

Supplementary Information

Estrogen-mediated Epigenetic Repression of Large Chromosomal Regions through DNA Looping

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Method

Immunofluorescence staining

Approximately 2,000 mammosphere-derived epithelial cells (MDECs) cells seeded collagen I-coated coverslips were fixed with methanol/acetone for 10 min. After blocking with 2.5% bovine serum albumin (Sigma) for 1 hr, these cells were incubated with anti-ESR1 antibody (Santa Cruz) overnight at 4°C. The corresponding secondary FITC-conjugated antibody was applied followed by DAPI staining (Molecular Probes) for the nuclei. Photographs were captured by Zeiss fluorescence microscopy (Zeiss). The percentages of ESR1 subcellular localization were calculated in ten different optical fields (~10 cells per field) by two independent researchers.

References

- Carroll, J.S., Meyer, C.A., Song, J., Li, W., Geistlinger, T.R., Eeckhoute, J., Brodsky, A.S., Keeton, E.K., Fertuck, K.C., Hall, G.F., et al. 2006. Genome-wide analysis of estrogen receptor binding sites. *Nat. Genet.* **38**: 1289-1297.
- Neve, R.M., Chin, K., Fridlyand, J., Yeh, J., Baehner, F.L., Fevr, T., Clark, L., Bayani, N., Coppe, J.P., Tong, F., et al. 2006. A collection of breast cancer cell lines for the study of functionally distinct cancer subtypes. *Cancer Cell* **10**: 515-527.

A

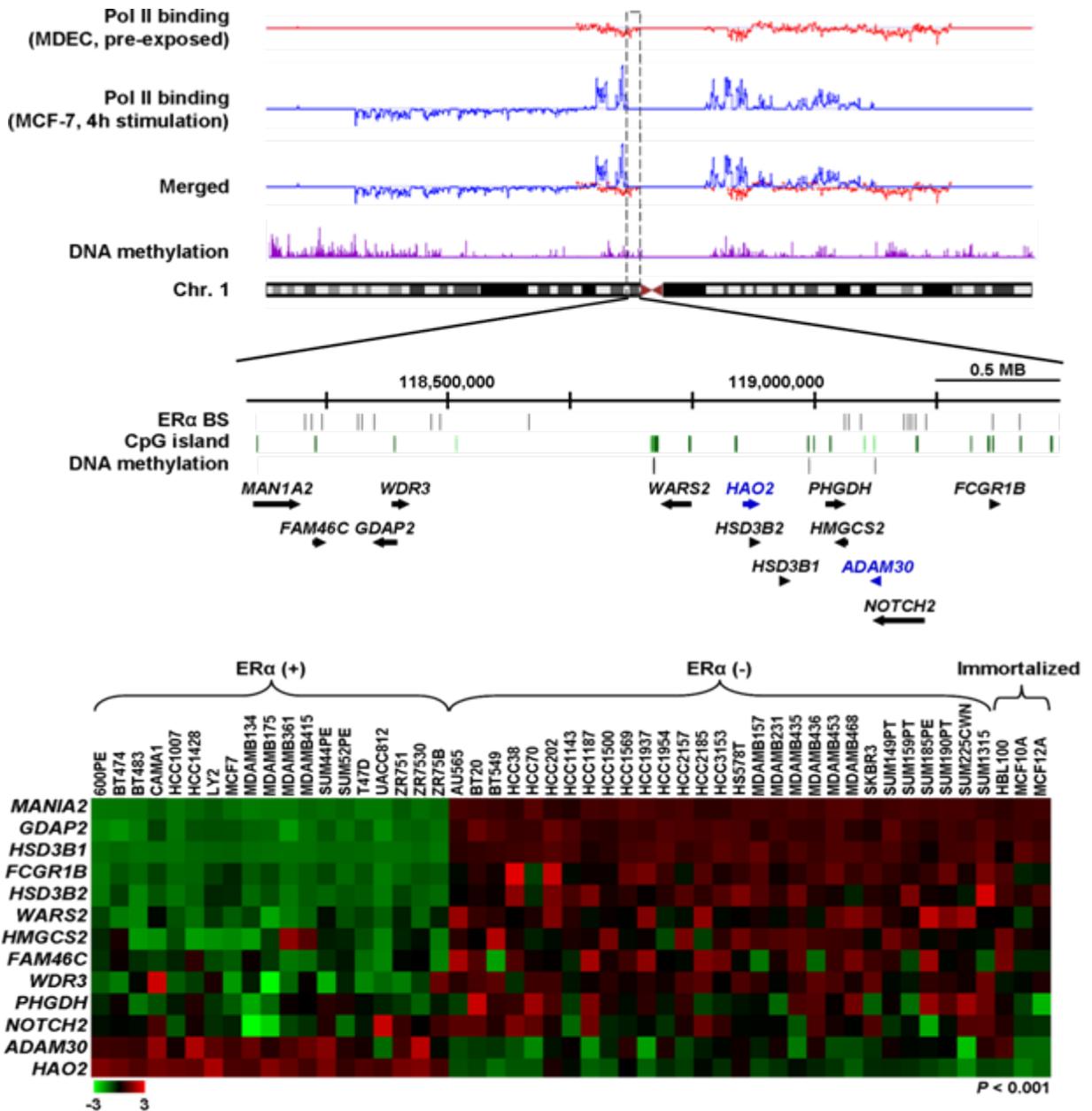
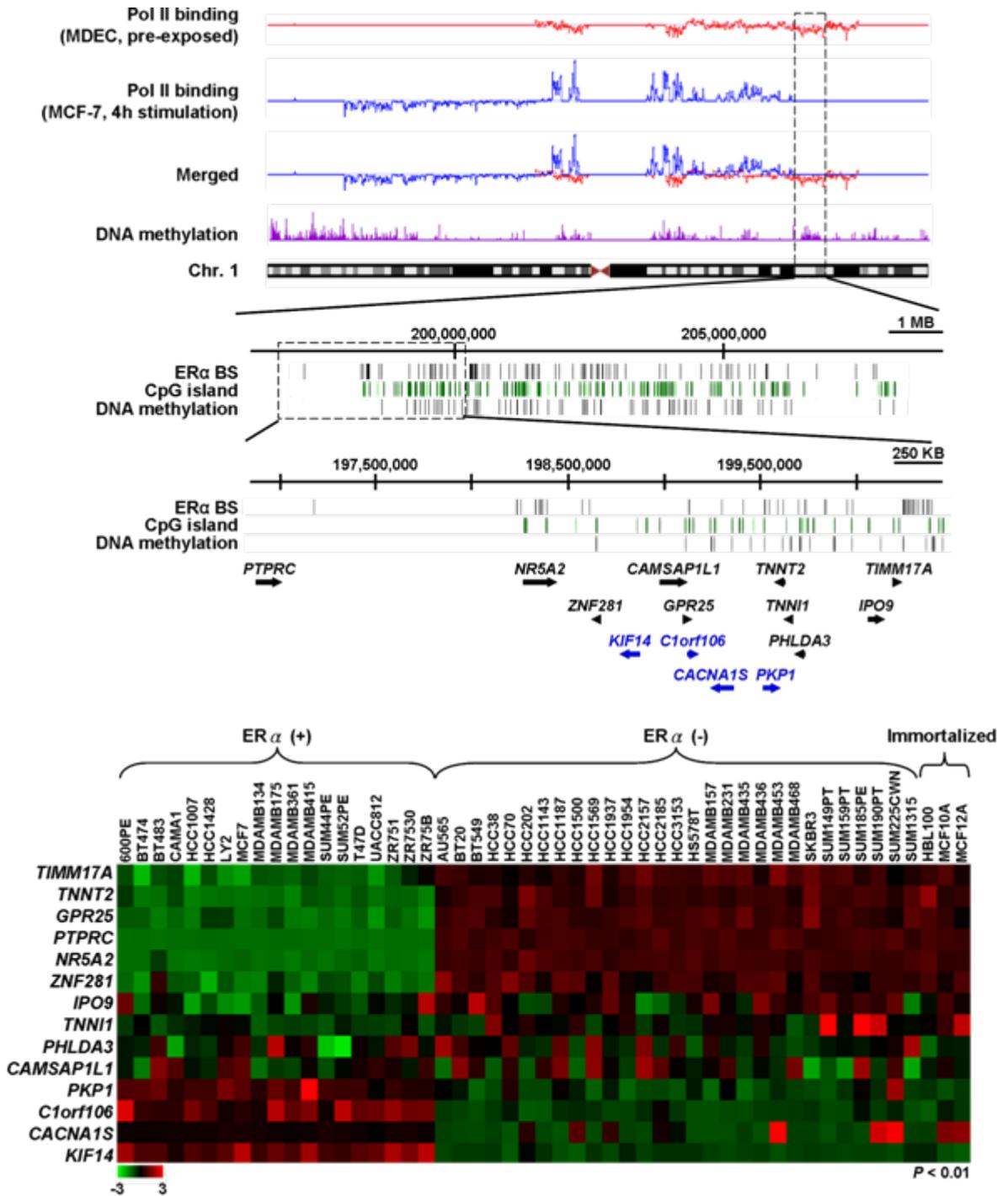
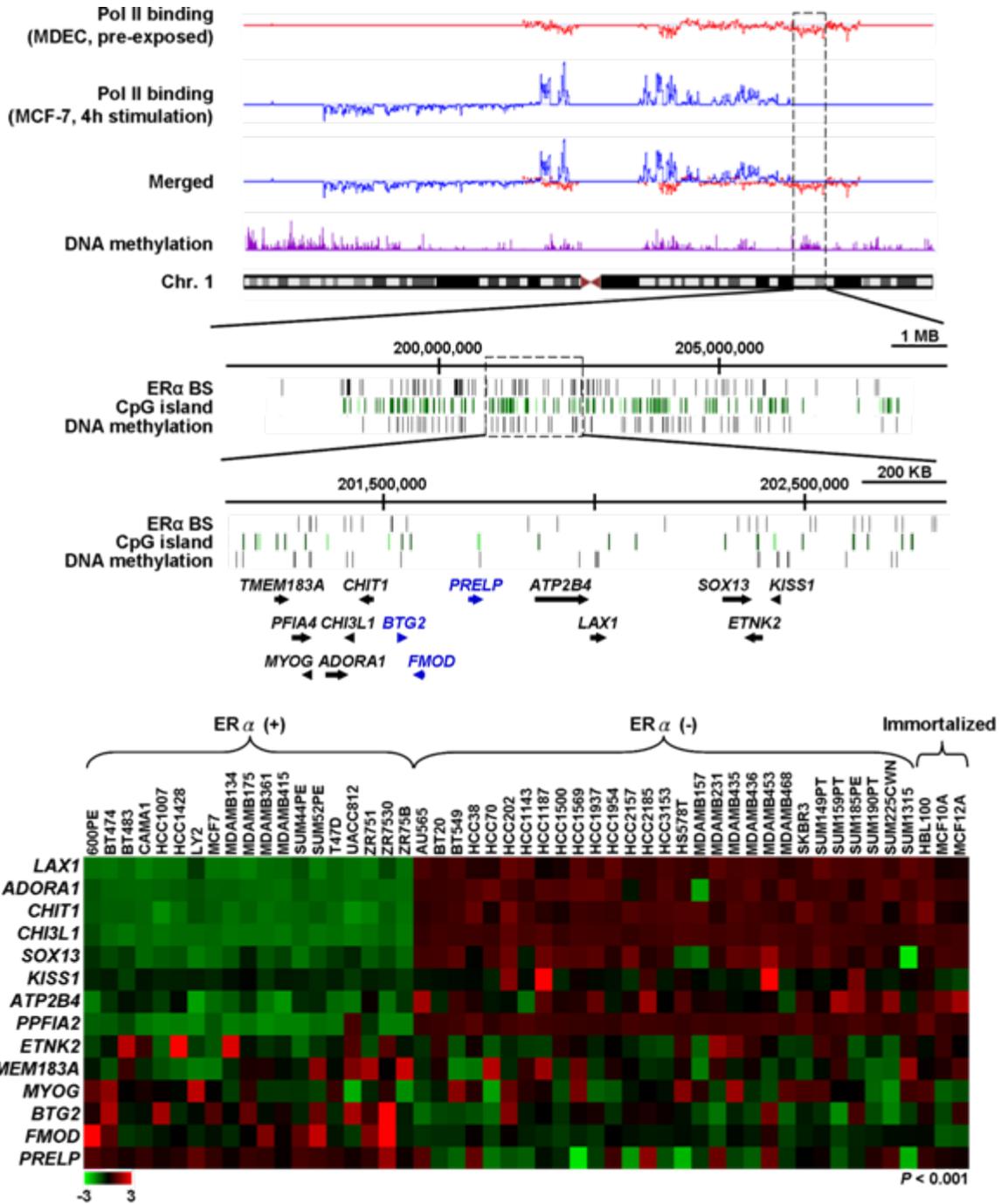


Figure S1. Integrative mapping of large genomic regions subjected to ER α -mediated epigenetic repression. (A-J) Schematic diagrams of concurrent silencing clusters. In upper panel, a gene cluster chosen from the region is concurrently down-regulated in MDECs (red track) and silenced in MCF-7 cells (blue track) with DNA hypermethylation (purple track). Within each gene cluster, concurrently down- or up-regulated genes were marked in black and blue arrows, respectively. In bottom panel, the gene cluster is concurrently silenced in ER α -positive breast cancer cell lines. *In silico* expression analysis of the interested gene cluster was performed based on 48 breast cancer cell panel (Neve et al. 2006). Statistical analysis used to distinguish ER α -positive from -negative breast cancer cell lines was calculated by Wilcoxon Rank Sum Test. A total 10 potential regions as shown: chr.1p12-p11.2 (A); chr.1q31.2-q32.1 (B); chr.1q32.1 (C); chr.1q41 (D); chr.3q27.2-q27.3 (E); chr.7p14.3-p14.1 (F); chr.7p12.3-p12.1 (G); chr.10q11.2 (H); chr.17q25.3 (I); chr.19p13.3 (J). Note: an additional gene cluster at 16p11.2 is shown in Figure 3 in the main text.

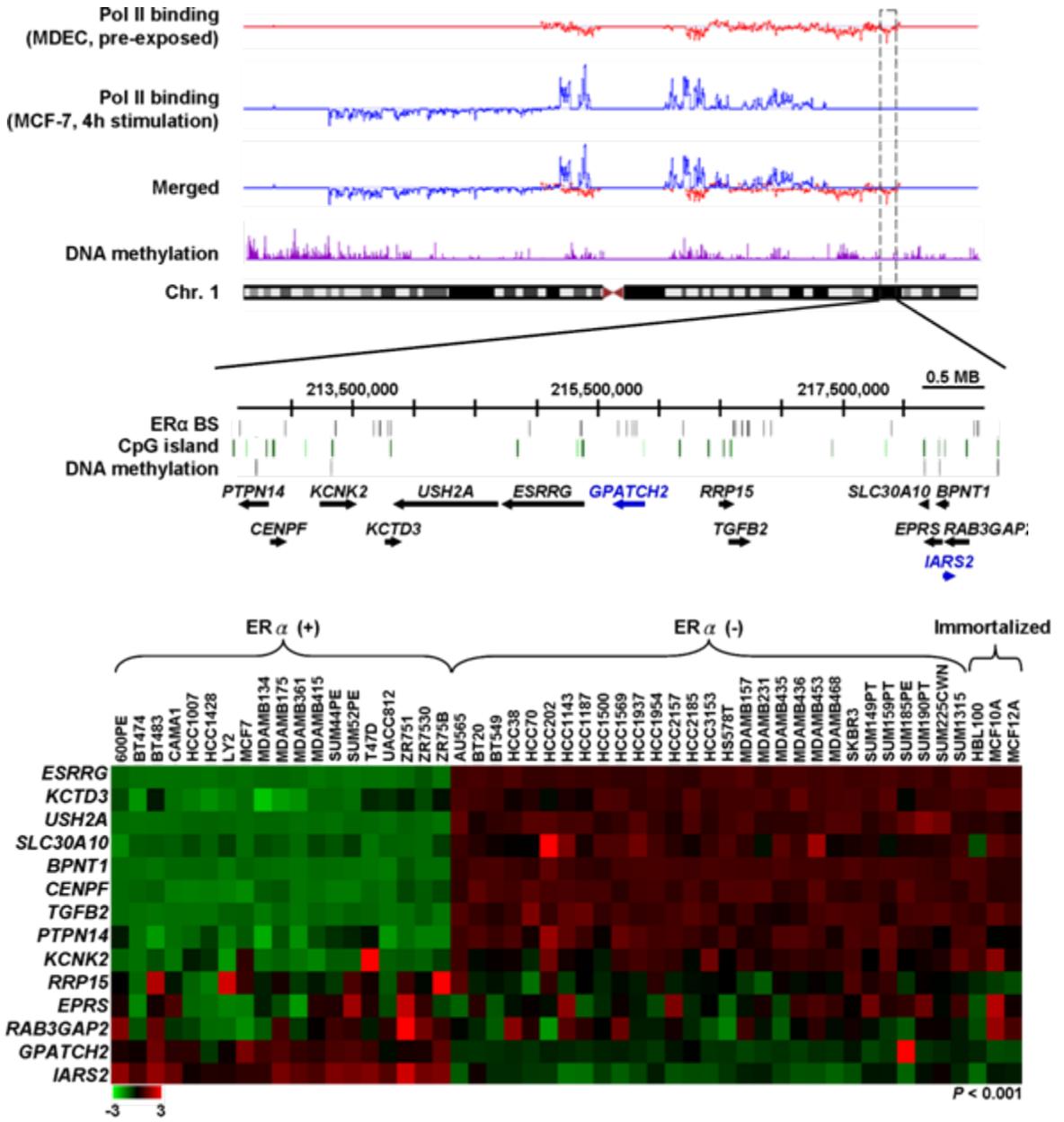
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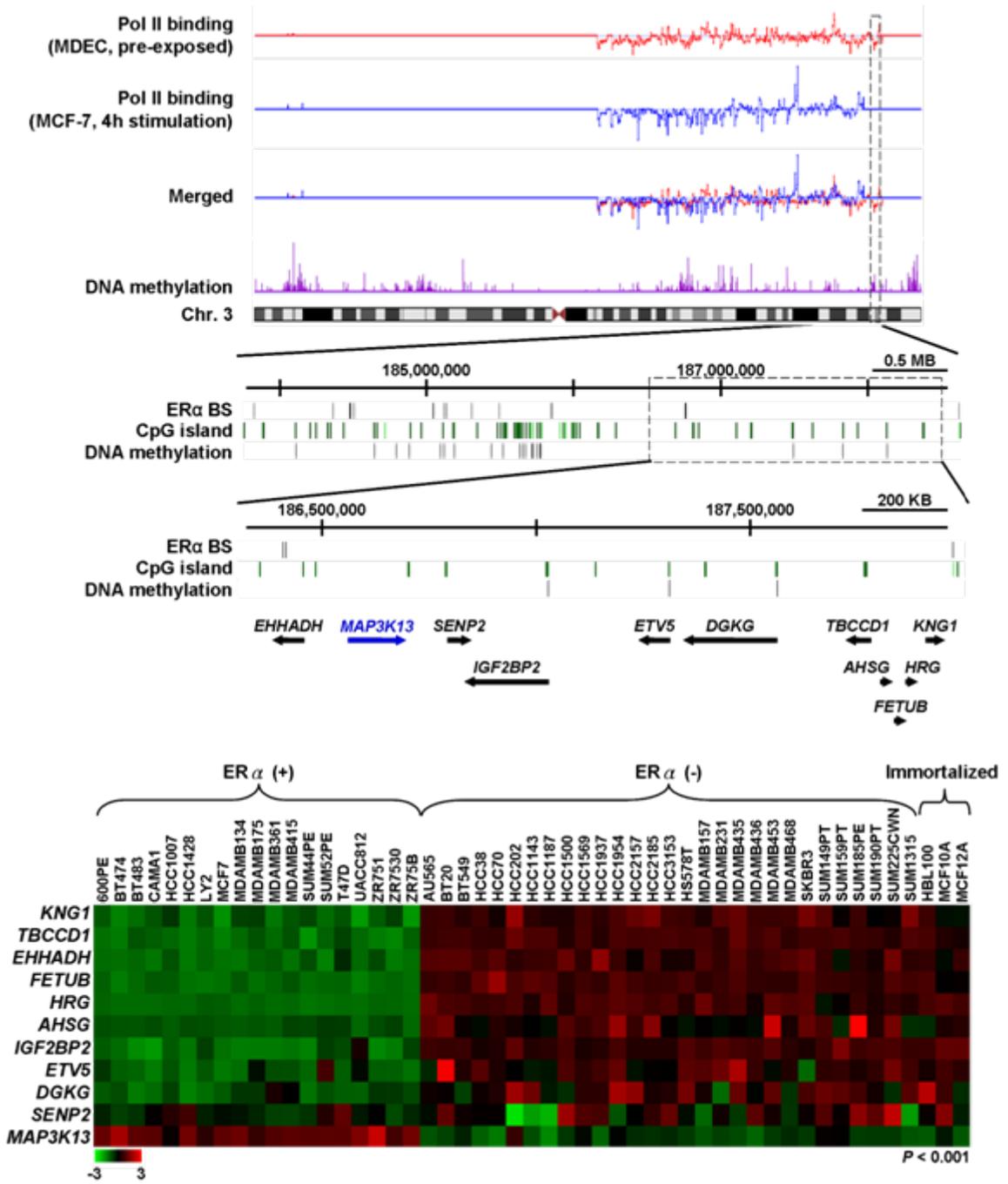
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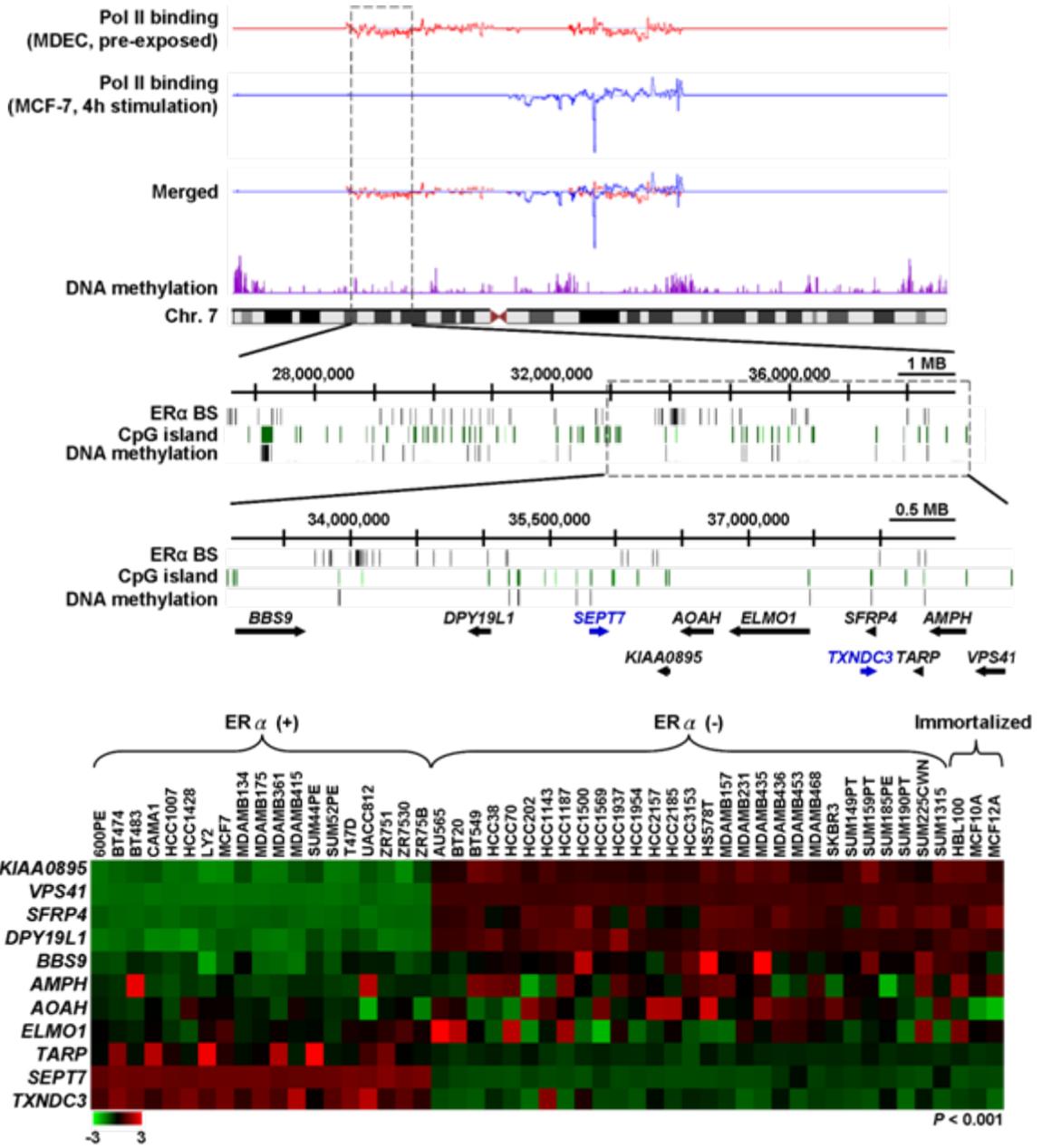
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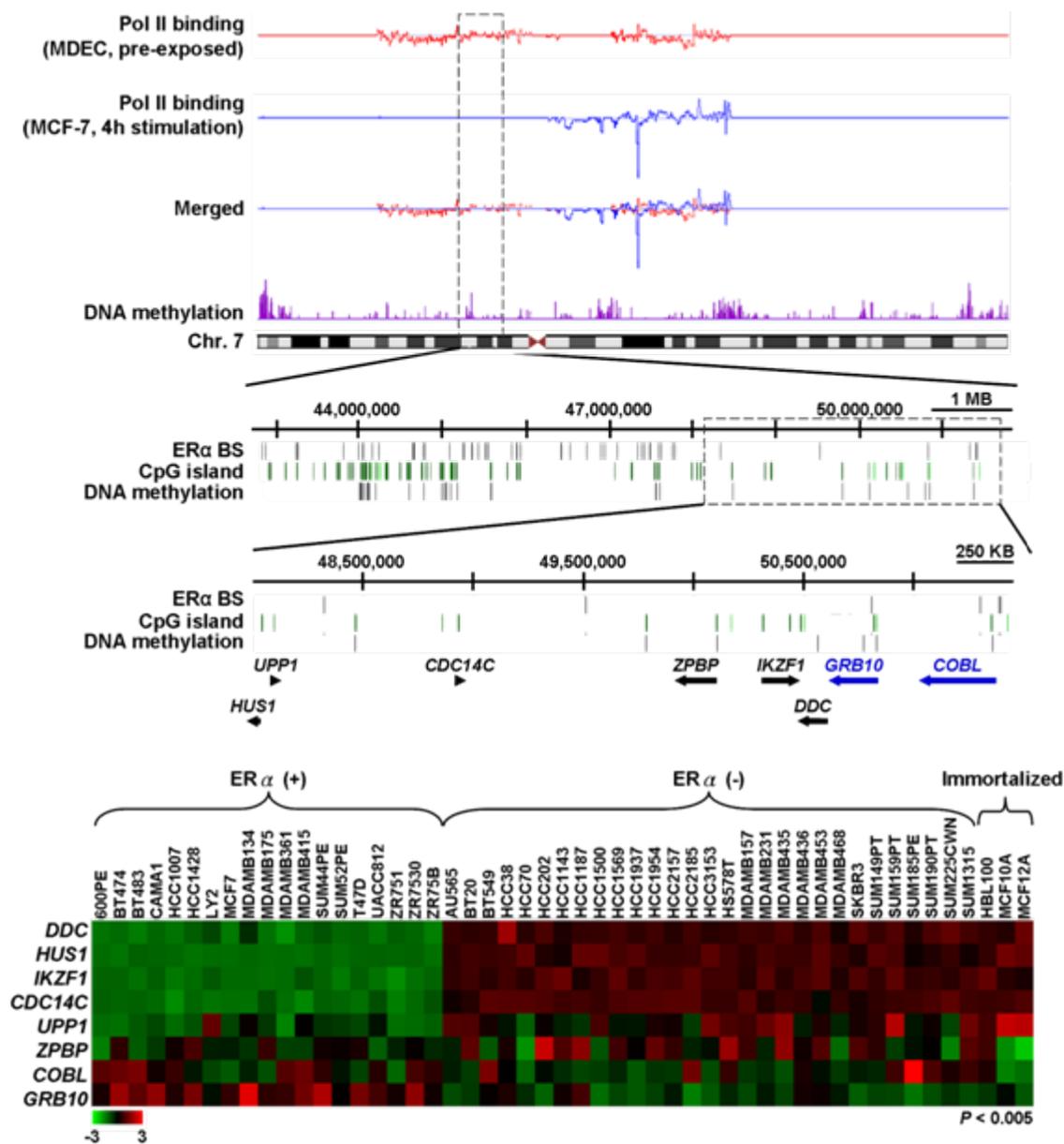
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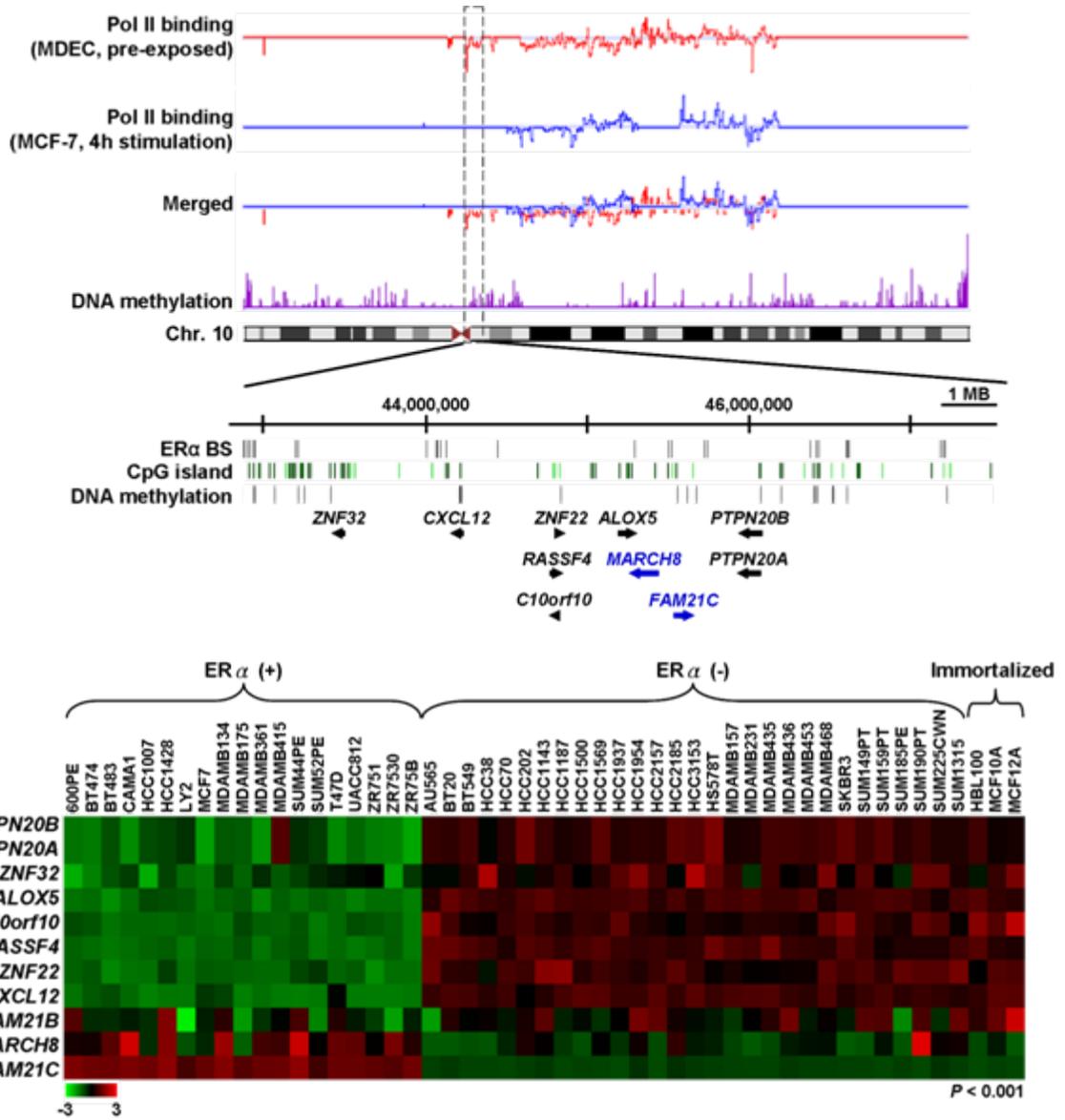
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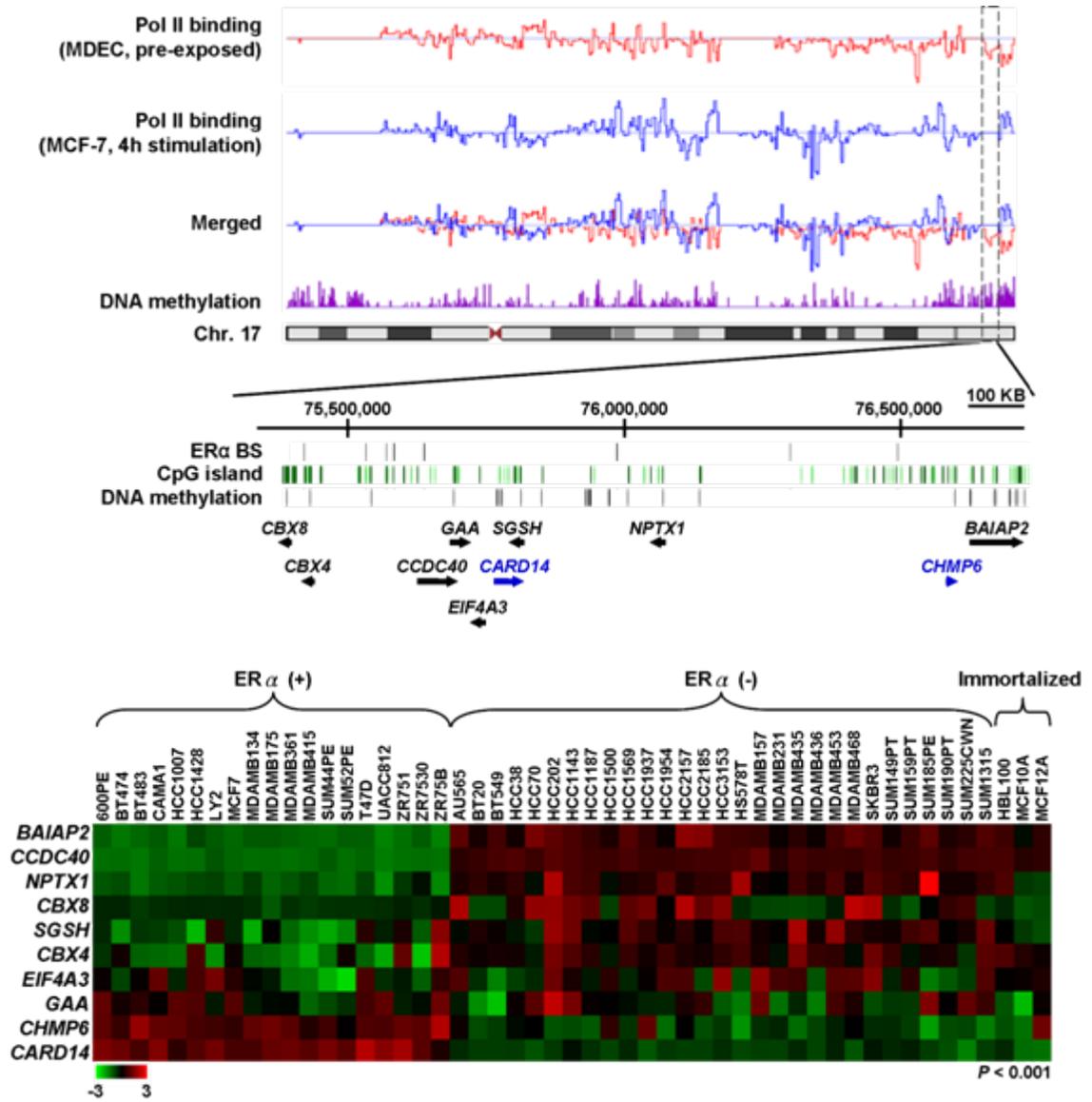


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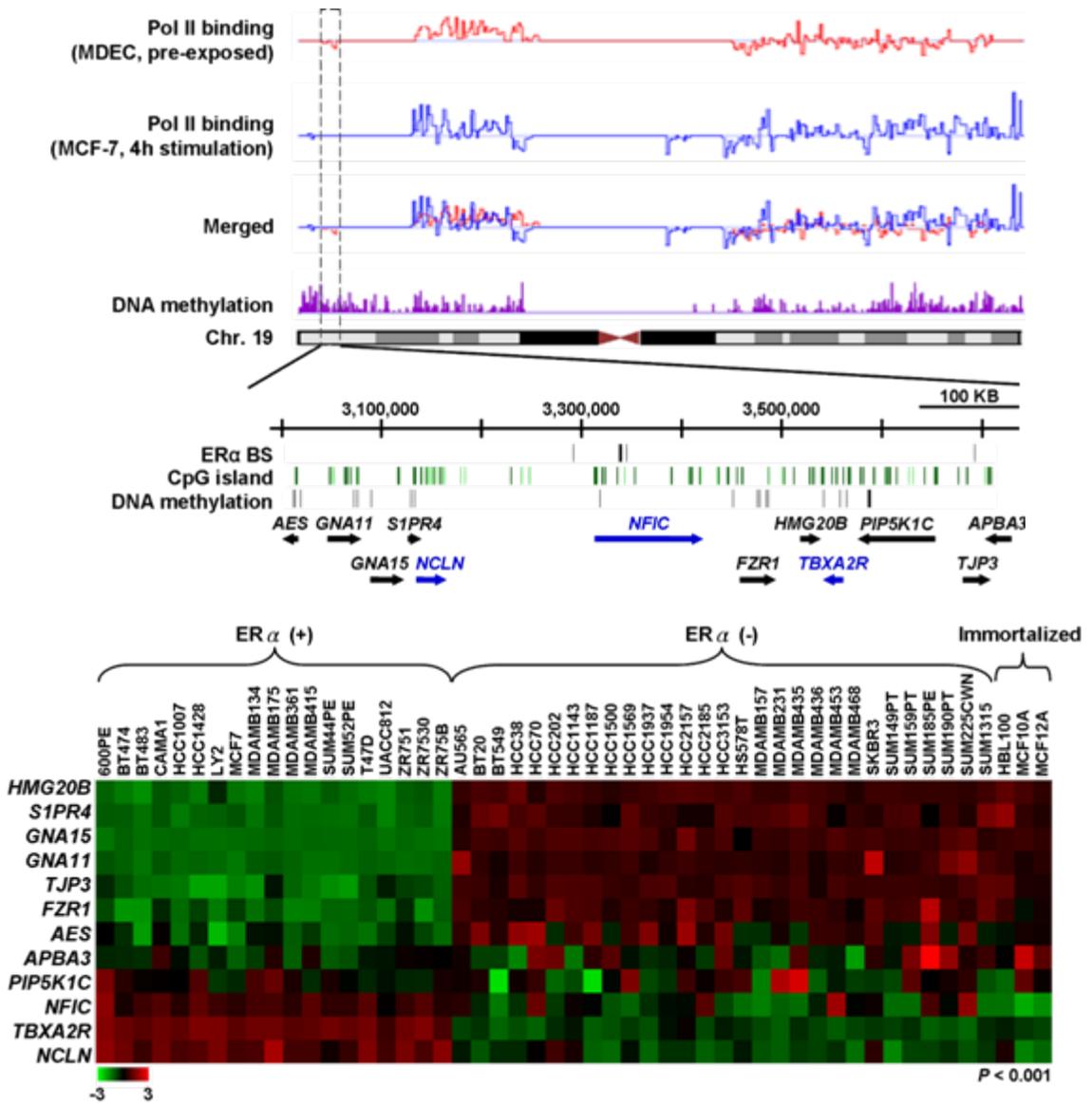


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J



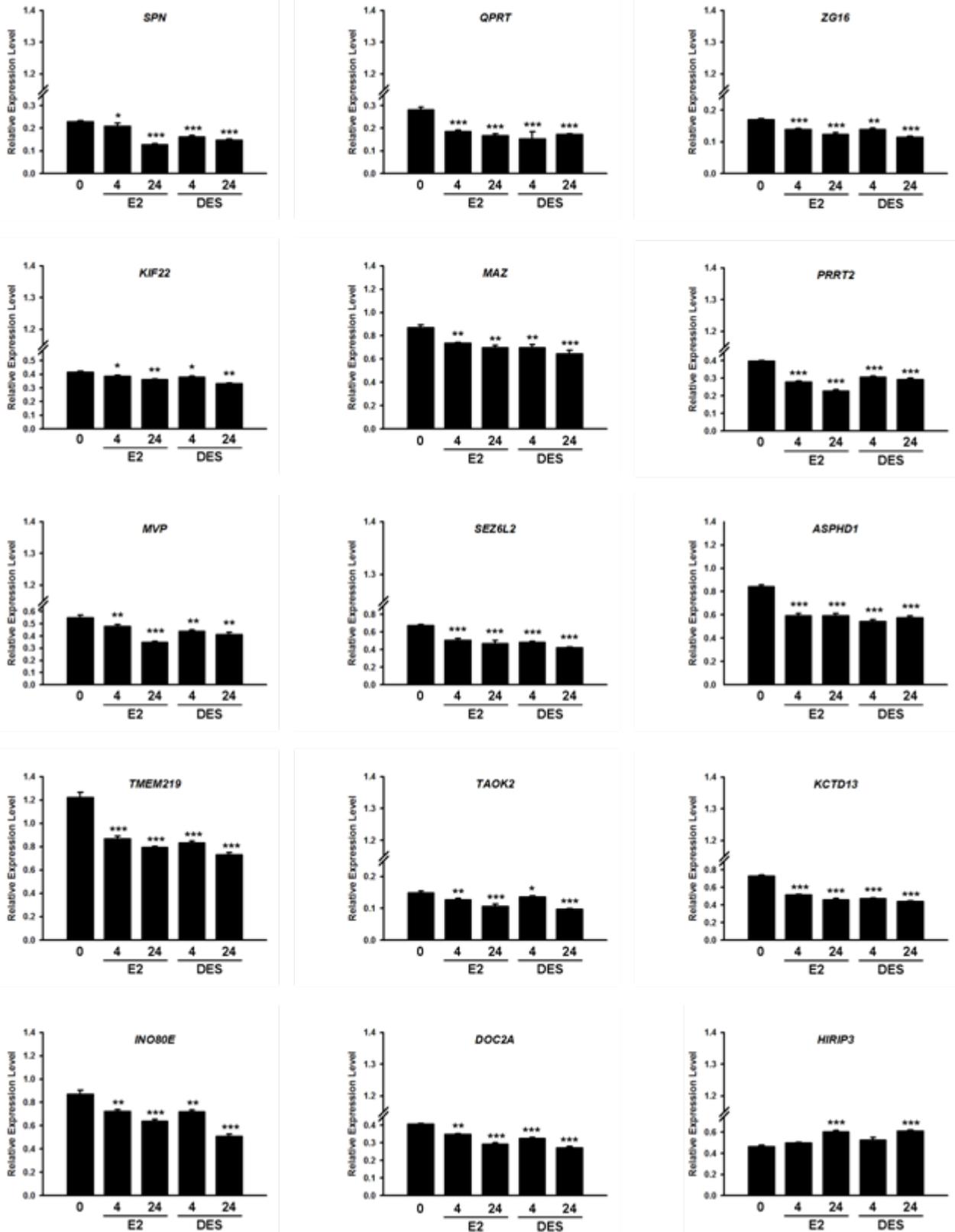


Figure S2. Coherent silencing of the 16p11.2 gene cluster upon short-term estrogen stimulations. Differentiated epithelial cells without prior exposure at the progenitor stage were stimulated with 17 β -estradiol (E2, 70 nM) or diethylstilbestrol (DES, 70 nM) and subjected to quantitative RT-PCR analysis at indicated time points. Mean \pm SD ($n=3$). ***, $p < 0.001$; **, $p < 0.01$; *, $p < 0.05$ (Student's t test), comparing to control cells (time point "0").

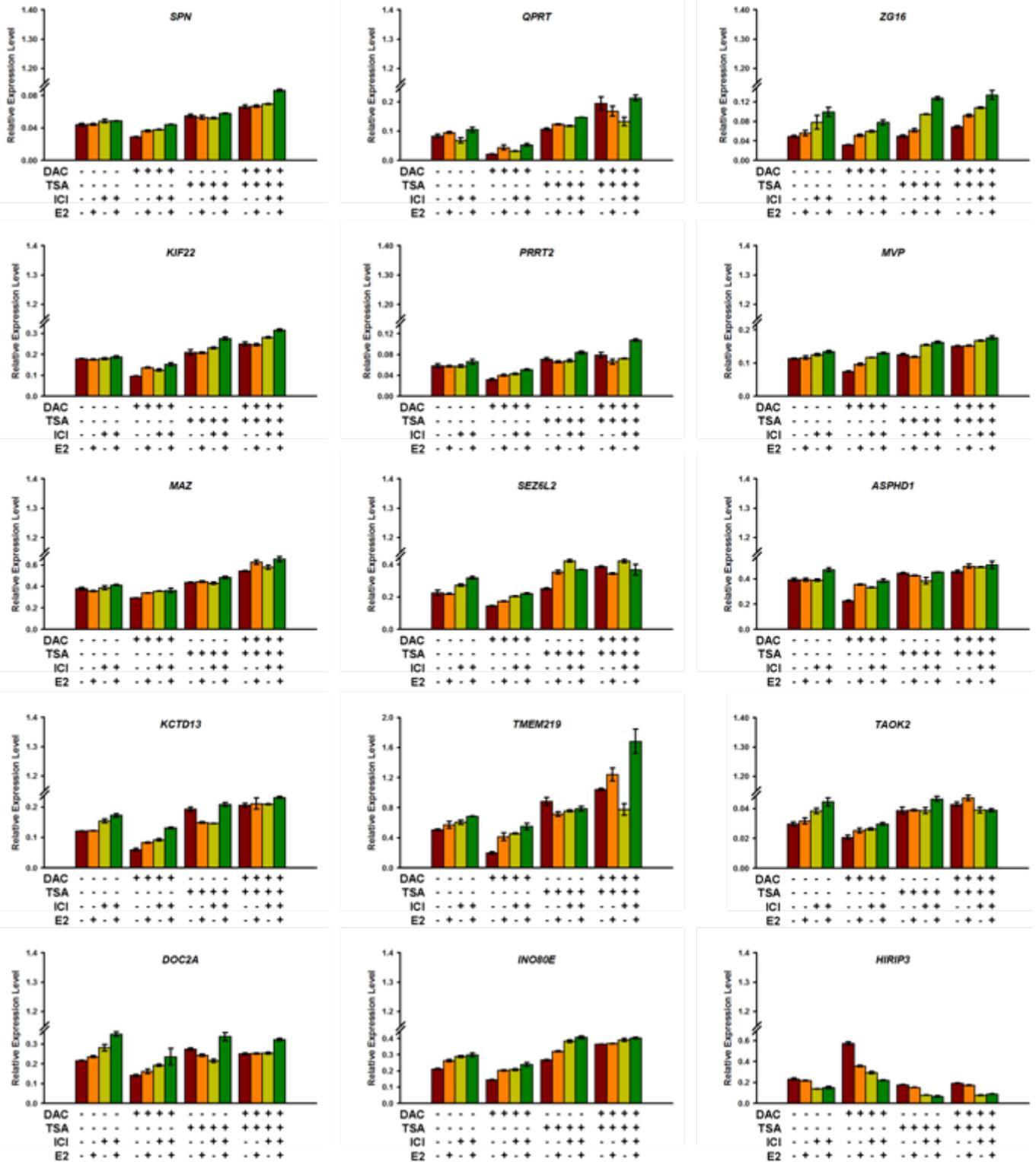


Figure S3. Epigenetic repression of the 16p11.2 cluster mediated by ER α -dependent pathway in MCF-7 cells. Cells were pretreated with 5-aza-2'-deoxycytidine (DAC, 1 μ M), trichostatin A (TSA, 1 μ M), and/or ER α antagonist, ICI182780 (ICI, 1 μ M) before 6 hrs stimulation of E2. Total RNA was addressed to quantitative RT-PCR analysis of the 16p11.2 gene cluster. Mean \pm SD (n=3).

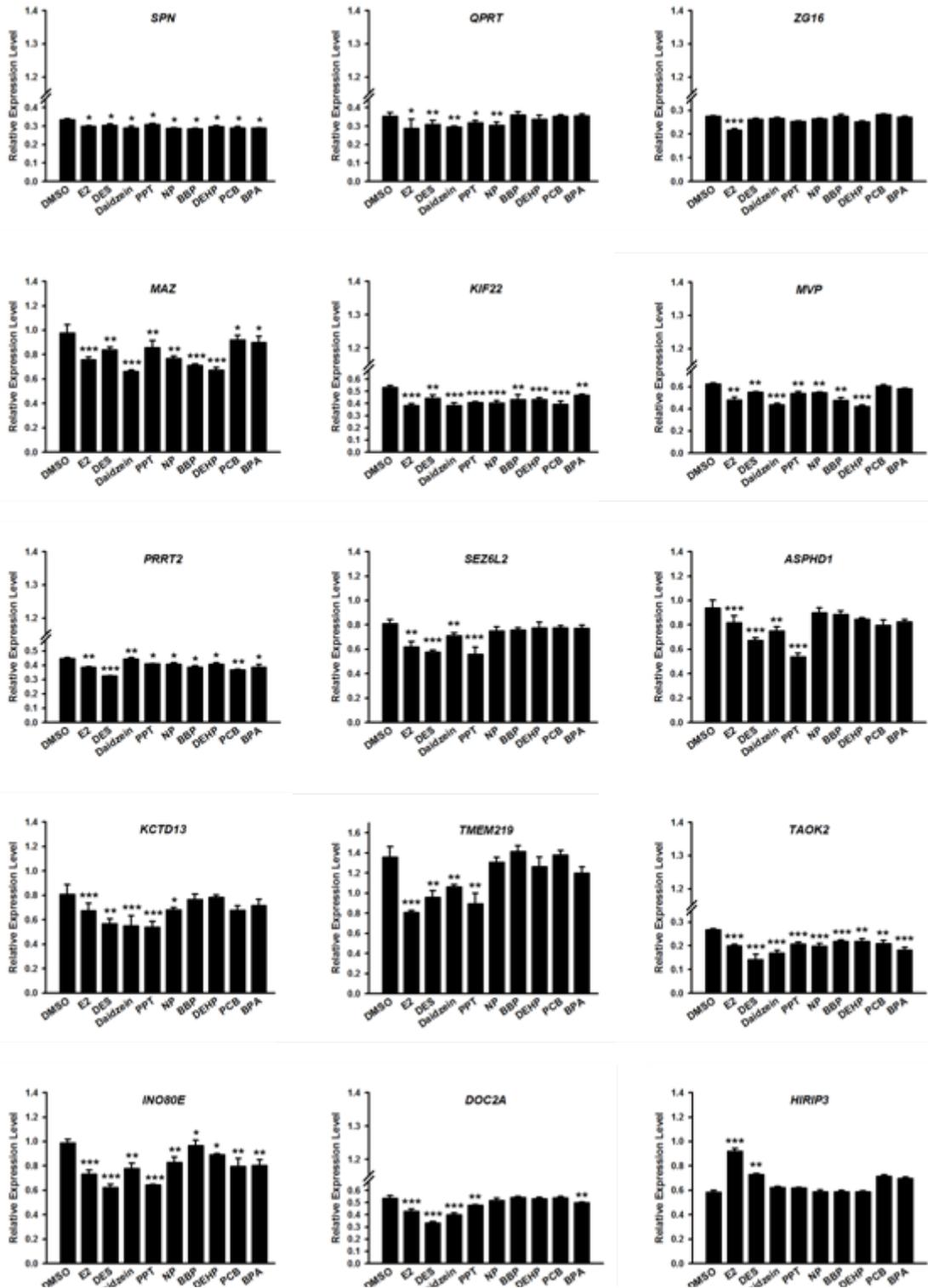


Figure S4. Concurrent repression of the 16p11.2 gene cluster in differentiated cells preexposed to endocrine disruptors. Progenitors were exposed to E2 (70 nM), diethylstilbestrol (DES, 70 nM), daidzein (10 μ M), 1,3,5-tris(4-hydroxyphenyl)-4-propyl-1H-pyrazole (PPT, 0.1 nM), 4-nonylphenol (NP, 1 μ M), N-butyl-benzyl phthalate (BBP, 10 μ M), di(2-ethylhexyl)-phthalate (DEHP, 10 μ M), 4,4'-dichloro-biphenyl (PCB, 0.1 nM), and bisphenol A (BPA, 4 nM) for 3 weeks. After the preexposure, MDECs with the absence of these chemicals were subjected to quantitative RT-PCR analysis. Data was calculated from three independent sets of MDEC samples. Mean \pm SE (n=9). ***, $p < 0.001$; **, $p < 0.01$; *, $p < 0.05$ (Student's t test), comparing to DMSO-preexposed cells.

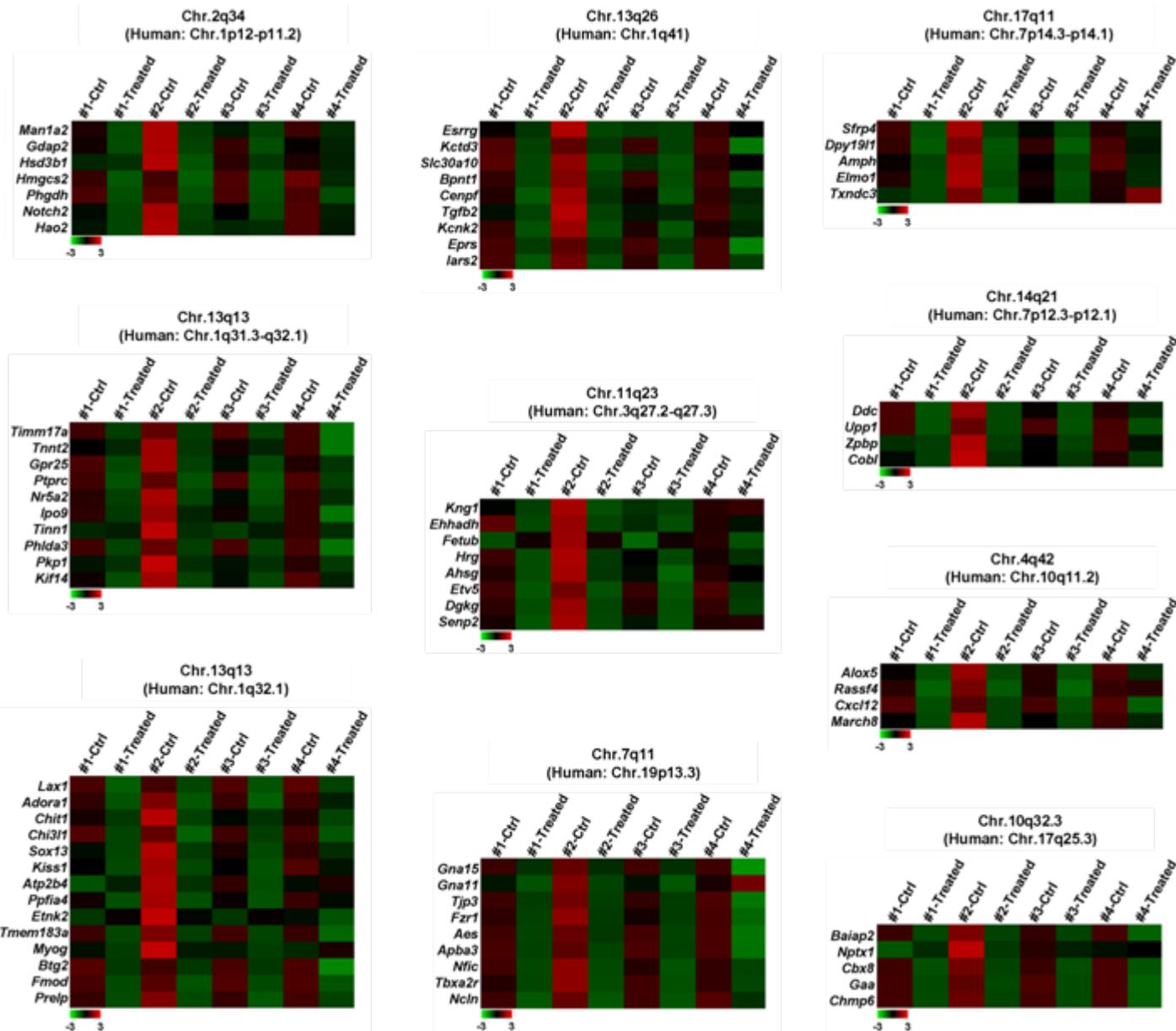
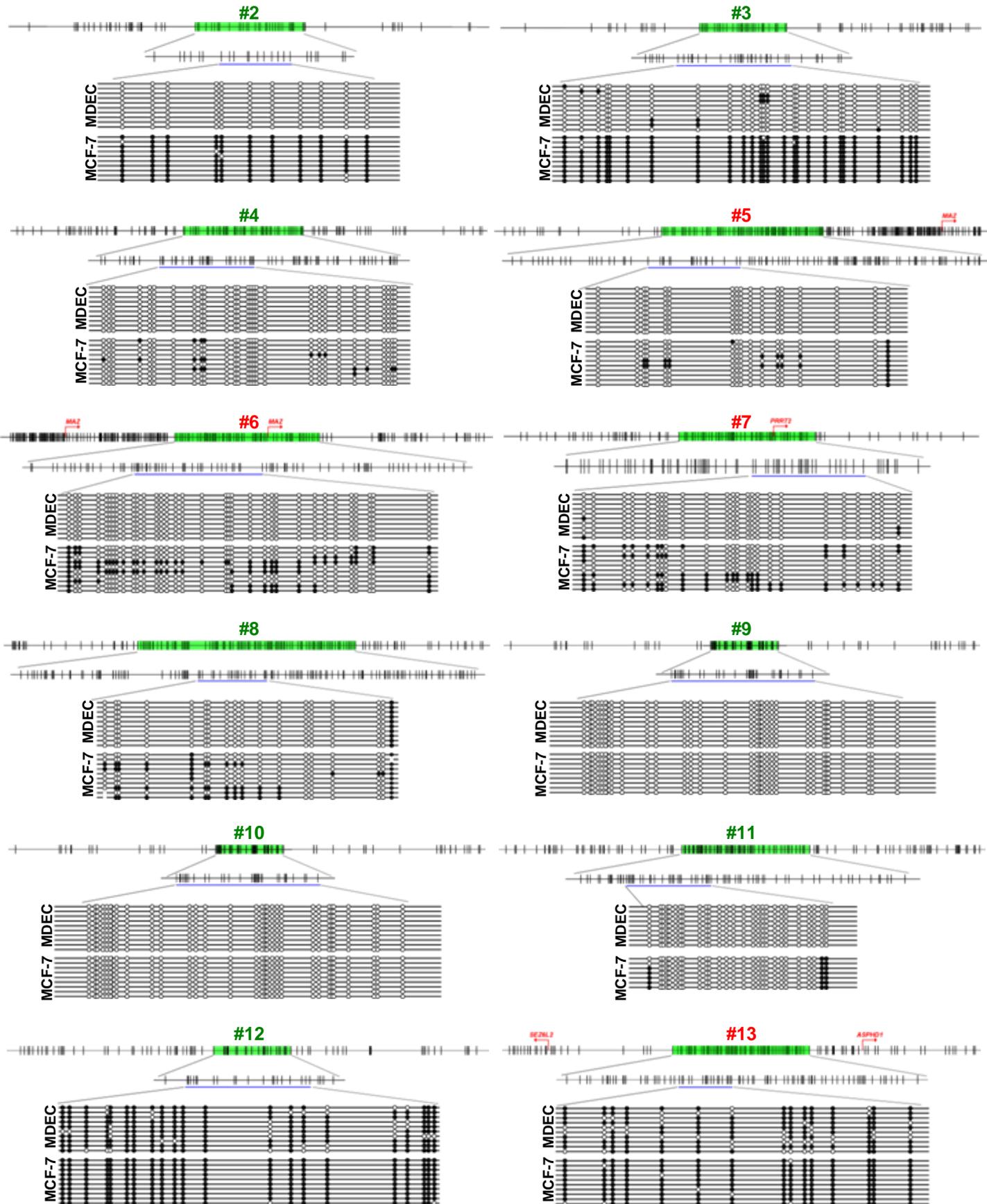


Figure S5. Gene expression profiling of homologous regions in a bisphenol A (BPA)-preexposed rat model. After birth, rats were exposed to sesame oil (Ctrl) or BPA (Treated; 250 $\mu\text{g}/\text{kg}$ BW) during the prepubertal period. Then, total RNA of mammary glands from 50-day-old rats ($n=4$) prepubertally exposed to BPA were collected for expression microarray analysis. Results of 10 homologous regions (total 75 genes) described in Figure S1A-J were shown as heat maps. Note: an additional region is shown in Figure 4D (see the main text).



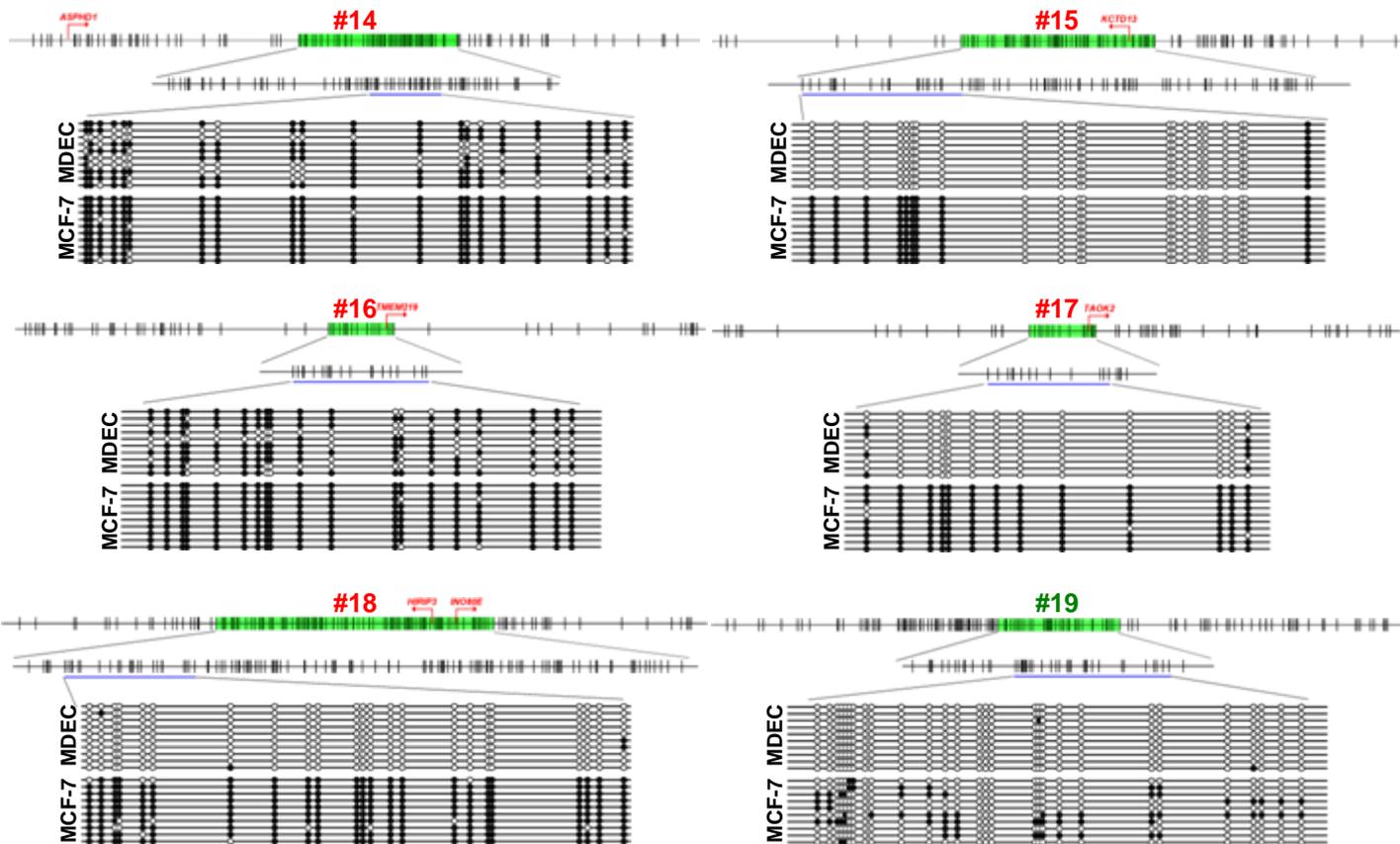


Figure S6. *De novo* DNA methylation analysis of CpG islands located on the 16p11.2 region. The diagrams indicated the 1-Kb upstream and downstream of the CpG islands. The green area is the CpG island. DNA methylation of 18 CpG islands located on 16p11.2 region was surveyed by bisulfite sequencing on normal (MDEC) and cancer (MCF-7) samples. Blue bars indicated the interrogated regions at CpG island area. The analyzed CpG islands located at the promoter and first exon regions of genes were labeled in red; others were labeled in green. Ten clones per CpG island were selected for sequencing. Black dot, methylated CG dinucleotides; white dot, unmethylated dinucleotides.

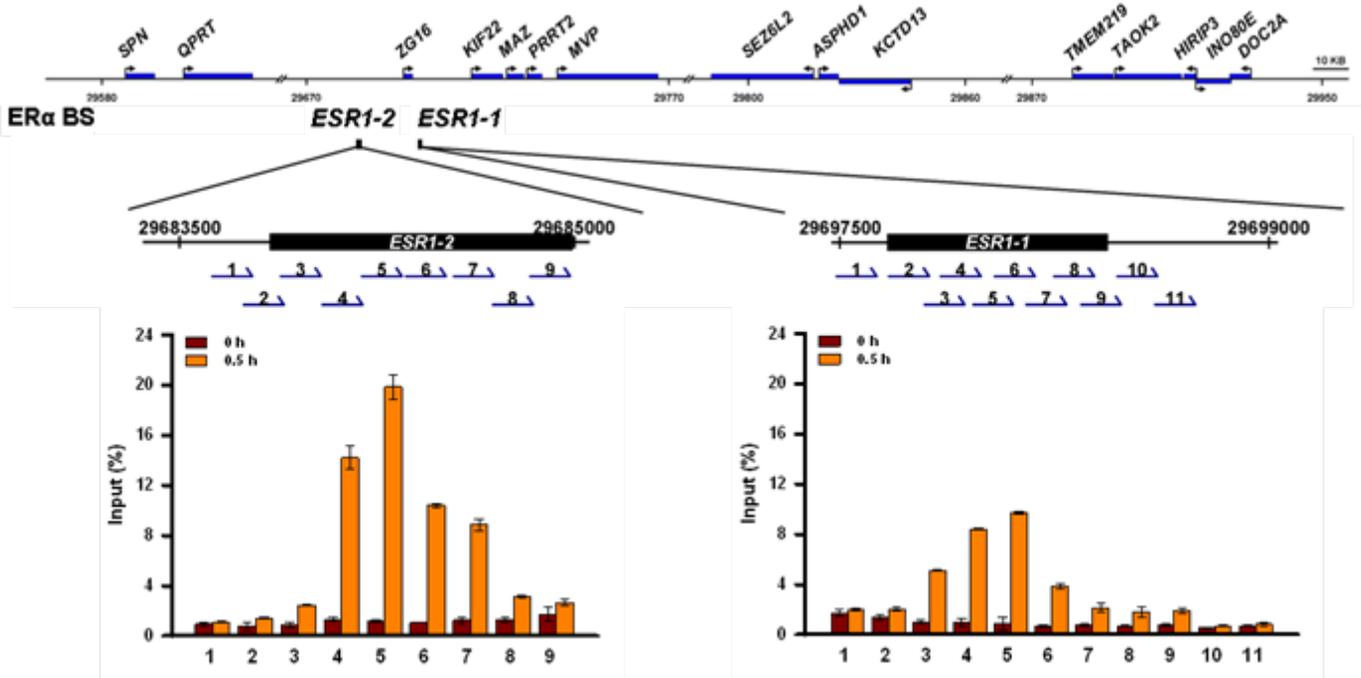
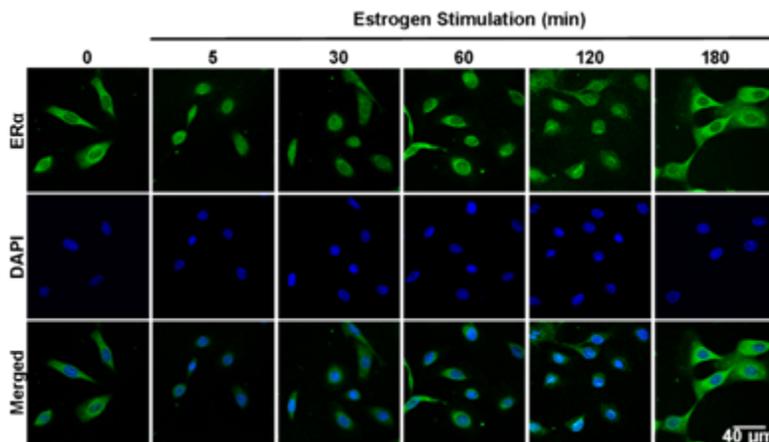


Figure S7. Recruitment of ER α onto the putative ER α binding sites upon estrogen stimulation. The diagram indicated the region surveyed by ER α -mediated chromatin immunoprecipitation (ChIP)-qPCR. Two ER α binding sites, *ESR1-1* and *ESR1-2*, were found in the 16p11.2 gene cluster. To determine whether ER α binds to these sites, MDECs without estrogen preexposure were stimulated by E2 for 0.5 hr, and then subjected to ChIP with anti-ER α antibody. ChIP-qPCR Was conducted to measure the enrichment of ER α binding on these two sites. Mean \pm SD (n=3).

A



B

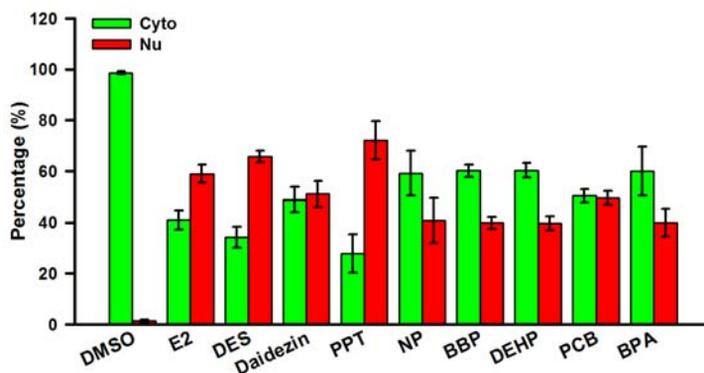


Figure S8. Nuclear internalization of ER α in breast epithelial cells exposed to xenoestrogens. (A) Time-course immunofluorescence (IF) analysis of ER α trafficking. Differentiated epithelial cells without prior exposure at the progenitor stage were stimulated with 17 β -estradiol (E2, 70 nM) and subjected to the IF analysis at indicated time points using an anti-ER α antibody (green). The protein was translocated from the cytoplasm into the nucleus at 5 min after stimulation, suggestive of the activation of ER α -mediated transcription. Nuclei were stained with DAPI (blue). (B) Nuclear ER α presented in MDECs preexposed to low-dose xenoestrogens and related compounds. Progenitor cells were exposed to E2 (70 nM), diethylstilbestrol (DES, 70 nM), daidzein (10 μ M), 1,3,5-tris(4-hydroxyphenyl)-4-propyl-1H-pyrazole (PPT, 0.1 nM), 4-nonylphenol (NP, 1 μ M), N-butyl-benzyl phthalate (BBP, 10 μ M), di(2-ethylhexyl)-phthalate (DEHP, 10 μ M), 4,4'-dichloro-biphenyl (PCB, 0.1 nM), and bisphenol A (BPA, 4 nM) for 3 weeks. Upon the removal of these compounds, progenitor cells were differentiated into epithelial cells for IF analysis. Subcellular localizations of ER α were scored from three independent sets of MDEC samples by two independent researchers. Mean \pm SD (n=3).

Table S1. Genomic information of 11 large chromosomal regions subjected to ER α -mediated epigenetic repression

Chromosome Region	Cluster Length (Mb)	No. Concurrent Silenced Genes^a	No. ERα BS^b	No. Methylated Regions^c	No. CpG Island^d
1p12-p11.2	3.10	11	21	4	24
1q31.3-q32.1	3.36	10	26	19	30
1q32.1	1.20	11	17	16	15
1q41	5.98	12	24	4	26
3q27.2-q27.3	1.56	10	2	3	11
7p14.3-p14.1	5.80	9	32	10	23
7p12.3-12.1	3.41	6	5	7	18
10q11.2	2.62	8	13	8	27
16p11.2	0.35	14	2	7	20
17q25.3	1.33	8	8	29	79
19p13.3	0.72	9	4	19	74

^a Number of concurrent silenced genes based on *in silico* analysis of 48 breast cancer cell lines (Neve et al. 2006).

^b ER α binding sites based on Carroll *et al* (Carroll et al. 2006).

^c Methylated regions based on MeDIP results of MCF-7 cells.

^d Number of CpG islands based on March 2006 build of the UCSC human genome browser.

Table S2. Descriptions of 14 concurrently down-regulated genes within the 16p11.2 cluster

Gene	Description	Cellular Component	Biological Functions
<i>SPN</i>	Sialophorin	extracellular space	negative regulation of cell adhesion
<i>QPRT</i>	Quinolate phosphoribosyltransferase	Cytosol	quinolate catabolic process
<i>ZG16</i>	zymogen granule protein 16 homolog	extracellular region	sugar binding
<i>KIF22</i>	kinesin family member 22	Nucleus	microtubule motor activity; mitosis
<i>MAZ</i>	MYC-associated zinc finger protein	Nucleus	a transcription factor with dual roles in transcription initiation and termination
<i>PRRT2</i>	proline-rich transmembrane protein 2	Membrane	response to biotic stimulus
<i>MVP</i>	major vault protein	nucleus; cytoplasm	required for normal vault structure; down-regulates INFG- mediated STAT1 signaling and subsequent activation of JAK; down-regulates SRC activity and signaling through MAP kinases.
<i>SEZ6L2</i>	seizure related 6 homolog (mouse)-like 2 isoform	endoplasmic reticulum membrane	specialized endoplasmic reticulum functions in neurons; a prognostic marker for lung cancers
<i>ASPHD1</i>	aspartate beta-hydroxylase domain containing 1	Membrane	oxidoreductase activity; peptidyl-amino acid modification
<i>KCTD13</i>	potassium channel tetramerisation domain containing 13	Nucleus	voltage-gated potassium channel activity and potassium ion transport; DNA replication
<i>TMEM219</i>	transmembrane protein 219	Membrane	
<i>TAOK2</i>	TAO kinase 2; serine/threonine-protein kinase TAO2	cytoplasmic vesicle membrane; nucleolus	response to stress; activates the JNK MAP kinase pathway through the specific activation of the upstream MKK3 and MKK6 kinases
<i>INO80E</i>	INO80 complex subunit E	Nucleus	component of the chromatin-remodeling INO80 complex
<i>DOC2A</i>	double C2-like domain-containing protein alpha	cytoplasmic vesicle; synaptic vesicle membrane	nervous system development; synaptic transmission; calcium dependent neurotransmitter

Table S3. Homology of the 16 p11.2 gene cluster between human and rat

Chromosome Region		No. Genes		Homology (%)
Human	Rat	Human	Rat	
1p12-p11.2	2q34	13	13	100
1q31.3-q32.1	13q13	14	11	79
1q32.1	13q13	14	14	100
1q41	13q26	14	13	93
3q27.2-q27.3	11q23	11	10	91
7p14.3-p14.1	17q11	11	8	73
7p12.3-12.1	14q21	8	7	88
10q11.2	4q42	11	6	55
16p11.2	1q36	15	12	80
17q25.3	10q32.3	10	8	80
19p13.3	7q11	12	12	100

Table S4. Microarray readouts of down-regulated rat genes

Gene Symbol		Entrez Id	Normalized Log2 Value							
Human	Rat		#1-Ctrl	#1-Treated	#2-Ctrl	#2-Treated	#3-Ctrl	#3-Treated	#4-Ctrl	#4-Treated
<i>ADORA1</i>	<i>Adora1</i>	29290	6.977173579	2.394873624	8.416844151	2.188023971	6.482624521	2.005236122	6.886918366	3.869014592
<i>ADORA1</i>	<i>Adora1</i>	29290	6.883259029	2.520805336	8.494018733	2.413233327	6.867521291	1.912084645	7.044599936	7.929176612
<i>ADORA1</i>	<i>Adora1</i>	29290	6.606311328	2.605203022	8.441030955	2.465156964	7.185553568	2.212963235	6.837257392	3.250666343
<i>ADORA1</i>	<i>Adora1</i>	29290	6.82358473	2.577517055	8.518584488	2.599228158	6.896811312	2.452681945	6.974341746	3.206333157
<i>ADORA1</i>	<i>Adora1</i>	29290	6.379584524	2.505458071	8.380154243	2.624365301	6.579771724	2.452681945	6.830150561	2.807435045
<i>ADORA1</i>	<i>Adora1</i>	29290	6.474353722	2.474428074	8.466291631	2.678181976	6.775926187	2.420967834	6.875501981	3.57575755
<i>ADORA1</i>	<i>Adora1</i>	29290	6.709905909	2.079523419	8.371734476	2.594028461	6.77496181	2.525411018	7.064606656	4.925321803
<i>ADORA1</i>	<i>Adora1</i>	29290	6.505563935	2.496409174	8.533848594	2.44066263	6.731128813	2.625391071	6.925798936	4.733907335
<i>ADORA1</i>	<i>Adora1</i>	29290	4.102169458	3.343790841	8.000438375	2.430121195	4.242597335	2.6232379	4.524087052	3.005914439
<i>ADORA1</i>	<i>Adora1</i>	29290	6.321169674	2.959499702	8.384145458	2.981668962	6.794929765	2.520021988	6.963623016	2.887825311
<i>ADORA1</i>	<i>Adora1</i>	29290	6.168612878	3.200618242	8.339459557	3.057874991	6.892499174	2.324507678	6.744338613	5.102299103
<i>AES</i>	<i>Aes</i>	29466	6.481556195	3.935425588	8.308944864	4.224752305	6.67819138	3.844009004	6.929860532	3.250202492
<i>AES</i>	<i>Aes</i>	29466	11.58107519	6.373799789	11.94728554	6.698164621	11.59825526	6.429531725	11.63233432	4.158737571
<i>AHSG</i>	<i>Ahsg</i>	25373	5.417032296	1.600622339	8.024968688	2.111138851	3.656510969	0.581627017	4.534128881	4.945827265
<i>AHSG</i>	<i>Ahsg</i>	25373	4.109455506	2.381263954	7.982214412	2.966213111	3.53961587	2.117550772	5.317048852	3.071970738
<i>ALOX5</i>	<i>Alox5</i>	25290	4.729848077	2.648039579	8.084560318	2.831549958	5.539279139	2.618201747	6.350021916	3.484610532
<i>AMPH</i>	<i>Amph</i>	60668	4.233831216	2.053304189	8.48417651	1.689499234	3.909607082	1.995114234	6.362647481	2.857679682
<i>APBA3</i>	<i>Apba3</i>	83611	9.16015772	4.615003671	9.749263996	4.554817771	9.250118725	4.617560159	9.22105466	3.004713779
<i>ATP2B4</i>	<i>Atp2b4</i>	29600	2.704481477	3.726820217	7.926702094	3.347965471	5.363421656	2.746520082	4.110089819	5.044937354
<i>BAIAP2</i>	<i>Baiap2</i>	117542	9.250396816	5.155258302	9.483732156	5.169682956	8.890309069	5.217615381	9.203956019	5.089625848
<i>BAIAP2</i>	<i>Baiap2</i>	117542	5.626276823	4.164434346	8.180657853	4.321234289	5.696888118	4.26456295	6.193212103	3.104963522
<i>BPNT1</i>	<i>Bpnt1</i>	64473	6.563246994	3.668527533	8.506228248	3.834173169	6.757632374	3.502676093	6.91304932	3.070261178
<i>BTG2</i>	<i>Btg2</i>	29619	12.00644968	6.194193051	11.17514753	6.278944828	11.58591997	6.25663022	11.65890163	2.970238012
<i>CACNA1S</i>	<i>Cacna1s</i>	116652	3.519049462	2.720596555	7.899418425	3.378087996	5.639453567	2.957055977	3.575146644	3.201662559
<i>CACNA1S</i>	<i>Cacna1s</i>	116652	5.859417321	3.573369026	8.561421292	4.411511459	6.377563214	3.553041306	6.057379764	3.087135773
<i>CBX8</i>	<i>Cbx8</i>	303731	7.118820603	3.317587299	8.517752942	3.659052835	6.968815965	3.364523584	7.423068849	3.232161314
<i>CENPF</i>	<i>Cenpf</i>	257649	5.968576599	1.959701568	8.095402077	2.250939232	5.526222248	2.014433063	6.275356223	3.941576877
<i>CENPF</i>	<i>Cenpf</i>	257649	4.328584451	2.525576628	7.996750292	4.124265381	4.04220242	2.662818709	4.765520131	3.041744587
<i>CHI3L1</i>	<i>Chi3l1</i>	89824	7.977138254	3.485102616	8.505115814	2.616142073	7.3712085	3.664190518	7.625657899	2.963558924
<i>CHIT1</i>	<i>Chit1</i>	289032	4.778604634	3.125247199	8.050750523	2.964830236	4.125608916	3.277679163	5.013333856	2.912252801
<i>CHMP6</i>	<i>Chmp6</i>	287873	9.207909236	4.655789644	9.745553258	4.838679296	8.958930498	4.726145188	8.992382725	2.833777258

Gene Symbol		Entrez Id	Normalized Log2 Value							
Human	Rat		#1-Ctrl	#1-Treated	#2-Ctrl	#2-Treated	#3-Ctrl	#3-Treated	#4-Ctrl	#4-Treated
<i>CHMP6</i>	<i>Chmp6</i>	287873	7.45593495	3.738145251	9.081228756	3.955647	7.646072948	3.728079442	7.959278651	4.45867721
<i>COBL</i>	<i>Cobl</i>	305497	4.999795936	2.924979548	8.043504172	3.463833465	3.59798058	2.87774647	4.699694172	2.829805874
<i>COBL</i>	<i>Cobl</i>	305497	2.704481477	2.670752345	7.911222492	2.745900193	4.593354121	3.010057886	5.06958647	2.968306805
<i>CXCL12</i>	<i>Cxcl12</i>	24772	11.64325613	3.814540175	12.08043874	4.555444351	11.25959435	3.878160275	12.1773754	3.04570475
<i>CXCL12</i>	<i>Cxcl12</i>	24772	12.59220855	3.875340312	12.55865461	4.510131467	11.93941416	3.854783554	12.54597181	3.132902488
<i>DDC</i>	<i>Ddc</i>	24311	7.261271152	3.200723309	9.189230624	3.525019544	5.599670387	3.329602603	6.323688392	4.315267022
<i>DGKG</i>	<i>Dgkg</i>	25666	5.474089379	2.46325754	8.232537643	2.661579726	5.260479419	2.40963301	5.666319623	2.801190429
<i>DOC2A</i>	<i>Doc2a</i>	65031	3.638197163	2.438998421	7.877084053	2.587433577	3.538994718	2.347392695	4.875940414	2.926304858
<i>DPY19L1</i>	<i>Dpy19l1</i>	315496	7.245048273	1.899069217	8.403872309	2.12601903	6.832119682	1.983052737	7.131480061	2.86793959
<i>DPY19L1</i>	<i>Dpy19l1</i>	315496	5.402623251	2.389347163	8.364389517	2.401552876	5.670336816	2.179148001	6.647190756	5.277767439
<i>EHHADH</i>	<i>Ehhadh</i>	171142	6.984250827	2.987885962	8.421128412	3.05161202	3.709886318	2.801505422	5.590392177	4.312011784
<i>ELMO1</i>	<i>Elmo1</i>	361251	6.147820474	2.142997389	8.034521749	1.930499591	4.204893111	1.889551596	5.647882458	2.911899947
<i>ELMO1</i>	<i>Elmo1</i>	361251	4.95586439	2.398649635	8.122935988	2.330351789	4.595426998	2.083741821	5.476274969	3.205098721
<i>ELMO1</i>	<i>Elmo1</i>	361251	4.746655775	1.952133365	8.209792433	2.208782191	5.118763109	2.055494901	5.237737424	3.437430864
<i>ELMO1</i>	<i>Elmo1</i>	361251	3.851115806	3.438828483	7.918000143	3.324588926	5.185773059	3.209461765	3.749119373	3.11149815
<i>EPRS</i>	<i>Eprs</i>	289352	11.55220547	5.961398825	12.50189215	6.211948207	11.53912886	6.018363701	11.55618772	2.780348848
<i>ESRRG</i>	<i>Esrrg</i>	360896	3.947039771	2.369793442	7.967237567	1.963608741	2.262851925	2.098054901	5.013039636	3.597561533
<i>ETNK2</i>	<i>Etnk2</i>	360843	3.38963261	4.676900967	8.513203917	4.354072445	3.415445208	4.692763653	4.242534213	2.83531933
<i>ETV5</i>	<i>Etv5</i>	303828	6.235350152	2.530565537	8.800302122	2.570647767	5.476339647	2.63836956	6.967716113	4.150268176
<i>ETV5</i>	<i>Etv5</i>	303828	9.628787379	2.910985619	10.64851631	3.211457769	9.708875219	2.76649154	9.767476576	3.475373744
<i>FETUB</i>	<i>Fetub</i>	83928	3.638903571	5.472504052	8.130170025	5.64375554	3.122180988	5.520513076	5.889428195	3.568398333
<i>FMOD</i>	<i>Fmod</i>	64507	11.12228802	3.720292998	11.82138169	3.287879027	11.5893186	3.727153151	11.35288865	3.263107792
<i>FZR1</i>	<i>Fzr1</i>	314642	6.225560862	3.652971351	8.468598261	3.805246519	5.672221883	3.755458818	6.796448932	2.783628456
<i>GAA</i>	<i>Gaa</i>	367562	8.844402926	3.876692878	9.756056931	3.969605569	9.197526585	3.849095561	8.997954466	3.118692888
<i>GDAP2</i>	<i>Gdap2</i>	362004	5.359803441	3.691478562	8.063224117	3.870482774	6.021913462	3.65589608	5.188495456	4.434903177
<i>GNA11</i>	<i>Gna11</i>	81662	4.071003082	2.477106006	8.015289291	2.858662256	4.205319854	2.321220476	5.392838936	7.696283383
<i>GNA15</i>	<i>Gna15</i>	89788	7.692101614	5.234415266	8.694235768	5.352873881	7.900940367	5.256529476	7.824785809	3.020473931
<i>GPR25</i>	<i>Gpr25</i>	363993	6.093650877	2.333592405	8.285864693	2.549527666	3.911235325	2.337138468	5.04834053	2.852716924
<i>HAO2</i>	<i>Hao3</i>	84029	3.169753674	1.943661609	8.098004526	2.275428057	2.75619492	2.560162034	5.745017326	3.094640562
<i>HIRIP3</i>	<i>Hirip3</i>	361650	11.63742712	5.05233052	12.05540302	5.405968876	11.7817384	5.123168597	11.49618737	3.884164288
<i>HMGCS2</i>	<i>Hmgcs2</i>	24450	8.141676748	2.823864698	8.590720257	2.582555834	8.975743708	3.072958141	10.01677215	4.551837809
<i>HRG</i>	<i>Hrg</i>	171016	5.36029502	2.200535764	7.94208144	2.645246465	3.957514898	2.316435827	4.528099771	2.872305054

Gene Symbol		Entrez Id	Normalized Log2 Value							
Human	Rat		#1-Ctrl	#1-Treated	#2-Ctrl	#2-Treated	#3-Ctrl	#3-Treated	#4-Ctrl	#4-Treated
<i>HSD3B1</i>	<i>Hsd3b1</i>	29632	3.691286526	3.465803323	8.131762869	2.729079062	5.363851424	3.309375087	5.087249148	3.812442974
<i>IARS2</i>	<i>Iars2</i>	364070	7.841452179	3.78504535	8.867989981	4.073947195	7.211029645	3.838201864	7.787923126	4.466261339
<i>IPO9</i>	<i>Ipo9</i>	304817	8.178943941	5.163561806	9.538081568	5.622555719	7.550570926	5.162633609	7.76462064	2.716664208
<i>IPO9</i>	<i>Ipo9</i>	304817	4.883496125	2.860673691	8.402118365	3.227941445	4.202305394	2.666488873	5.975092629	2.845072024
<i>IPO9</i>	<i>Ipo9</i>	304817	6.251605417	4.463595106	8.42465555	5.022375724	5.699028483	4.532901758	6.295572668	2.900049482
<i>KCNK2</i>	<i>Kcnk2</i>	170899	5.795726748	2.412329394	8.219181608	2.515601485	5.16678438	2.277763492	5.253974598	3.616181159
<i>KCTD13</i>	<i>Kctd13</i>	293497	7.30994765	2.784741557	8.353896025	3.063540154	6.289943085	2.656950618	6.181543386	2.87491591
<i>KCTD3</i>	<i>Kctd3</i>	305055	9.331419481	4.682414665	9.748696924	4.995829606	8.641019868	4.687809763	8.991123529	2.948253586
<i>KIF14</i>	<i>Kif14</i>	360849	4.333406922	1.818766447	8.180175872	2.14793234	3.540153016	2.082634903	6.065847585	3.02180888
<i>KIFF22</i>	<i>Kif22</i>	293502	8.719046023	3.68685822	10.16049322	3.873923797	7.330535875	3.682174644	7.322530025	2.875267654
<i>KISS1</i>	<i>Kiss1</i>	289023	4.296316478	2.5696947	8.167343683	2.609078569	4.380454205	2.35997674	6.310771709	3.890930362
<i>KNG1</i>	<i>Knng1</i>	24903	4.530492164	2.204122916	8.188863855	2.409083632	2.404629583	2.22824679	5.999067049	6.537732709
<i>KNG1</i>	<i>Knng1</i>	24903	3.455876073	2.896922291	7.904540806	1.966955747	3.415234085	2.840825014	4.004827957	4.218382434
<i>LAX1</i>	<i>Lax1</i>	498232	8.80861975	2.316528272	8.578633662	3.27998166	9.122553649	2.780325578	9.461184763	3.440397122
<i>MAN1A2</i>	<i>Man1a2</i>	295319	5.136454881	2.648321564	8.380263441	3.002393496	3.859508403	2.881622107	5.848594019	3.414025184
<i>MARCH8</i>	<i>March8</i>	312656	4.425256903	2.832352038	8.000201656	3.046036168	4.407004119	2.971265836	5.651908005	3.619955156
<i>MVP</i>	<i>Mvp</i>	64681	9.313516707	4.737312561	9.328155208	4.515468326	9.955627769	4.73035009	9.528590086	3.157379439
<i>MYOG</i>	<i>Myog</i>	29148	3.638722065	2.74211961	7.858101348	3.419271856	3.479279043	2.723628634	3.147217649	4.512977062
<i>NCLN</i>	<i>Ncln</i>	314648	11.54203405	5.500237625	11.44775796	5.544986698	11.13472846	5.53119602	11.93746343	4.624638229
<i>NCLN</i>	<i>Ncln</i>	314648	6.295520344	3.512977722	8.646139036	3.490186963	6.743414206	3.576871275	7.087443194	6.689407498
<i>NFIC</i>	<i>Nfic</i>	29228	6.114245326	2.770656412	7.968974033	2.74240506	5.429232596	2.478732039	5.735757002	2.907932165
<i>NOTCH2</i>	<i>Notch2</i>	29492	4.520802111	3.114746447	8.674397901	3.223158191	4.702999163	3.102708176	6.682939486	4.037572681
<i>NPTX1</i>	<i>Nptx1</i>	266777	2.705252915	3.530036191	7.858162507	3.29022449	5.093280202	3.754314381	4.032349043	4.362598905
<i>NR5A2</i>	<i>Nr5a2</i>	60349	5.016415282	2.465398574	8.121458292	2.383914525	3.762504916	2.093542143	5.346956325	2.926678491
<i>PHGDH</i>	<i>Phgdh</i>	58835	12.65529078	5.806849837	13.15710211	5.702931712	12.6175021	5.827046662	12.65723171	5.96158449
<i>PHLDA3</i>	<i>Phlda3</i>	363989	8.363478579	4.494943452	9.399588018	4.642276175	8.616161719	4.518974145	8.512316546	2.999620469
<i>PKP1</i>	<i>Pkp1</i>	304822	5.11770642	4.669288515	8.458728931	4.689393261	5.137448017	4.642420564	6.04035984	4.501221631
<i>PPFIA4</i>	<i>Ppfia4</i>	140592	6.294806765	2.48098771	9.191704553	2.452863514	5.82816603	2.42885778	7.748862572	2.886957193
<i>PPFIA4</i>	<i>Ppfia4</i>	140592	4.685862075	2.322316763	8.109751274	2.304785441	3.540235636	2.327492941	5.376725821	5.412783867
<i>PPFIA4</i>	<i>Ppfia4</i>	140592	3.839267338	2.92122318	8.188421667	2.868799565	4.940112499	2.597034221	4.473017678	4.388036219
<i>PRELP</i>	<i>Prelp</i>	84400	6.520255296	2.556747222	8.723950342	2.595279982	6.458744386	2.196241136	6.933154229	2.871521763
<i>PTPN14</i>	<i>Ptpn14</i>	305064	5.951630239	4.589304447	9.036971373	4.697293457	5.55480331	4.643656987	5.548717681	2.942905127

Gene Symbol		Entrez Id	Normalized Log2 Value							
Human	Rat		#1-Ctrl	#1-Treated	#2-Ctrl	#2-Treated	#3-Ctrl	#3-Treated	#4-Ctrl	#4-Treated
<i>PTPRC</i>	<i>Ptprc</i>	24699	7.873078385	1.822396778	8.683820022	2.135898506	7.652045248	2.14895865	8.423650724	2.996865403
<i>PTPRC</i>	<i>Ptprc</i>	24699	7.95760638	3.210639921	8.076991141	2.77396605	8.376559545	2.452681945	7.670520132	3.2832021
<i>PTPRC</i>	<i>Ptprc</i>	24699	6.444064663	3.43771496	8.130478207	3.678456382	7.407607172	3.488410951	7.249884248	4.02781552
<i>QPRT</i>	<i>Qprt</i>	293504	8.970923696	2.404826254	8.814459306	2.757178387	8.938933643	2.599262892	9.020298059	6.362612128
<i>RAB3GAP2</i>	<i>Rab3gap2</i>	289350	8.597509813	4.182657856	9.791433083	4.29505194	8.668175216	4.325688123	9.091107221	3.318271101
<i>RAB3GAP2</i>	<i>Rab3gap2</i>	289350	11.22945913	5.697359604	11.26507036	5.792461525	11.07933347	5.747037169	10.92063658	3.317743202
<i>RASSF4</i>	<i>Rassf4</i>	362423	6.729691787	2.900060744	8.723279425	3.14369479	6.622276238	2.809226379	7.017127024	6.686977815
<i>SENP2</i>	<i>Senp2</i>	78973	6.81475869	2.902333146	8.249751701	3.278752262	4.802705409	3.071809314	5.119349116	4.504353708
<i>SENP2</i>	<i>Senp2</i>	78973	3.169845269	2.141967243	7.954889549	2.405285637	3.122368076	2.130420414	5.316637513	6.099010445
<i>SEZ6L2</i>	<i>Sez6l2</i>	308988	5.788296798	3.578722909	8.457989134	3.50075728	4.80024811	3.590665201	6.066524124	2.951333762
<i>SEZ6L2</i>	<i>Sez6l2</i>	308988	3.001311846	2.296618733	7.960524695	2.267227441	3.414637681	1.995114234	4.476808584	3.492040429
<i>SFRP4</i>	<i>Sfrp4</i>	89803	6.576453912	1.901361095	8.388339063	1.908679426	4.624797345	1.548678224	5.660942761	2.69733715
<i>SFRP4</i>	<i>Sfrp4</i>	89803	5.911700334	2.236442877	8.047115756	2.312087334	4.946221067	2.091671948	5.285468028	2.896528525
<i>SFRP4</i>	<i>Sfrp4</i>	89803	4.148588174	0.905084371	7.905616795	2.2569776	1.511868139	2.16820008	3.604972138	3.030912634
<i>SLC30A10</i>	<i>Slc30a10</i>	289353	6.679459313	2.363865414	8.232552408	2.131180349	3.040170416	2.068934418	5.609565067	4.248751868
<i>SOX13</i>	<i>Sox13</i>	289026	3.579818331	2.309906643	7.906190369	2.525337864	4.539102263	2.181757133	4.99043498	2.840195741
<i>SPN</i>	<i>Spn</i>	24796	11.53625452	3.093050104	10.23425897	3.098157534	11.16028882	3.138353316	10.93954247	4.642678258
<i>SPN</i>	<i>Spn</i>	24796	4.880798297	2.513246145	8.022977152	2.601054579	5.750599888	3.164984198	6.002077898	3.009271415
<i>TAOK2</i>	<i>Taok2</i>	64666	9.273532983	4.165875988	9.095419138	4.152299428	8.940601199	4.191085868	9.187140361	2.93624209
<i>TBXA2R</i>	<i>Tbxa2r</i>	24816	5.934051455	3.196298421	8.59400229	3.039456311	6.644002622	2.919174881	6.322629805	3.166047752
<i>TGFB2</i>	<i>Tgfb2</i>	81809	3.739089679	2.519128717	8.375261372	2.529961702	3.656848321	3.197628619	5.672955756	2.956051242
<i>TIMM17A</i>	<i>Timm17a</i>	54311	8.366124056	4.845231934	9.300005188	4.896128982	8.716306725	4.761119169	8.481765406	3.283287834
<i>TJP3</i>	<i>Tjp3</i>	314640	7.617610942	4.434115314	9.076937662	4.385945401	7.376836739	4.424703065	8.101452159	2.863349877
<i>TMEM183A</i>	<i>Tmem183a</i>	289034	7.103285201	3.966900528	8.77421543	4.122078326	7.311617073	3.969139554	7.019034225	3.120314612
<i>TNNI1</i>	<i>Tnni1</i>	29388	3.638197163	3.795408806	8.028298709	3.485308092	3.20169374	3.840994675	5.462415861	3.499915952
<i>TNNT2</i>	<i>Tnnt2</i>	24837	5.468687325	4.585564535	8.478813699	4.278978003	5.824560193	4.650639716	6.618502632	3.017450904
<i>TXNDC3</i>	<i>Txndc3</i>	364729	3.086794597	2.336399523	7.974426445	1.85559389	4.655995997	2.259216012	5.318743544	8.033411724
<i>UPP1</i>	<i>Upp1</i>	289801	8.336073275	4.176822323	9.12221777	4.464275248	8.313873131	4.171137334	8.276562407	4.258675195
<i>ZG16</i>	<i>Zg16</i>	171449	4.639724888	3.658771077	8.067058697	3.332874972	5.86073245	3.769103196	4.418025299	3.299325019
<i>ZBPB</i>	<i>Zbpb</i>	498415	3.245614759	2.882200628	7.979710178	2.872390163	4.349479736	2.777328312	5.838604088	3.807737291

Table S5. Primer information for PCR-based assays**(A) Primer sequences for RT-qPCR**

Name	Forward	Reverse
<i>SPN</i>	ACAACAGCAGTGACAGACACC	GAAGTTGAGGGAGGTAGGGC
<i>QPRT</i>	CAGACAGCTGCAAGTCACCA	CTGACCAAGGCTGCGTAGTT
<i>ZG16</i>	ATTCTGGCAACCAGTTGGAC	CATAGTCGCTCCACACCTTG
<i>KIF22</i>	CCAAGGAGGGAGTGGAATG	TCCAATCTTGCTTAGCCGAC
<i>MAZ</i>	TCGGCTTATATTTTCGGACCA	CATTGGACAAACCTCACCAGT
<i>PRRT2</i>	CTCCCTAGCTGACTTGCTCC	GGAAATAGCAGAGACAGCGG
<i>MVP</i>	GTTCCCATCTGAGGCG	GGATGCGGATGATGAACTCT
<i>SEZ6L2</i>	ACTCCTGGCCAACTCATCC	AAGCCACAGCTCAGGAGGTA
<i>ASPHD1</i>	TCGAAGCTTTATGAGTGCCA	CAGCCAGGAGGGATCTTTAG
<i>KCTD13</i>	CTGCCGGAGAGTACGAGAGA	GATGTCACCATGGGGATGAG
<i>TMEM219</i>	TGAGCCCTAGAATGGGTGAG	AAGCCACAGAAGAGAAGCA
<i>TAOK2</i>	GGCACCATAGTGACCCCTAC	CCTGAAGAAGAGCTCAGCC
<i>DOC2A</i>	TGACTTACAGCGGGATCACA	GCGGATCTCCCAATAAACT
<i>HIRIP3</i>	CCAGGGAAGACAACTGGAC	CAAAGTAGTCTGGGCTGGA
<i>INO80E</i>	CTGCAGTACGAGAACGTGGA	CGGTGTGTCAGACAACCTTG
<i>ACTB</i>	CAACTGGGACGACATGGAGA	ACGTACATGGTGGGGTGTG

(B) Primer sequences for ChIP-qPCR

Name	Forward	Reverse
#1	ACAGAGG GATAAGGAGATTAAGGCA	AGGACCGCCACCTTCTTCAT
#2	AGTCCACGGGCCTGTTAGA	GGCAACGTAGCAAACTCCTATCA
#3	CAGTGCTGCGTCCTTATCAGC	ACCCTGTGCAGCCCAATG
#4	CCCACTTTCTGGTTCAGAAGCT	TGAGAAAACCTCTGCAATGAAACAG
#5	GCCATTTTAAAGCTAAGGAACTGA	CCTAACTCCATCCTTTTTGATCTCA
#6	GCATGGACTTCTGCTCTCGC	CAGGGAATCACGGGACTCA
#7	TGCACTTCCCATTGGACTGACT	TCATCTATTTATCCCAATATGCCA
#8	CTGACAGATGGCAGATTTAGGT	GTAACCTAAGGTCACCACCAGCAG
#9	TCAGGAGGTGAGGTTACACAAT	CTGACAGTTTCAGATGCAAAGCA
#10	ATTACGTTACGCAGCCATCATCA	GCAATAGATATAACGAGTTTTCTTTGGG
#11	AGCTACTCAACGGACTGCTGTACTC	CGGCGAAGCGTGGAAAA
#12	CTACAGAACCGACCAGACGTGATA	TTTCTTGCCCTCCGTGGGTG
#13	TGGCAGTTCGCTCTCTGGTTTA	TGGCCCAGGACATGTTTTGA
#14	CAAAGTTGGTCCCTGCTTCTTCT	CTCCAATCTTGCTTAGCCGACA
#15	GTGTCAGAGAAGACCACCCAGATT	GCCCCGCCTAGAAAAACA
#16	GGGTCCAGATAGGAAGTGAGCAA	CGCGATCTGAATGGCAAGAG
#17	GGCAAAGGTTGTACCTTCATAAGGT	CTTTTTCCCCTGACAGATTCTCAAG
#18	TCGGCCTGTGCGAGTGCTA	CATCCAACAAGATCCAGACTCTCAG
#19	TGCACTCAGCCATAAATCGTGT	CATGCTCTTCCCTGGCAAGAT
#20	GGGTGCAGTGTCCGTACCTG	CCCGCAACGTGCTGTTTTG
#21	TCCAAGAATGTGACCTGTACCCATT	GCCCTGCATGGAGGAGTAAGAA
#22	GAGACCCTGTCCCCTATCGATC	GAAGGACTCCATCTGTTTCCC
#23	GATCACCTCAACAGTCACGTCAGA	TGACTCAGACAGCTACCATGAGGAT
#24	CCTGCACGGGTAGCAGAGAA	TAGCCACTTGCAAGGTTGACC
#25	GCGACTACCCCGATCTCT	AAAGATAAACGGAGACGGAGGAA
#26	ATTATGCCCCCTGTTACATTCA	GCCCATTCACCCGAGCTA
#27	CTCCCCCGACCTTTTGT	TGTGTTGTCCAGGCTTTTTATGAG
#28	CCACCCAGTCTTATTTACAGGAC	GGGAAGAAGGTGGAGACACAGAA
#29	TGGTAAGTTCTGTCTCCATAGGGCT	TCTCCACGACCTCCACTTCT
#30	AAAACCTGGGATGCAGAATGCAG	TTTGGTTTACTGGAGAAGCCAGAG
#31	CTCGTTAACCCTTCCGTTTGTG	CACTTTCATTCTGGTGGTATCCTT
#32	GCCTGTGAGAACATATCACACTCATTAC	AAATGGCCAACTTTGTGCAGT
#33	CATCTCTGAGCCTTAGTTTCTTATCTG	CGCCATACTGTCCGGTGTG

(continued)

Name	Forward	Reverse
#34	TTGTGTTCAATATCCAGTCTGCTC	CGAGAACTGCTGTTGGGTTAAGTC
#35	CTGGGAAGGAGTCAGTCATAACAAT	AAAGAACACCCCAATTTCAGCC
#36	GCTCTGAAACAGCAGAGATAGC	GAGACAATACACCTACACCAGCCA
#37	CCCCCGACCTTTTGTCTAC	TCACTGTGTTGTCCAGGCTTTTTAT
#38	CTCCTGACCTCGTGATCAATCC	CTGTAACCTTGACACCCCAACAA
#39	ACTTCAGGGCACACTAGCCTCA	GGGATTCTAGGTTGAAAAGAACAGC
#40	GGGCCAGGAACGTCTTTAATCTTAT	GGGCTTTTCGACAGTTTGACTCA
#41	AAACCACCATCCCCTAGATCCA	GCCACATCAAGCAACCCATAATA
#42	GGCTGGGTAATAAACCAAACGATAC	ACGATGCTGGCTTGTTAAAGAGA
#43	GGAAGTGGAAAGGCAATCTAGGTCT	TGCTTCTAACAGCTGCAGAGAAATC
ESR1-1-1	GCCTCTGGGCTCAGTAAACTCAG	CATTTGGGTTGGTATGGCCAT
ESR1-1-2	TCAGGGACATTGAAGGTAGCATC	CGTCCTTCAACTTAGACCTAGCAGA
ESR1-1-3	AGGAGTGCCTGGGTCAATCAA	GGGCTAGGAGAGCGACTGTCA
ESR1-1-4	TTGCTCTTTTCTTCCCCTCCA	CCTGGTATCTCACTTACTGGCATTG
ESR1-1-5	CAGAATGTTGACAGTCGCTCTCC	GCCTTCCCAAGTCCCCAATA
ESR1-1-6	AGTCGCTCTCCTAGCCCTTCTCT	TGCCCAAGGCTGCCTTC
ESR1-1-7	TCTGGCAATGCCAGTAAGTGAGATA	AAGCCAACCTCCAAAAGCCT
ESR1-1-8	GGACTTGGGAAGGCAGCCT	TTCTCTGCATCACCCCTGTTC
ESR1-1-9	TCTCCCTCCAACCTCCTGCTTG	GCCAGAATGAGAGAATCGCTTTC
ESR1-1-10	TCAGCCTGGGCAAGATGC	CCATGCCTGGCTAATTTTTTTG
ESR1-1-11	CAAGACCCCATCTCTACCGAAG	AGGCAATCCTCCCGCCT
ESR1-2-1	TGGAACAAGCTGGGTTTTGC	CCCACCCAAATTAAGTAGTTGCTAA
ESR1-2-2	CCAGCGTGAATGGCTGTCA	CCTGGGCAACAAAGGGAGA
ESR1-2-3	AGTGCAATCTCAGCTCACTACAACC	GCGTGGTAGCACACACCTGTTA
ESR1-2-4	CCTCTCACCTTGACCCAGCAT	CCTGGATGGTGACCAGGTTTC
ESR1-2-5	CACCTTGACCCAGCATTGCT	GCAAGCCTGGATGGTGACC
ESR1-2-6	CGTCTGACAGCACTGGATCCT	AAAAGCGGTCGATAAAGTCAACAT
ESR1-2-7	CCCCAGCTGTCTGATCCTT	GCACAGGACTGGAGATGTTTGG
ESR1-2-8	CTGTCCAAACATCTCCAGTCTCG	GCTACCGAGTGAGACTCTGTGTCA
ESR1-2-9	AGTGGCATGATCTTGGCTCAC	GAGGTGGTGCCTGCCTGTA

(C) Primer sequences for 3C-qPCR

Name	Sequence
ESR1-1-1	CTACGCACAGAGAAGGGCTAGG
ESR1-1-2	AGCACGGCACAGAGAAGGG
ESR1-1-3	CTCCGCACAGAGAAGGGCTA
ESR1-1-4	AGGCACAGAGAAGGGCTAGGA
ESR1-1-5	GTAGGGTAAGGCACAGAGAAGGG
ESR1-1-6	GACGGCACAGAGAAGGGCTA
ESR1-1-7	AGACGGACGGCACAGAGAAG
ESR1-1-8	AGTACGGCACAGAGAAGGGCTA
ESR1-1-9	GGACGCACAGAGAAGGGCTA
ESR1-1-10	TGTCTACCCCAAAGCGGTACAA
ESR1-1-11	CCTTCCCAAGACACACCCTGTA
ESR1-1-12	CGATGAGCTCTCCGCACAGA
ESR1-1-13	TGAAACCCTCCGCACAGAGA
ESR1-1-14	GAACCGTCTCCTCGGGTTTC
ESR1-1-15	CAACGGGTGGCACAGAGAAG
ESR1-1-16	GTGCGGGTCGATTAATAAACAC
ESR1-1-17	GTCGTCGTAAAGGCACAGAGAAG
ESR1-1-18	CGCTAACCGCACAGAGAAGG
ESR1-1-19	TGACCGGCACAGAGAAGGG
ESR1-1-20	AGGCACAGAGAAGGGCTAGGA

(continued)

Name	Sequence
ESR1-1-21	GACGGCACAGAGAAGGGCTA
ESR1-1-22	GAATACAGCGCACAGAGAAGGG
ESR1-1-23	AAGAGGGTGGCACAGAGAAGG
ESR1-1-24	AGCACGGCACAGAGAAGGG
ESR1-1-25	CGGCACAGAGAAGGGCTAGG
ESR1-1-26	CTCCGCACAGAGAAGGGCTAG
ESR1-1-27	TTCCGCACAGAGAAGGGCTA
ESR1-1-28	CCGCACAGAGAAGGGCTAGG
ESR1-1-29	GACGCACAGAGAAGGGCTAGG
ESR1-1-30	CCGGCACAGAGAAGGGCTA
ESR1-1-31	GGAAGGCACAGAGAAGGGCTAG
ESR1-1-32	AAGGTCTCTCTCGCACAGAGA
ESR1-1-33	CTCCGCACAGAGAAGGGCTA
ESR1-1-34	AGGCACAGAGAAGGGCTAGGA
ESR1-1-35	GGAGGAGGCACAGAGAAGGG
ESR1-1-36	CTCCGCACAGAGAAGGGCTA
ESR1-1-37	CTCCGCACAGAGAAGGGCTA
ESR1-1-38	AAGAGGACGGCACAGAGAAGG
ESR1-1-39	GACGGCACAGAGAAGGGCTA
ESR1-1-40	CTCCGCACAGAGAAGGGCTA
ESR1-1-C1	TGCCTGGGTCAATCAAGTCAA
ESR1-1-C2	TGCCTGGGTCAATCAAGTCAAC
ESR1-1-P1	TGCTCTTTTCTTCCCCTCCAGCCC
ESR1-2-1	TGAAGGTAGTTACTCCCAGTGCTGT
ESR1-2-2	AGTCAGGAGTAGCGTGGAGTGG
ESR1-2-3	TGGAAGCCAGTGCTGTCAGA
ESR1-2-4	TTACCCAGTGCTGTCAGACGG
ESR1-2-5	TCCTATCTGCCAGTGCTGTCAG
ESR1-2-6	AGGACCCCAGTGCTGTCAGA
ESR1-2-7	AGGCGGTACCAGTGCTGTCA
ESR1-2-8	TGTCCCTCCAGTGCTGTCAGA
ESR1-2-9	GACGTACCAGTGCTGTCAGACG
ESR1-2-10	TTATGGTCATTCCAAGTCCGGT
ESR1-2-11	GGTGTGAGTACAGGAATGGGAC
ESR1-2-12	AGGACCCCAGTGCTGTCAGA
ESR1-2-13	TGATGTCCGAATTGGAGGACTC
ESR1-2-14	CCTGTACCAGTGCTGTCAGACG
ESR1-2-15	AAGGTCCAGTGCTGTCAGACG
ESR1-2-16	TCTTAGTCACCCAGTGCTGTCAGA
ESR1-2-17	CCATTCTCGCTCGCCGAC
ESR1-2-18	AGGGTCGATGAGTCCTCCGA
ESR1-2-19	GATCCCTACCCAGTGCTGTCAG
ESR1-2-20	ATCCCAGTGCTGTCAGACGG
ESR1-2-C1	TTGAAACCTGGTCACCATCCA
ESR1-2-C2	TTGAAACCTGGTCACCATCCAG
ESR1-2-P1	TGCCTTGGCCATCAGGTTCCCT
GAPDH_F	TAGTAGCCGGGCCCTACTTT
GAPDH_R	TCCTCCTGTTTCATCCAAGC

(D) Primer sequence for bisulfite sequencing.

Name	Forward	Reverse
CpG_#2	TGTTTATTGTTTGTGTTGGG	ACCCATACTTCTCCACCAAC
CpG_#3	TTTTGTTGGGGTTGTAGT	TTAACAACCATCCCTCCCT

(continued)

Name	Forward	Reverse
CpG_#4	TAGAAAGTAAAGGGAAAGGGA	CCTCTCCCAAATTCCACC
CpG_#5	TGAAGGTGAAGTTAYGGTTTTG	CAACCCCAAAAATCAAAC
CpG_#6	GTGTTTTAGTTGAGYGGAGT	ACACCRAAAAAAACTCTTACC
CpG_#7	GATTTGTTTTTTTTYGGGTTG	ATCCCCTATCAACCCCTC
CpG_#8	GTGGTATTTTTATTGTGGGTTG	TCTCCACACCCRAACAC
CpG_#9	AGAGTTTTTAGTTTTGGYGTT	AACCCCAACAACAAACAAAAC
CpG_#10	ATTYGTATTGTTGTTTTGGTTTTG	TAAACAACCRAACTCCCAACCT
CpG_#11	GTTGGAGGTTGGTATYGTGGTT	AAACCCRCAACCTATCTTC
CpG_#12	GATTTGTTTTTAGTTTTTTTTGTGT	AACCCCAAAACAAAAAAC
CpG_#13	GAGGGTTTGGGGGTTTTTAG	CRCCCCATTCAAAAAC
CpG_#14	GGTGAGTTGYGAGGTTGG	ACCCCTCCCCRAAAAAC
CpG_#15	ATGTATTGTGATTTTGGTAAGTTTTG	CTCTAAACCCRAACTTATTACT
CpG_#16	AAGTAGATTTAGAAGGATTTGGAGTG	ACCCAAAACCCCAAAAATAA
CpG_#17	TATGGTAGYGGGGGGTAG	AACCCAAAAACRAACAAC
CpG_#18	GTAGTAAGTTTTYTTTTYGT	ATTCACCCRTAACTTCTTC
CpG_#19	ATTATTTTTGGGAGATTTGGT	TAAACTCCCAACCTAACTC