 12 | 25 | 8  | 8 | 2  | 0  | 0 | 0 | 0 | 0 | 0 |
| Tumor-74                 | 0  | 0  | 0  | 0 | 0  | 0  | 0 | 0 | 0 | 0 | 0 |
| Tumor-75                 | 0  | 0  | 0  | 0 | 0  | 0  | 0 | 0 | 0 | 0 | 0 |
| Tumor-76                 | 1  | 0  | 1  | 1 | 1  | 2  | 1 | 2 | 1 | 0 | 2 |
| Tumor-77                 | 6  | 16 | 10 | 8 | 19 | 7  | 4 | 5 | 3 | 2 | 7 |
| <hr/>                    |    |    |    |   |    |    |   |   |   |   |   |
| Breast Cancer Cell Lines |    |    |    |   |    |    |   |   |   |   |   |
| <hr/>                    |    |    |    |   |    |    |   |   |   |   |   |
| 184A1                    | 0  | 7  | 5  | 6 | 1  | 3  | 1 | 0 | 0 | 0 | 1 |
| AU565                    | 1  | 5  | 4  | 1 | 0  | 0  | 0 | 0 | 0 | 0 | 0 |
| BT549                    | 1  | 12 | 4  | 1 | 1  | 1  | 3 | 1 | 0 | 0 | 0 |
| HCC1395                  | 1  | 0  | 3  | 0 | 2  | 4  | 1 | 0 | 0 | 0 | 0 |
| HCC1569                  | 7  | 1  | 0  | 2 | 4  | 10 | 8 | 4 | 0 | 0 | 0 |
| HCC1937                  | 1  | 1  | 1  | 4 | 4  | 2  | 0 | 1 | 0 | 0 | 0 |
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|             |   |   |    |    |   |   |   |    |   |   |   |
|-------------|---|---|----|----|---|---|---|----|---|---|---|
| HCC1143     | 0 | 0 | 0  | 0  | 0 | 0 | 0 | 0  | 0 | 0 | 0 |
| HCC1428     | 2 | 0 | 2  | 0  | 2 | 0 | 1 | 0  | 0 | 0 | 0 |
| HCC202      | 1 | 5 | 1  | 2  | 0 | 5 | 0 | 0  | 2 | 0 | 0 |
| HCC3153     | 9 | 1 | 4  | 0  | 1 | 1 | 1 | 0  | 0 | 0 | 0 |
| MDAMB436    | 3 | 7 | 2  | 0  | 1 | 2 | 0 | 0  | 0 | 0 | 0 |
| SUM102PT    | 0 | 3 | 4  | 2  | 4 | 3 | 2 | 1  | 1 | 0 | 0 |
| SUM185PE    | 0 | 2 | 0  | 1  | 1 | 1 | 3 | 0  | 1 | 0 | 0 |
| 600MPE      | 3 | 3 | 6  | 1  | 2 | 0 | 0 | 0  | 0 | 0 | 0 |
| HCC1500     | 2 | 1 | 0  | 1  | 1 | 1 | 0 | 0  | 0 | 0 | 0 |
| HCC1806     | 0 | 0 | 0  | 0  | 0 | 0 | 0 | 0  | 0 | 0 | 0 |
| HS578T      | 1 | 6 | 3  | 1  | 1 | 2 | 0 | 0  | 0 | 0 | 0 |
| MCF12A      | 6 | 8 | 19 | 9  | 8 | 4 | 2 | 4  | 4 | 2 | 0 |
| MDAMB175VII | 3 | 7 | 3  | 5  | 2 | 2 | 3 | 10 | 4 | 0 | 2 |
| MDAMB453    | 7 | 8 | 11 | 10 | 2 | 3 | 4 | 3  | 5 | 1 | 1 |
| SUM1315MO2  | 2 | 3 | 3  | 0  | 0 | 0 | 1 | 0  | 0 | 0 | 0 |

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|         |    |    |   |   |   |   |   |   |   |   |   |
|---------|----|----|---|---|---|---|---|---|---|---|---|
| SUM52PE | 11 | 11 | 7 | 3 | 2 | 7 | 2 | 2 | 6 | 2 | 0 |
| MX-1    | 0  | 1  | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |

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**Table S2.** Association between RPRM methylation of Promoter region and clinicopathological features.

| Clinicopathological features | <i>n</i> | Percentage-methylated relative of CGIs RPRM |           | <i>p</i> |
|------------------------------|----------|---|-----------|----------|
|                              |          | Low   | High      |          |
|                              |          | 32  | 45        |          |
| Age (year; mean 60)          | 26       |   |           | 0.134    |
| ≤ 60                         | 19       | 12 (62.3%)                                  | 7 (36.8%) |          |
| > 60                         | 7        | 7 (100%)                                    | 0 (0.0%)  |          |
| Tumor Size *                 | 25       |   |           | 0.724    |
| T1                           | 4        | 3 (75.0%)                                   | 1 (25.0%) |          |
| T2                           | 19       | 13 (68.4%)                                  | 6 (31.6%) |          |
| T3                           | 2        | 2 (100%)                                    | 0 (0.0%)  |          |
| Lymph node metastasis        | 26       |   |           | 1.000    |
| No                           | 16       | 12 (75.0%)                                  | 4 (25%)   |          |
| Yes                          | 10       | 7 (70.0%)                                   | 3 (30.0%) |          |
| Elston Grade                 | 26       |   |           | 0.659    |
| Well differentiated          | 2        | 2 (100%)                                    | 0 (0.0%)  |          |
| Moderately differentiated    | 11       | 8 (72.7%)                                   | 3 (27.3%) |          |
| Poorly differentiated        | 13       | 9 (69.2%)                                   | 4 (30.8%) |          |
| Estrogen receptor            | 26       |   |           | 0.010    |
| ERα-negative                 | 11       | 11 (100%)                                   | 0 (0.0%)  |          |
| ERα-positive                 | 15       | 8 (53.3%)                                   | 7 (46.7%) |          |
| Progesterone Receptor        | 26       |   |           | 0.665    |
| PR-negative                  | 14       | 11 (78.6%)                                  | 3 (21.4%) |          |
| PR-positive                  | 12       | 8 (66.7%)                                   | 4 (33.3%) |          |

\* 1 case were excluded from that analysis due by missing information.

**Table S3.** Spearman correlation between methylation intensity of reads by each 100-bp and relative expression of RPRM mRNA.

|                                    |                         | <b>MBDCap-seq CGIs (chr2: 154042600 - 154043700)</b> |           |           |           |           |           |           |           |           |           |           |
|------------------------------------|-------------------------|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                                    |                         | 154042600  | 154042800 | 154042900 | 154043000 | 154043100 | 154043200 | 154043300 | 154043400 | 154043500 | 154043600 | 154043700 |
| Relative expression of RPRM (Log2) | <i>n</i>                | 18   | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        |
|                                    | Correlation Coefficient | -0.479   | -0.224    | -0.348    | -0.499    | -0.390    | -0.376    | -0.475    | -0.628    | -0.544    | -0.412    | -0.444    |
|                                    | Significance            | 0.047  | 0.318     | 0.157     | 0.035     | 0.109     | 0.124     | 0.044     | 0.005     | 0.02      | 0.089     | 0.065     |