

Supplementary Material

Genomic characterization of ER-positive primary tumors and corresponding relapses identifies potentially targetable alterations

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Supplementary Table 1. Mutually exclusive genes in patients' primary tumors (a) and relapse tumors (b), filtered for $p < 0.1$.

a.

Gene_1	Gene_2	p_value	BH_adjusted_q_value
<i>FAT1</i>	<i>MAP3K1</i>	0.0273	0.3574
<i>GATA3</i>	<i>TP53</i>	0.0287	0.3574
<i>BRCA2</i>	<i>PIK3CA</i>	0.0323	0.3574
<i>NOTCH2</i>	<i>PIK3CA</i>	0.0345	0.3574
<i>CDC27</i>	<i>PIK3CA</i>	0.0373	0.3574
<i>FOXA1</i>	<i>TP53</i>	0.0481	0.4349
<i>CHD3</i>	<i>FAT1</i>	0.0555	0.4349
<i>ALB</i>	<i>PIK3CA</i>	0.0606	0.5803
<i>ATRX</i>	<i>PIK3CA</i>	0.0606	0.5803
<i>CDC27</i>	<i>CHD4</i>	0.0790	0.6188
<i>MSH6</i>	<i>TP53</i>	0.0805	0.6188
<i>NOTCH1</i>	<i>TP53</i>	0.0805	0.6188
<i>TAF1</i>	<i>TP53</i>	0.0805	0.6188
<i>ALK</i>	<i>NOTCH2</i>	0.0845	0.6188
<i>NF1</i>	<i>NOTCH2</i>	0.0845	0.6188
<i>KMT2D</i>	<i>PIK3CA</i>	0.0849	0.6188
<i>JAK1</i>	<i>PIK3CA</i>	0.0970	0.6579

b.

Gene_1	Gene_2	p_value	BH_adjusted_q_value
<i>CDH1</i>	<i>TP53</i>	0.0137	0.2919
<i>GATA3</i>	<i>TP53</i>	0.0567	0.9386
<i>CDC27</i>	<i>SMC1A</i>	0.0591	0.9386
<i>CDH1</i>	<i>ZFHX3</i>	0.0591	0.9386
<i>DICER1</i>	<i>FAT1</i>	0.0603	0.9386
<i>CDC27</i>	<i>PIK3CA</i>	0.0685	0.9386
<i>ALB</i>	<i>ARHGAP35</i>	0.0766	0.9386
<i>EP300</i>	<i>PIK3CA</i>	0.0956	0.9386
<i>CDH1</i>	<i>NOTCH2</i>	0.0999	0.9386

BH=Benjamini Hochberg

Supplementary Table 2. Genes with differences in the total copy number (TCN) between the patients' primary and relapse tumors, as determined by the Wilcoxon signed-rank test.

Gene	p_value	Higher in tumor sample	BH adjusted q_value
<i>AKT3</i>	0.0343	Primary	0.3850
<i>ELF3</i>	0.0358	Primary	0.3850
<i>FH</i>	0.0343	Primary	0.3850
<i>SOX9</i>	0.0358	Primary	0.3850
<i>ALB</i>	0.0079	Relapse	0.2358
<i>ANKRD11</i>	0.0100	Relapse	0.2358
<i>ASXL1</i>	0.0449	Relapse	0.4057
<i>CBL</i>	0.0089	Relapse	0.2358
<i>CDH1</i>	0.0151	Relapse	0.2358
<i>CHD3</i>	0.0001	Relapse	0.0139
<i>CHEK1</i>	0.0089	Relapse	0.2358
<i>CTCF</i>	0.0275	Relapse	0.3377
<i>CYLD</i>	0.0253	Relapse	0.3227
<i>DNMT3B</i>	0.0449	Relapse	0.4057
<i>ESR1</i>	0.0218	Relapse	0.2997
<i>FANCA</i>	0.0249	Relapse	0.3227
<i>GPR126</i>	0.0024	Relapse	0.1382
<i>GPS2</i>	0.0001	Relapse	0.0139
<i>HIST1H1C</i>	0.0484	Relapse	0.4057
<i>HIST1H1E</i>	0.0484	Relapse	0.4057
<i>HIST1H3B</i>	0.0484	Relapse	0.4057
<i>HIST1H3C</i>	0.0484	Relapse	0.4057
<i>HIST1H3H</i>	0.0484	Relapse	0.4057
<i>HLA-A</i>	0.0484	Relapse	0.4057
<i>INPPL1</i>	0.0491	Relapse	0.4057
<i>INTS4</i>	0.0070	Relapse	0.2358
<i>KDR</i>	0.0131	Relapse	0.2358
<i>KIT</i>	0.0131	Relapse	0.2358
<i>KMT2A</i>	0.0151	Relapse	0.2358
<i>LATS1</i>	0.0070	Relapse	0.2358
<i>MAP2K4</i>	0.0011	Relapse	0.0787
<i>NCOR1</i>	0.0002	Relapse	0.0153
<i>NQO1</i>	0.0151	Relapse	0.2358
<i>PARK2</i>	0.0162	Relapse	0.2421
<i>PDGFRA</i>	0.0131	Relapse	0.2358
<i>SDHD</i>	0.0204	Relapse	0.2928
<i>TGFBR2</i>	0.0062	Relapse	0.2358
<i>TP53</i>	0.0001	Relapse	0.0139
<i>WWOX</i>	0.0100	Relapse	0.2358
<i>ZBTB16</i>	0.0151	Relapse	0.2358
<i>ZFHX3</i>	0.0151	Relapse	0.2358

BH=Benjamini Hochberg

Supplementary Table 3. Single-nucleotide variations (SNVs) and copy number variations (CNVs) in the tumors of the patients that were associated with a worse overall survival.

Gene	Sample	Alteration_type	p_value	BH_adjusted_q_value
<i>AKT3</i>	Primary	Amplification	0.047	0.33
<i>ALK</i>	Primary	Amplification	0.0001	0.0047
<i>ARHGAP35</i>	Primary	SNV	0.027	0.37
<i>ARID5B</i>	Primary	Deletion	0.048	0.33
<i>ARID5B</i>	Primary	SNV	0.031	0.37
<i>ATR</i>	Primary	Amplification	0.022	0.23
<i>B2M</i>	Relapse	Amplification	0.0048	0.084
<i>BCL10</i>	Primary	Amplification	0.00013	0.005
<i>BCL6</i>	Primary	Amplification	0.038	0.32
<i>BLM</i>	Relapse	Amplification	0.041	0.33
<i>BMPRI4</i>	Relapse	Deletion	0.027	0.27
<i>BRAF</i>	Primary	Amplification	0.022	0.23
<i>BRCA1</i>	Primary	Deletion	0.024	0.25
<i>BRCA1</i>	Relapse	SNV	0.0061	0.23
<i>BTG2</i>	Primary	Amplification	0.028	0.27
<i>CDC27</i>	Primary	Deletion	0.016	0.2
<i>CDH1</i>	Primary	SNV	0.0055	0.23
<i>CDK6</i>	Primary	Amplification	0.0062	0.1
<i>CDKN2C</i>	Primary	Amplification	0.01	0.14
<i>CHD3</i>	Primary	SNV	0.0014	0.089
<i>CSDE1</i>	Primary	Amplification	0.0078	0.11
<i>CTNNB1</i>	Primary	SNV	0.037	0.37
<i>DPYD</i>	Primary	Amplification	0.0001	0.0047
<i>EIF4A2</i>	Primary	Amplification	0.038	0.32
<i>ELF3</i>	Primary	Amplification	0.017	0.204
<i>EPHB1</i>	Primary	Amplification	0.022	0.23
<i>ERBB2</i>	Primary	Deletion	0.0075	0.11
<i>EZH2</i>	Primary	Amplification	0.022	0.23
<i>FH</i>	Primary	Amplification	0.047	0.33
<i>FOXL2</i>	Primary	Amplification	0.022	0.23
<i>FUBP1</i>	Primary	Amplification	0.00059	0.021
<i>GATA2</i>	Primary	Amplification	0.015	0.199
<i>GATA3</i>	Primary	Amplification	0.027	0.27
<i>GATA3</i>	Relapse	SNV	0.046	0.37
<i>GREM1</i>	Relapse	Amplification	0.0048	0.084
<i>GSK3B</i>	Primary	Amplification	0.015	0.2
<i>GTF2I</i>	Primary	Amplification	0.037	0.32
<i>H3F3A</i>	Primary	Amplification	0.021	0.23
<i>HGF</i>	Primary	Amplification	0.037	0.32
<i>HRAS</i>	Primary	Amplification	0.042	0.33
<i>HSD3B1</i>	Primary	Amplification	0.0078	0.11
<i>IDH2</i>	Relapse	Amplification	0.041	0.33
<i>IGF1R</i>	Relapse	Amplification	0.0042	0.082

<i>INPPL1</i>	Primary	Amplification	0.0065	0.1
<i>INTS4</i>	Primary	Amplification	0.0028	0.07
<i>INTS4</i>	Relapse	Amplification	0.04	0.33
<i>JAK1</i>	Primary	Amplification	0.019	0.22
<i>JUN</i>	Primary	Amplification	0.019	0.22
<i>KEL</i>	Primary	Amplification	0.022	0.23
<i>KMT2C</i>	Primary	Amplification	0.022	0.23
<i>KNSTRN</i>	Relapse	Amplification	0.0048	0.084
<i>MAP2K1</i>	Relapse	Amplification	0.0048	0.084
<i>MAP3K13</i>	Primary	Amplification	0.038	0.32
<i>MCL1</i>	Primary	Amplification	0.047	0.33
<i>MDM4</i>	Primary	Amplification	0.028	0.27
<i>MEN1</i>	Primary	Amplification	0.0065	0.1
<i>MGA</i>	Relapse	Amplification	0.0048	0.084
<i>MGA</i>	Primary	SNV	0.038	0.37
<i>MUTYH</i>	Primary	Amplification	0.01	0.14
<i>MYCL</i>	Primary	Amplification	0.0055	0.092
<i>NF1</i>	Primary	Deletion	0.0052	0.088
<i>NOTCH2</i>	Primary	Amplification	0.016	0.2
<i>NRAS</i>	Primary	Amplification	0.0078	0.11
<i>NTRK1</i>	Primary	Amplification	0.017	0.2
<i>PARP1</i>	Primary	Amplification	0.021	0.23
<i>PIK3CA</i>	Primary	Amplification	0.016	0.2
<i>PIK3CB</i>	Primary	Amplification	0.022	0.23
<i>PIK3CG</i>	Primary	Amplification	0.012	0.17
<i>PMS2</i>	Primary	Amplification	0.039	0.32
<i>POLQ</i>	Primary	Amplification	0.015	0.2
<i>POT1</i>	Primary	SNV	0.029	0.37
<i>PRKCI</i>	Primary	Amplification	0.016	0.2
<i>PRSSI</i>	Primary	Amplification	0.022	0.23
<i>PTEN</i>	Primary	Deletion	0.025	0.25
<i>PTPRD</i>	Primary	Deletion	0.026	0.26
<i>RAC1</i>	Primary	Amplification	0.039	0.32
<i>RAD51</i>	Relapse	Amplification	0.0048	0.084
<i>RHEB</i>	Primary	Amplification	0.022	0.23
<i>RIT1</i>	Primary	Amplification	0.017	0.2
<i>RPL5</i>	Primary	Amplification	0.0001	0.0047
<i>RPS6KA4</i>	Primary	Amplification	0.0065	0.1
<i>SDHAF2</i>	Primary	Amplification	0.0065	0.1
<i>SDHC</i>	Primary	Amplification	0.047	0.33
<i>SMAD2</i>	Relapse	Deletion	0.043	0.33
<i>SMAD3</i>	Relapse	Amplification	0.034	0.3
<i>SMAD4</i>	Primary	Amplification	0.019	0.22
<i>SMAD4</i>	Relapse	Deletion	0.043	0.33
<i>SMC3</i>	Primary	Deletion	0.0014	0.045
<i>SOX2</i>	Primary	Amplification	0.016	0.2
<i>SPEN</i>	Relapse	SNV	0.0092	0.28
<i>SPRED1</i>	Relapse	Amplification	0.0048	0.084

<i>SPTA1</i>	Primary	Amplification	0.047	0.33
<i>STAT3</i>	Primary	Deletion	0.024	0.25
<i>SUZ12</i>	Primary	Deletion	0.021	0.23
<i>TBL1XR1</i>	Primary	Amplification	0.016	0.2
<i>TCF12</i>	Relapse	Amplification	0.0048	0.084
<i>TCF7L2</i>	Primary	Deletion	0.0014	0.045
<i>TP63</i>	Primary	Amplification	0.038	0.32
<i>TPMT</i>	Primary	Amplification	0.024	0.25

BH=Benjamini Hochberg, SNV=single-nucleotide variation

Supplementary Table 4. Genes with correlations between the normalized copy number and gene expression in the patients' tumor samples.		
Gene	p_value	BH_adjusted_q_value
<i>ARHGAP35</i>	0.0472	0.2610
<i>ARID5B</i>	0.0143	0.1311
<i>ASXL2</i>	0.0062	0.0944
<i>ATM</i>	0.0264	0.1998
<i>BAP1</i>	0.0000	0.0019
<i>BCL2L1</i>	0.0007	0.0234
<i>BCL6</i>	0.0125	0.1311
<i>BRD4</i>	0.0024	0.0495
<i>CCND1</i>	0.0000	0.0000
<i>CCND3</i>	0.0426	0.2592
<i>CDH1</i>	0.0016	0.0354
<i>CDKN1A</i>	0.0192	0.1652
<i>CDKN2A</i>	0.0014	0.0354
<i>CHD3</i>	0.0388	0.2592
<i>CHEK1</i>	0.0001	0.0025
<i>CIC</i>	0.0143	0.1311
<i>CTLA4</i>	0.0127	0.1311
<i>CYLD</i>	0.0472	0.2610
<i>DAXX</i>	0.0040	0.0665
<i>ELF3</i>	0.0043	0.0685
<i>ERBB2</i>	0.0268	0.1998
<i>ETV6</i>	0.0378	0.2592
<i>EZH2</i>	0.0039	0.0665
<i>FAT1</i>	0.0014	0.0354
<i>FGFR1</i>	0.0000	0.0000
<i>FGFR2</i>	0.0003	0.0097
<i>FLT3</i>	0.0230	0.1832
<i>GNA11</i>	0.0143	0.1311
<i>GNAS</i>	0.0000	0.0004
<i>GPS2</i>	0.0414	0.2592
<i>H3F3C</i>	0.0383	0.2592
<i>IDH2</i>	0.0000	0.0019
<i>INTS4</i>	0.0000	0.0000
<i>IRS2</i>	0.0111	0.1278

<i>KEAP1</i>	0.0446	0.2610
<i>KEL</i>	0.0280	0.2038
<i>KLF4</i>	0.0114	0.1278
<i>KMT2B</i>	0.0253	0.1974
<i>LATS1</i>	0.0000	0.0004
<i>LZTR1</i>	0.0157	0.1385
<i>MDM2</i>	0.0110	0.1278
<i>MED12</i>	0.0453	0.2610
<i>MEN1</i>	0.0211	0.1723
<i>MSH3</i>	0.0475	0.2610
<i>PDGFRA</i>	0.0016	0.0354
<i>PIK3CD</i>	0.0424	0.2592
<i>PIK3CG</i>	0.0289	0.2057
<i>PIM1</i>	0.0136	0.1311
<i>PPM1D</i>	0.0410	0.2592
<i>PPP4R2</i>	0.0105	0.1278
<i>RAD50</i>	0.0436	0.2610
<i>RAD51C</i>	0.0027	0.0531
<i>RNF43</i>	0.0145	0.1311
<i>ROS1</i>	0.0417	0.2592
<i>RPTOR</i>	0.0008	0.0245
<i>SDHB</i>	0.0205	0.1716
<i>SOCS1</i>	0.0079	0.1100
<i>SOX9</i>	0.0104	0.1278
<i>STK11</i>	0.0072	0.1049
<i>TAF1</i>	0.0029	0.0534
<i>ZBTB16</i>	0.0084	0.1120

BH=Benjamini Hochberg