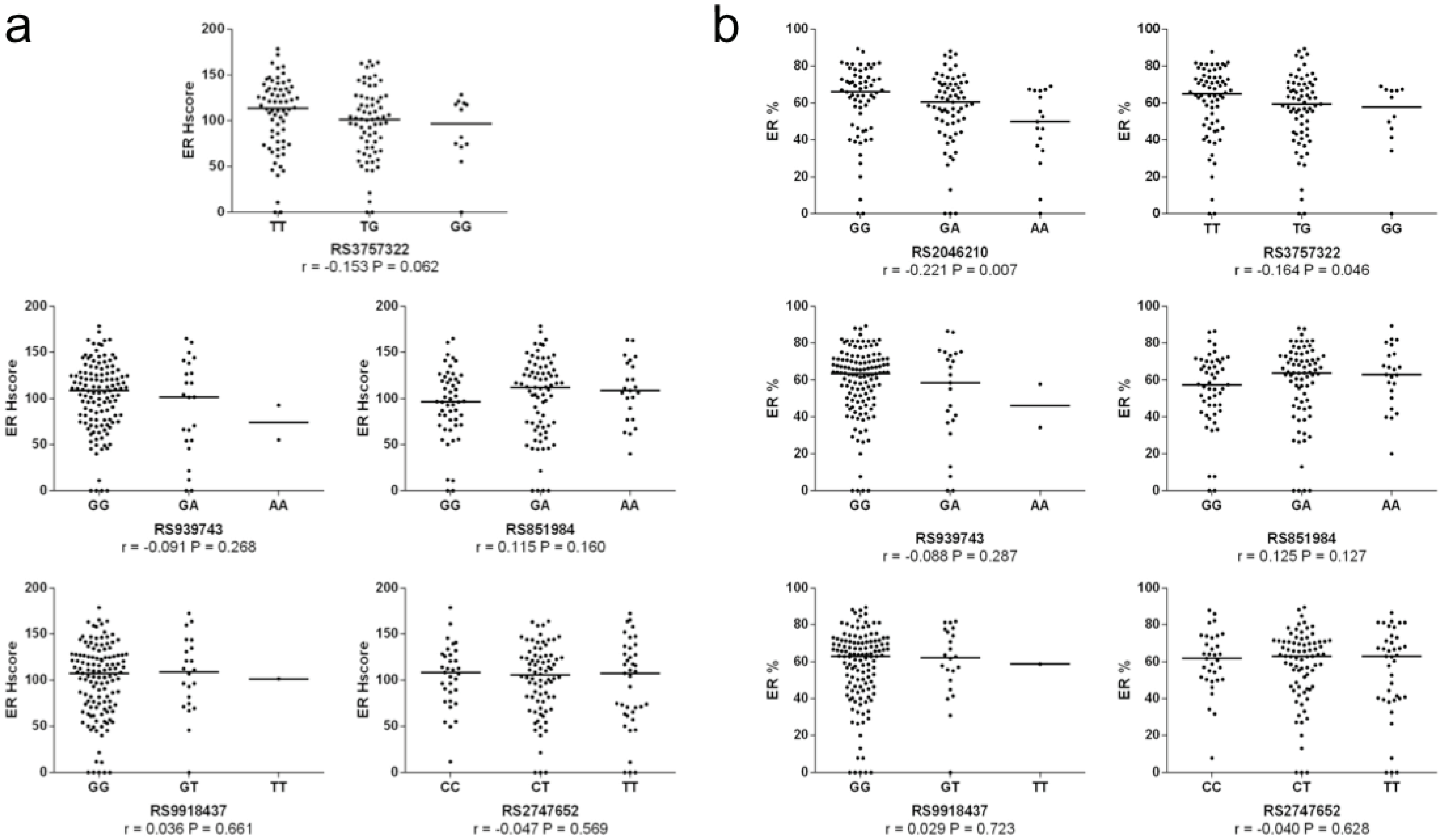
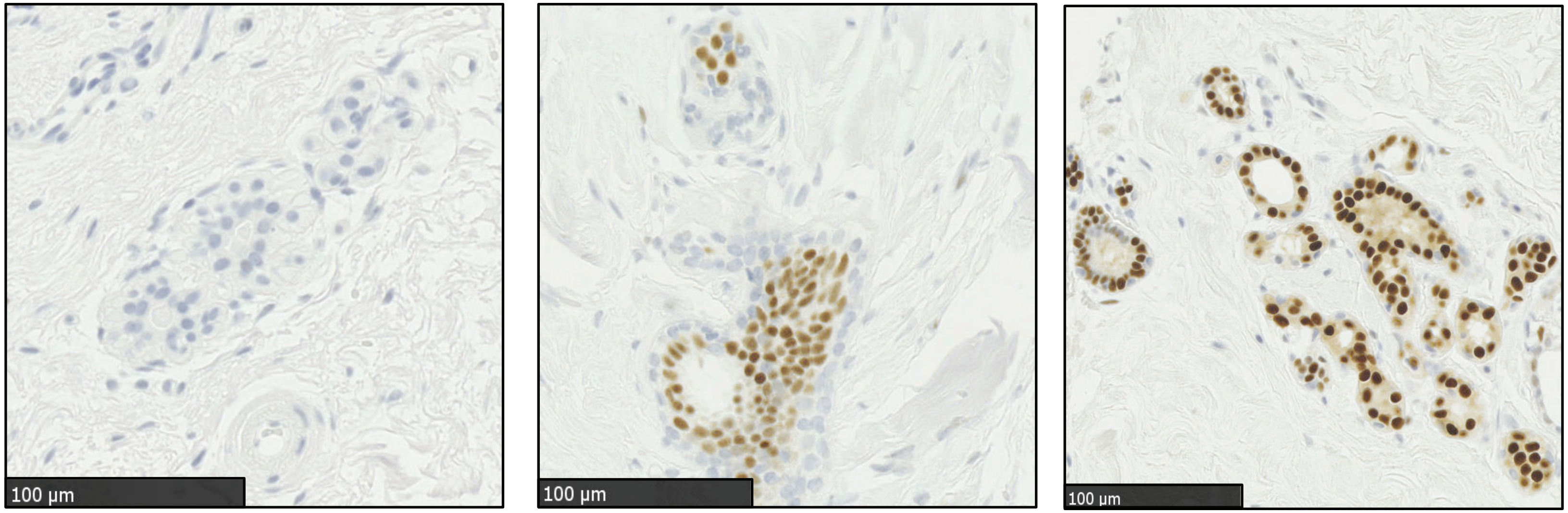


Supplementary Figure 1. Spearman correlations of the signal-representative SNP genotypes (signal 1:rs2046210 and rs3757322; signal 2:rs9397437; signal 3:rs851984; signal 4:rs9918437; signal 5:rs2747652) with estrogen receptor (ER) immunohistochemistry levels measured as ER Hscore **(a)** and ER percentage **(b).**

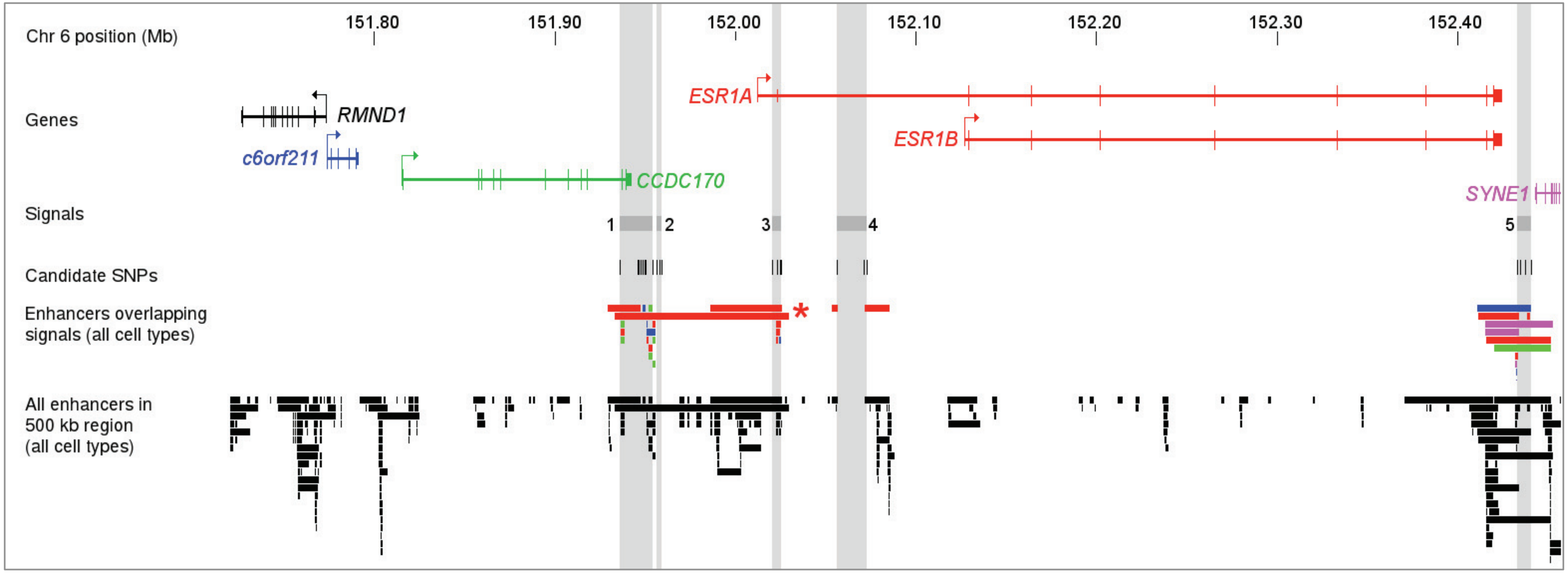


none

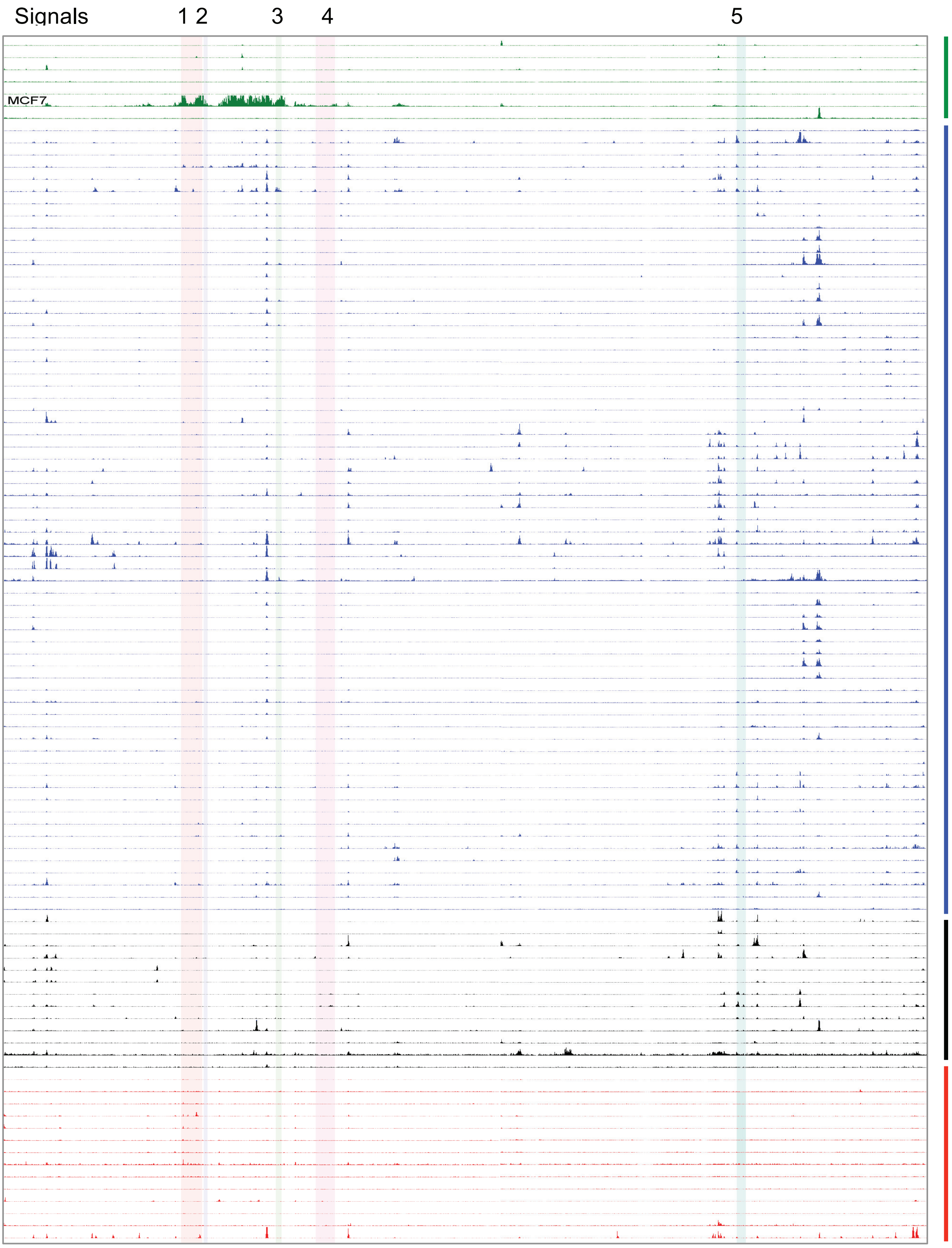
weak

strong

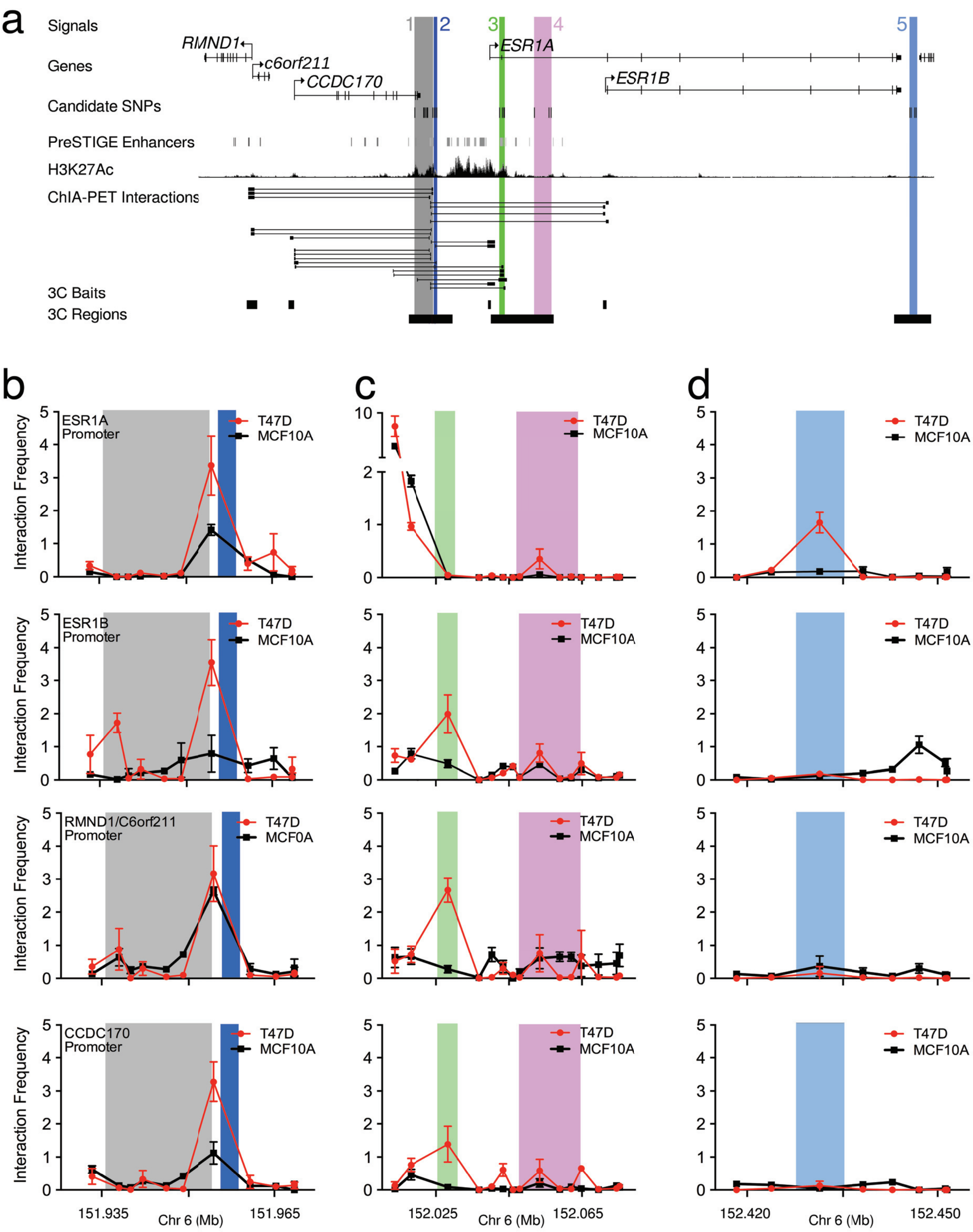
Supplementary Figure 2. Representative ER immunohistochemical stains. The H-scores for each image are: none=127 (ER$^-$), weak=117 (ER$^+$) and strong=66.2 (ER$^+$).



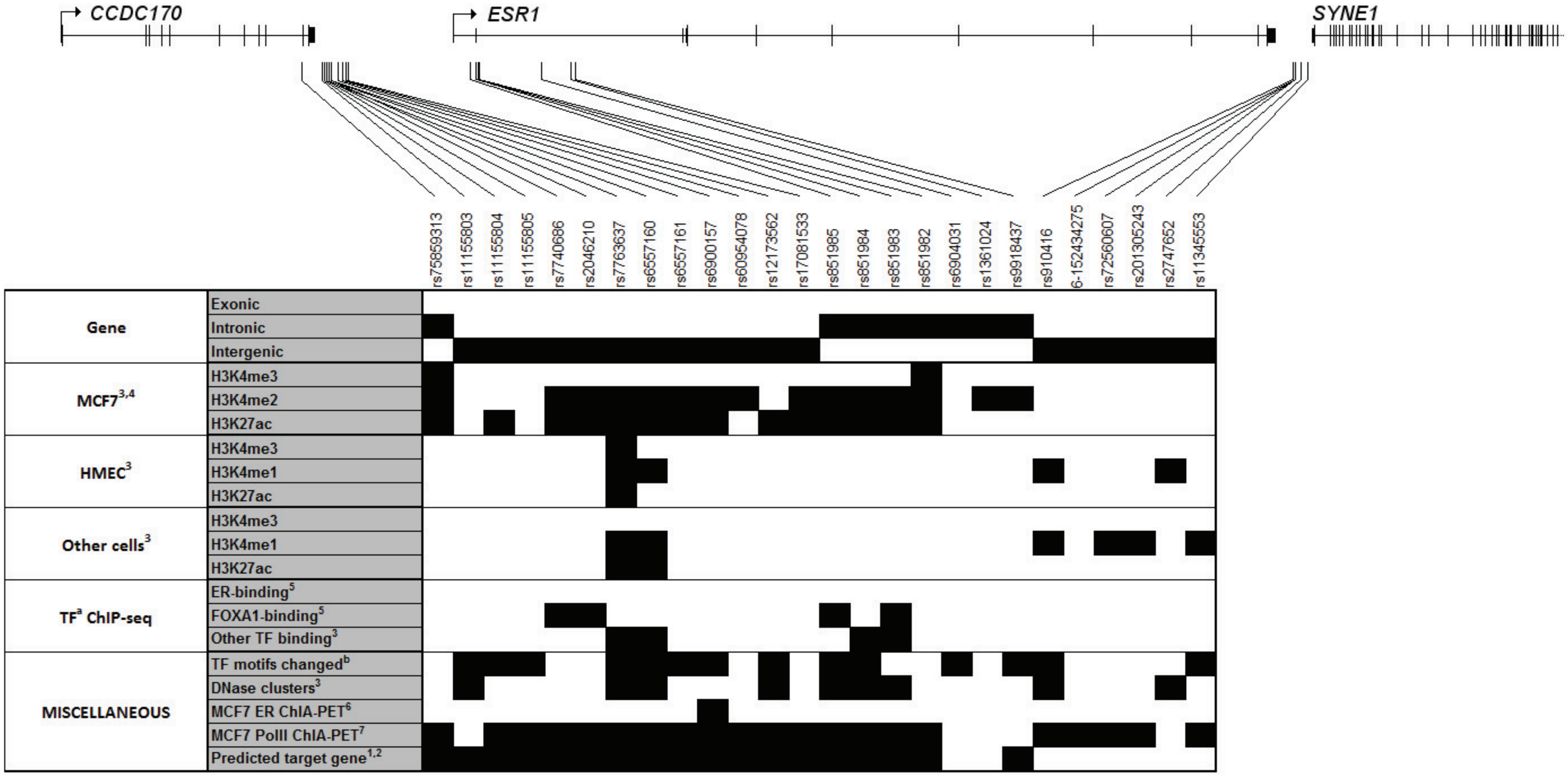
Supplementary Figure 3. Landscape of predicted enhancers at 6q25.1. Signals 1-5 are shown as numbered grey vertical stripes with candidate causal variants represented by black ticks. *RMND1*, *C6orf211*, *CCDC170, ESR1* and *SYNE1* gene structures are depicted with exons (vertical boxes) joined by introns (lines). *ESR1* has two proximal promoters (transcripts *ESR1A* and *ESR1B*). The subset of enhancers, including the super enhancer (red asterisk), predicted in Corradin *et al*[1] and Hnisz *et al*[2], which overlap candidate functional variants are shown as colored bars, where the color matches its predicted gene target. The location of all predicted enhancers from all cell types are depicted in the bottom panel as black bars.



Supplementary Figure 4. Alignment of H3K27ac histone modifications from >100 cell lines and tissues. ChIP-seq data for H3K27ac were visualized using the Washington University EpiGenome Browser. Tracks are colored by tissue type, with cancer cell lines in green, adult tissues in blue, fetal tissue in black, embryonic and pluripotent cells in red. Signals 1-5 are numbered and represented by vertical shaded regions.



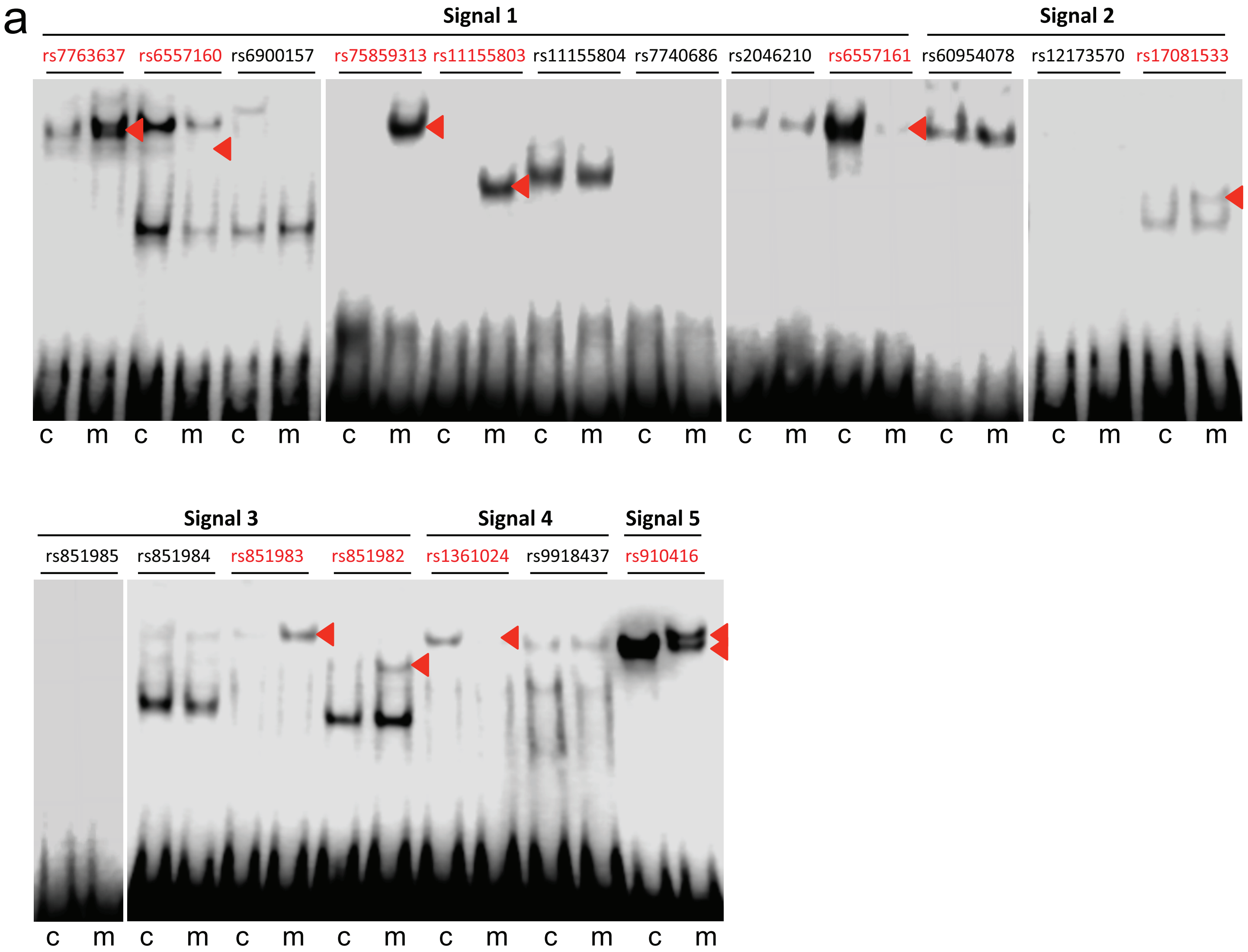
Supplementary Figure 5. Chromatin configuration across the 6q25.1 region. (a) Signals 1-5 are numbered and shown as colored stripes. *RMND1*, *C6orf211*, *CCDC170,* and *ESR1* gene structures are depicted with exons (vertical boxes) joined by introns (lines). Gene-enhancer predictions from PreSTIGE[1], ChIP-seq binding profiles for H3K27ac[2] and ENCODE RNAPII ChiA-PET interactions in MCF7s are shown. 3C anchor points (3C baits) and sequences interrogated (3C regions) are depicted as black boxes and grey shading. 3C interaction profiles in ER$^+$ T47D and ER$^-$ MCF10A breast cell lines for signals 1 and 2 **(b)**, signals 3 and 4 **(c)**, or signal 5 **(d).** 3C libraries were generated with *EcoRI,* with the anchor points set at the *ESR1*, *RMND1/C6orf211 or CCDC170* promoter regions. Graphs represent three biological replicates. Error bars represent SD.

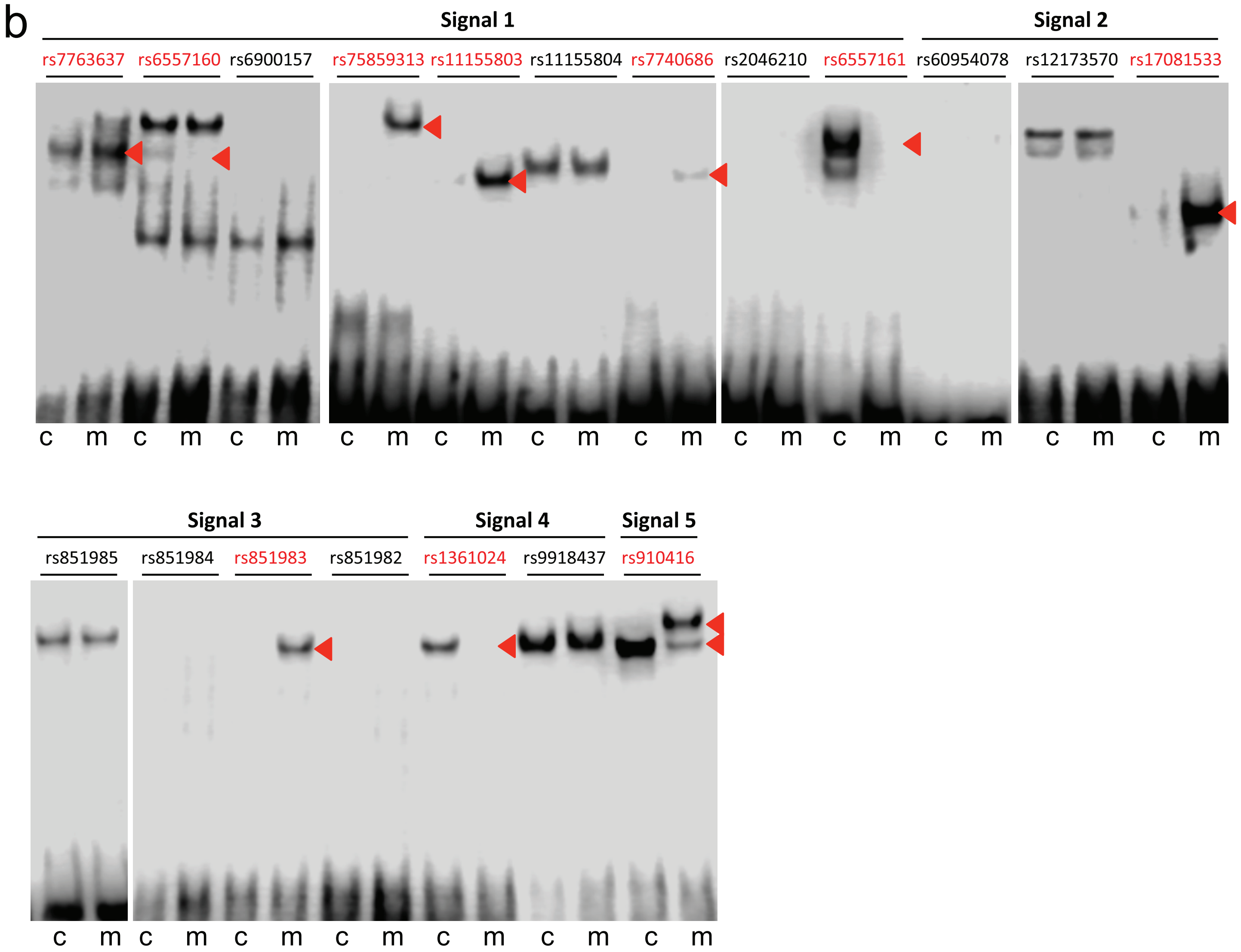


		rs75859313	rs11155803	rs11155804	rs11155805	rs7740686	rs2046210	rs7763637	rs6557160	rs6557161	rs6900157	rs60954078	rs12173562	rs17081533	rs851985	rs851984	rs851983	rs851982	rs6904031	rs1361024	rs9918437	rs910416	6-152434275	rs72560607	rs201305243	rs2747652	rs11345553
Gene	Exonic																										
	Intronic	■													■	■	■	■	■	■	■						
	Intergenic		■	■	■	■	■	■	■	■	■	■	■	■								■	■	■	■	■	■
MCF7[3,4]	H3K4me3	■																■									
	H3K4me2	■				■	■	■	■	■	■	■		■	■	■	■	■		■	■						
	H3K27ac	■		■		■	■	■	■	■	■		■	■	■	■	■	■									
HMEC[3]	H3K4me3							■																			
	H3K4me1							■	■													■				■	
	H3K27ac							■																			
Other cells[3]	H3K4me3																										
	H3K4me1							■	■													■		■	■		■
	H3K27ac							■	■																		
TF[a] ChIP-seq	ER-binding[5]																										
	FOXA1-binding[5]					■	■								■		■										
	Other TF binding[3]							■	■							■	■										
MISCELLANEOUS	TF motifs changed[b]		■	■	■			■	■	■	■		■		■	■			■		■	■					■
	DNase clusters[3]		■					■	■				■		■	■	■					■				■	
	MCF7 ER ChIA-PET[6]										■																
	MCF7 PolII ChIA-PET[7]	■		■	■	■	■	■	■	■	■	■	■	■	■	■	■	■				■	■	■	■		■
	Predicted target gene[1,2]	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■			■						

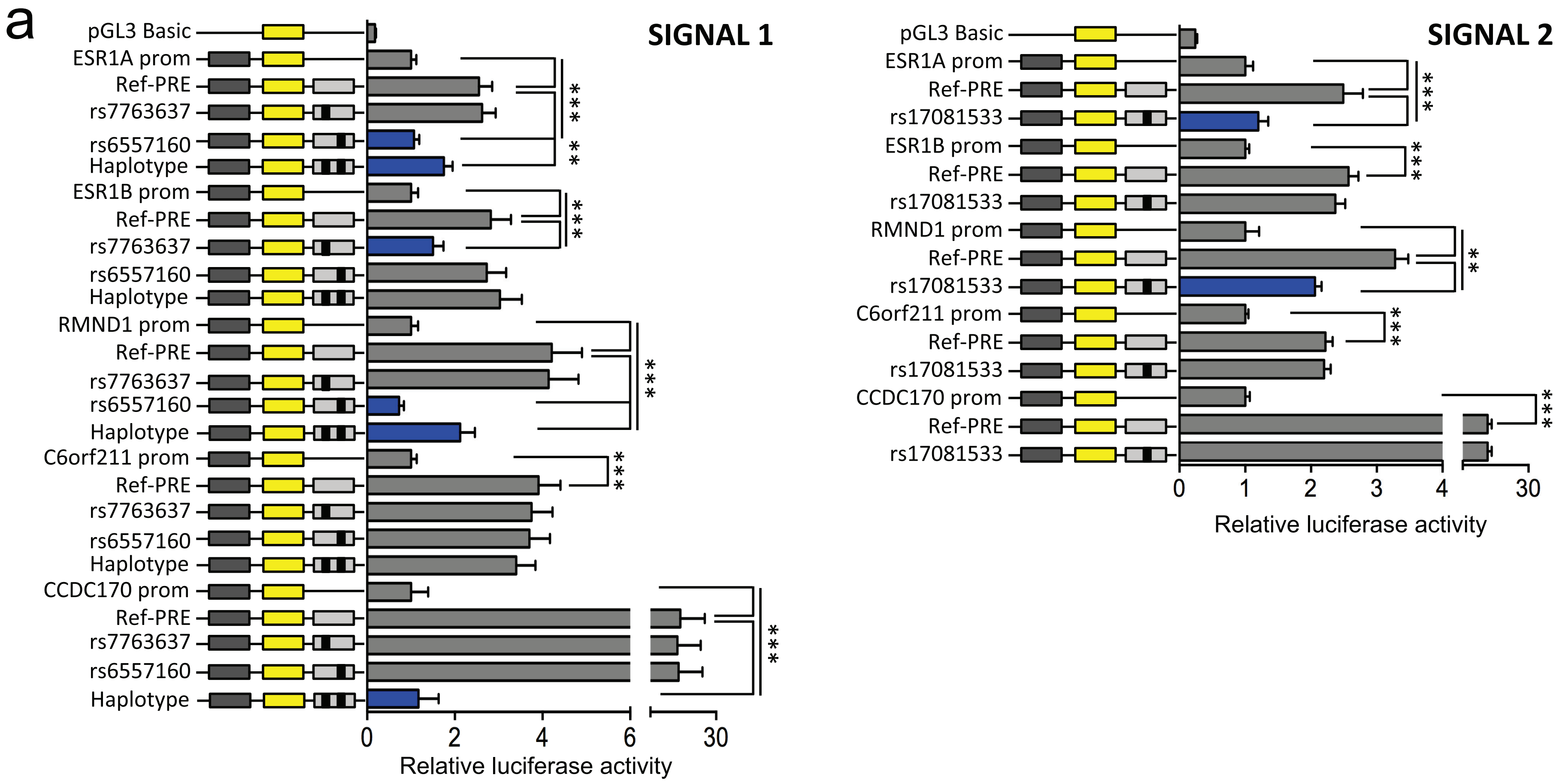
[a] TF=transcription factor; [b] TF binding site prediction using Haploreg[3]

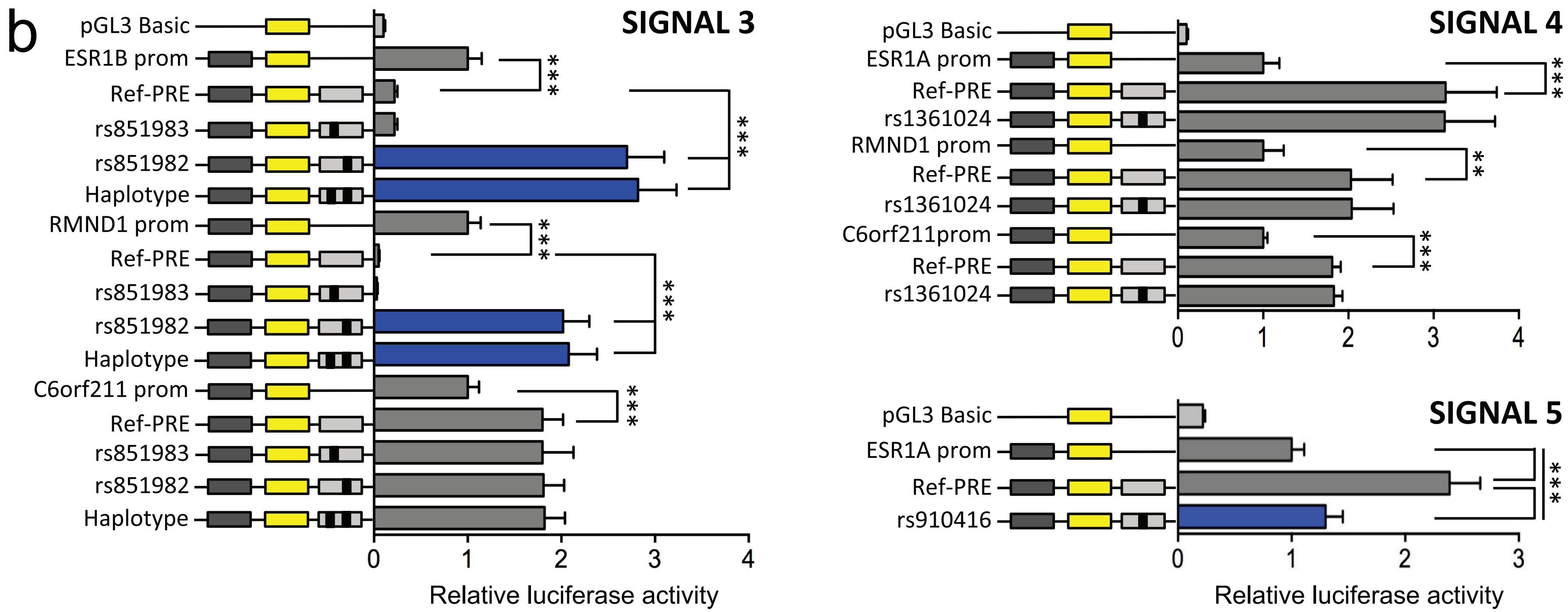
Supplementary Figure 6. Annotation of epigenetic marks (black boxes) coinciding with candidate causal variants across 6q25.


a
Signal 1
Signal 2
rs7763637
rs6557160
rs6900157
rs75859313
rs11155803
rs11155804
rs7740686
rs2046210
rs6557161
rs60954078
rs12173570
rs17081533
c m c m c m c m c m c m c m c m c m c m c m c m
Signal 3
Signal 4
Signal 5
rs851985
rs851984
rs851983
rs851982
rs1361024
rs9918437
rs910416
c m c m c m c m c m c m c m

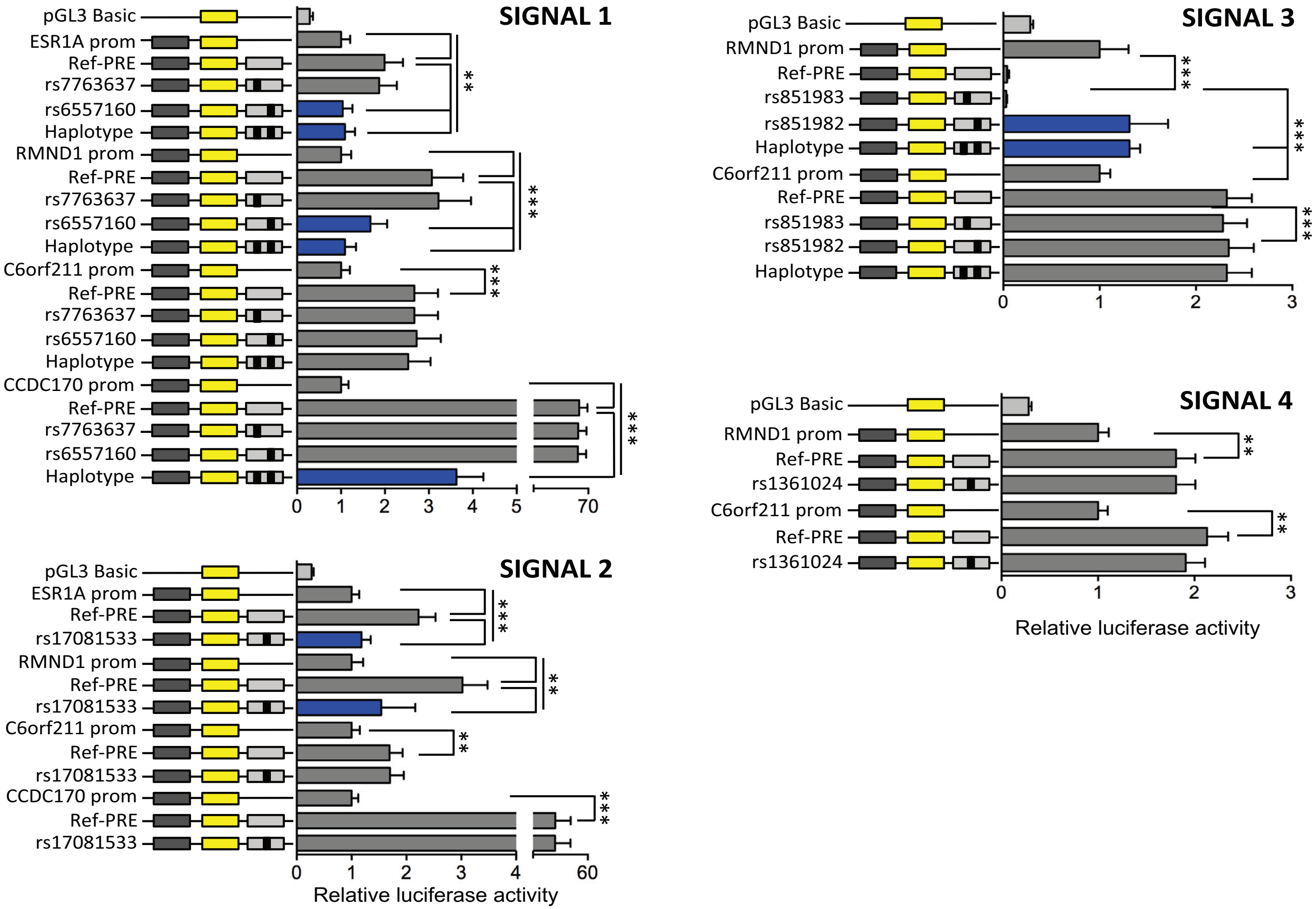


Supplementary Figure 7. EMSAs for 19/26 candidate SNPs to detect allele-specific binding of nuclear proteins. Oligonucleotides were incubated with ER^+ MCF7 **(a)** or ER^- Bre80 **(b)** nuclear extracts. Red arrowheads show bands of different mobility detected between the common (c) and minor (m) alleles.

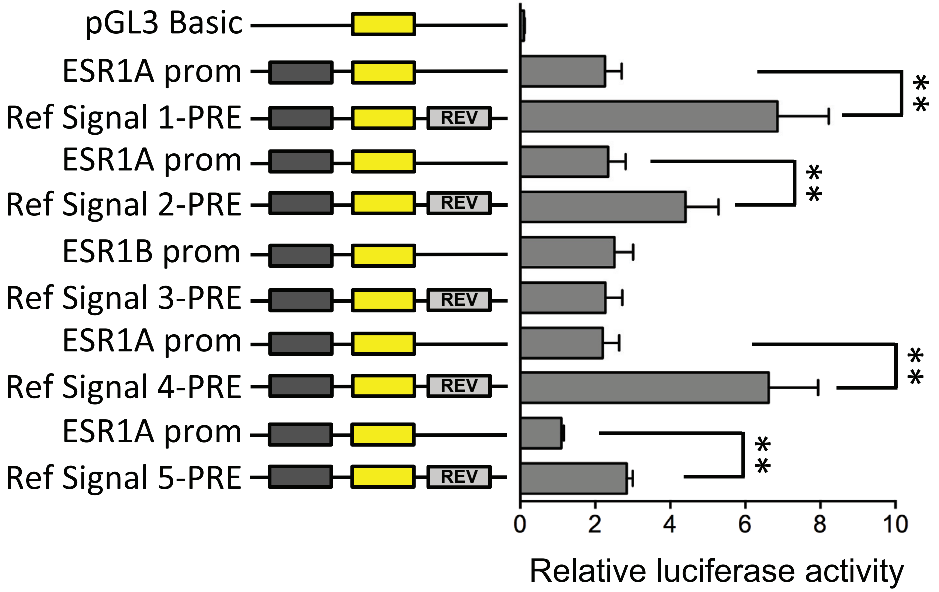

a
SIGNAL 1
pGL3 Basic
ESR1A prom
Ref-PRE
rs7763637
rs6557160
Haplotype
ESR1B prom
Ref-PRE
rs7763637
rs6557160
Haplotype
RMND1 prom
Ref-PRE
rs7763637
rs6557160
Haplotype
C6orf211 prom
Ref-PRE
rs7763637
rs6557160
Haplotype
CCDC170 prom
Ref-PRE
rs7763637
rs6557160
Haplotype
***
**
***
***
***
***
0
2
4
6
30
Relative luciferase activity
SIGNAL 2
pGL3 Basic
ESR1A prom
Ref-PRE
rs17081533
ESR1B prom
Ref-PRE
rs17081533
RMND1 prom
Ref-PRE
rs17081533
C6orf211 prom
Ref-PRE
rs17081533
CCDC170 prom
Ref-PRE
rs17081533
***
***
**
***
***
0
1
2
3
4
30
Relative luciferase activity



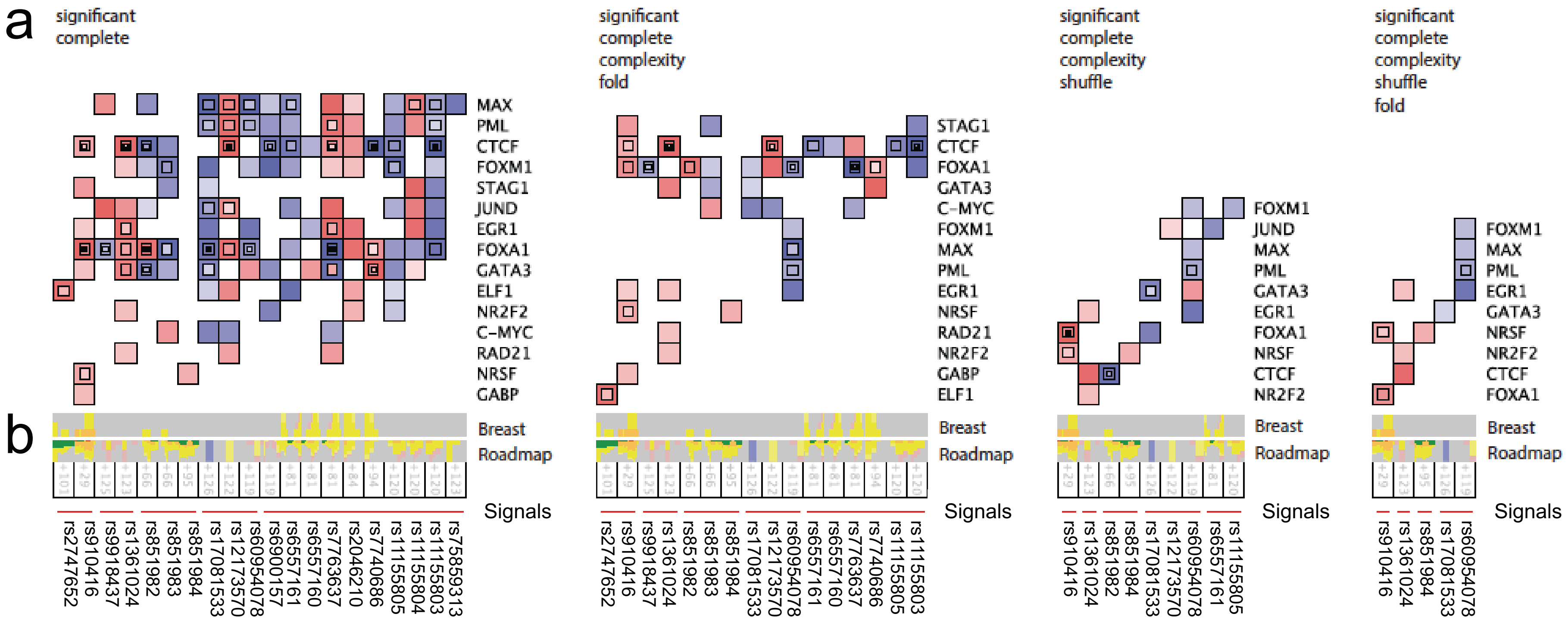
Supplementary Figure 8. Luciferase reporter assays following transfection of ER$^+$ BT474 breast cancer cells. Putative regulatory elements (PREs) located within signals 1-2 **(a)** and signals 3-5 **(b)** containing the major SNP alleles were cloned downstream of target gene promoter-driven luciferase constructs (prom) for the creation of reference (Ref-PRE) constructs. Minor SNP alleles were engineered into the constructs and are designated by the rs ID of the corresponding SNP. Haplotype denotes a construct that contains the minor alleles of both candidate SNPs within either signals 1 or 3. Error bars denote 95% confidence intervals from three independent experiments performed in duplicate. P-values were determined by 2-way ANOVA followed by Dunnett's multiple comparisons test (**P<0.01, ***P<0.001).



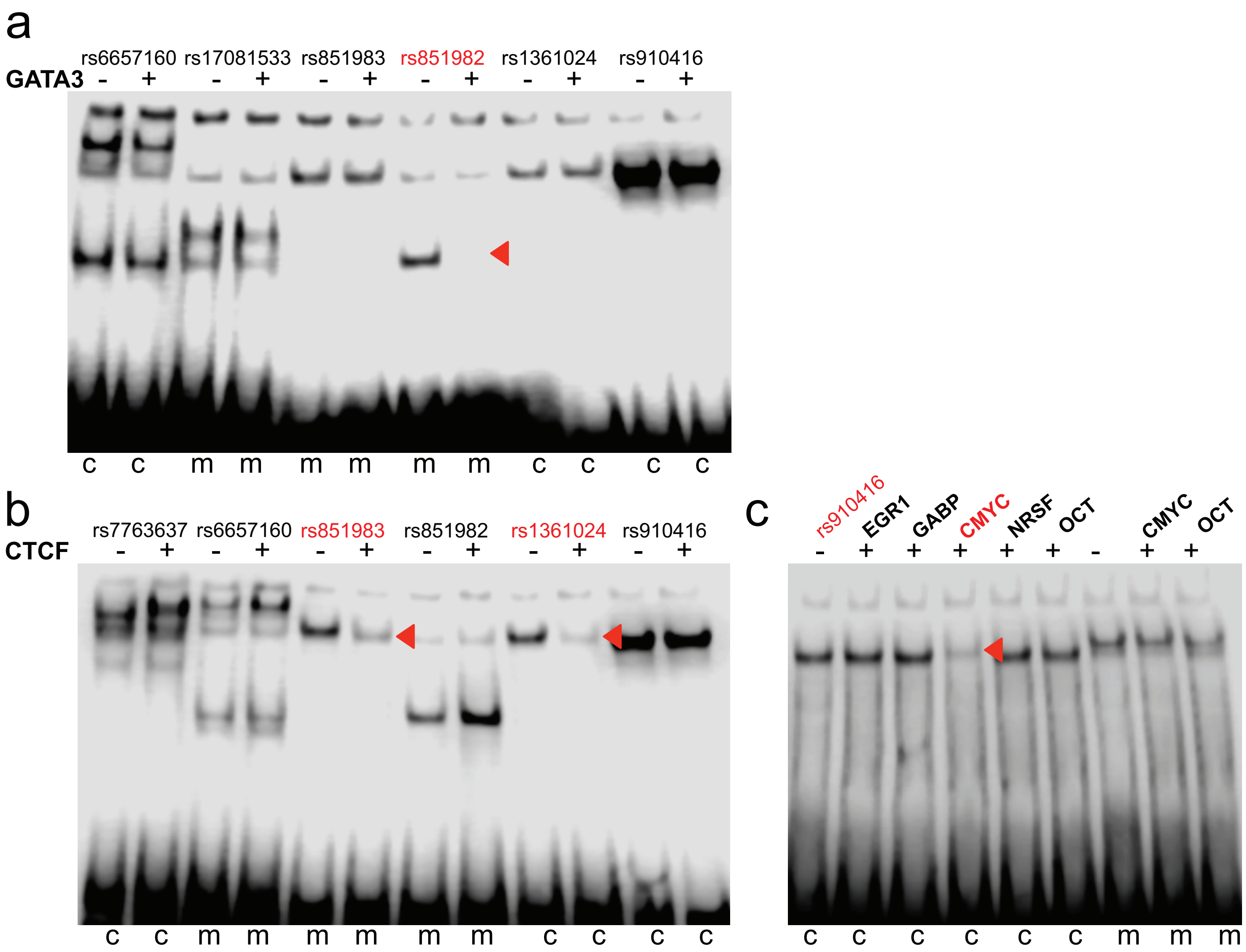
Supplementary Figure 9. Luciferase reporter assays following transfection of ER$^-$ Bre-80 breast cells. Putative regulatory elements (PREs) located within signals 1-4 containing the major SNP alleles were cloned downstream of target gene promoter-driven luciferase constructs (prom) for the creation of reference (Ref-PRE) constructs. Minor SNP alleles were engineered into the constructs and are designated by the rs ID of the corresponding SNP. Haplotype denotes a construct that contains the minor alleles of both candidate SNPs within either signals 1 or 3. Error bars denote 95% confidence intervals from three independent experiments performed in duplicate. P-values were determined by 2-way ANOVA followed by Dunnett's multiple comparisons test (**P<0.01, ***P<0.001).



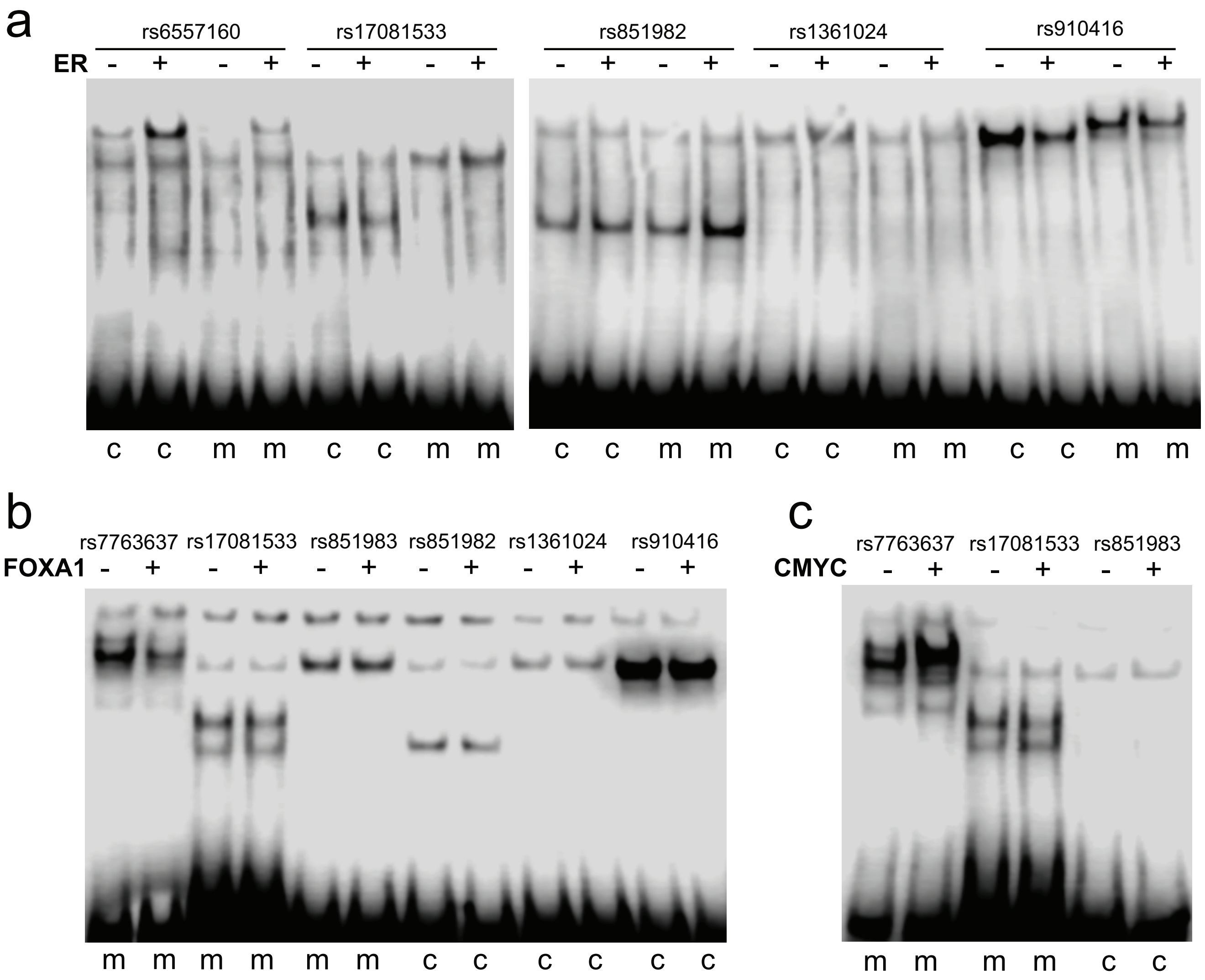
Supplementary Figure 10. Luciferase reporter assays following transfection of ER$^+$ MCF7 breast cancer cells. Putative regulatory elements (PRE) located within signals 1-5 containing the major SNP alleles were cloned in the reverse direction (REV) downstream of *ESR1* promoter-driven luciferase constructs (prom). Error bars denote 95% confidence intervals from three independent experiments performed in duplicate. P-values were determined by 2-way ANOVA followed by Dunnett's multiple comparisons test (**P<0.01).



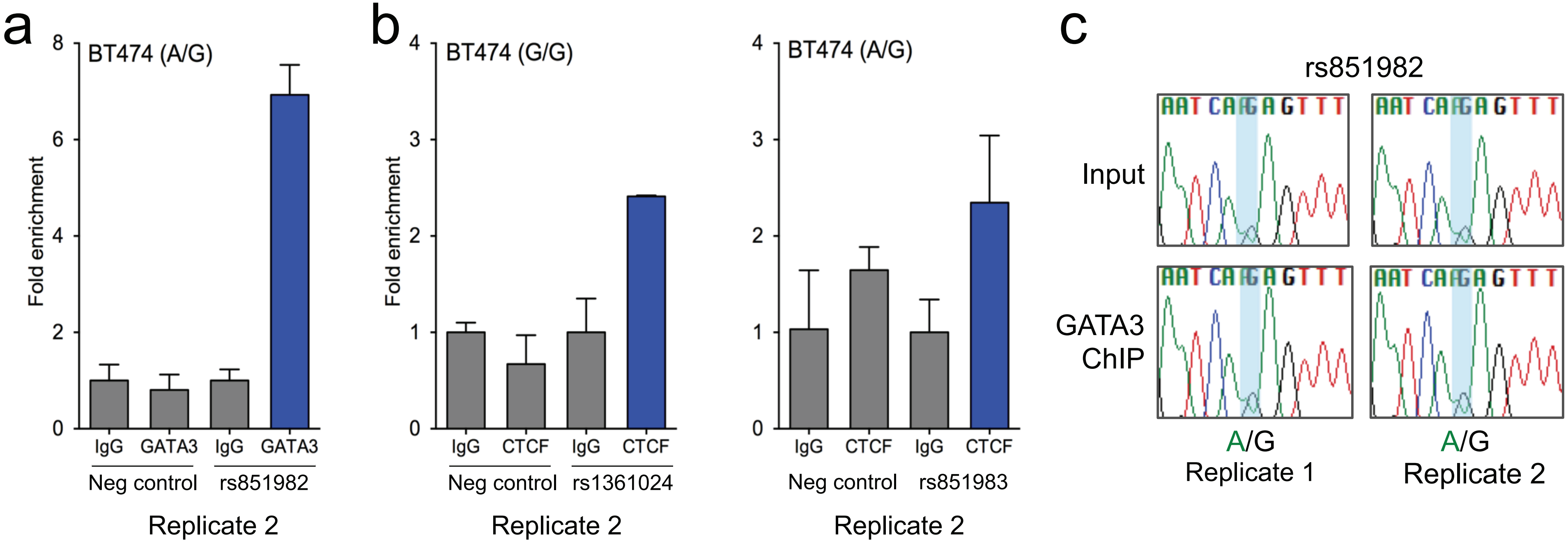
Supplementary Figure 11. IGR^4 plots for all 26 candidate causal variants. (a) Affinity modulation for candidate causal SNPs in each signal for a set of breast related transcription factors shown as a heatmap with nested cells. The color in each cell depicts the -log10 of the p-value for that SNP and factor. Blue indicates that the alternate allele has a higher affinity than the reference allele; red indicates the opposite. Multiple replicates for each factor are displayed as nested cells. The colors along the contours of the superimposed squares also represent the -log10 p-values for significant results across replicates. Replicates are sorted so the most significant p-value is on the outside. Each panel, from left to right, shows results for a more stringent set of filters on the results (See Methods). **(b)** Stacked histograms at the base of each column depict the chromatin diversity for the local context around each SNP. Chromatin states were obtained from the NIH Roadmap Epigenomics Project in breast tissues (HMEC, vHMEC, vHMMC) and across all 127 profiled epigenomes. In all cases, chromatin states were taken from the 15-state ChromHMM models and colors were chosen based on the standard color assignments from the Roadmap Consortium. Centered within the annotation for each SNP is the chromatin state directly under it; on either side of this center annotation lie bar charts of the values 1000bp in each direction. In order to increase the visibility of subtle regional state changes, at each coordinate the number of cells with quiescent (unmarked) chromatin states was tallied, and the minimum value across the window was subtracted from the bar charts and presented as a separate number below.



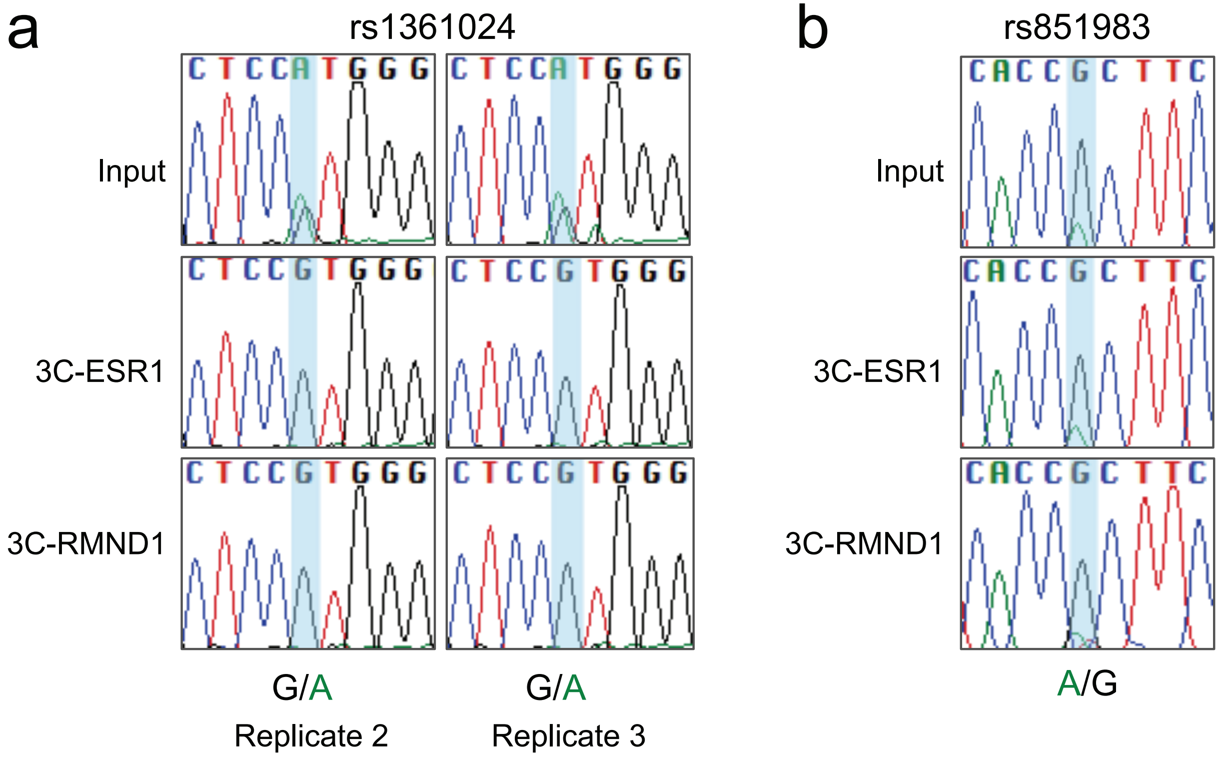
Supplementary Figure 12. EMSAs for prioritized candidate causal SNPs to identify candidate nuclear proteins. Competitor oligonucleotides for predicted transcription factors (100-fold molar excess) were incubated with ER$^+$ MCF7 nuclear extracts. Red arrowheads indicate bands that were competed for complex formation on either the common (c) or minor (m) alleles of prioritized SNPs.



Supplementary Figure 13. EMSAs for prioritized candidate causal SNPs to identify candidate nuclear proteins. Competitor oligonucleotides for additional predicted transcription factors (100-fold molar excess) were incubated with ER^+ MCF7 nuclear extracts.



Supplementary Figure 14. GATA3 and CTCF binding *in vivo*. Replicate ChIP-qPCR results against GATA3 **(a)** or CTCF **(b)** in ER$^+$ BT474 breast cancer cells. Error bars denote SD (N=2). A region within the second intron of *ESR1* served as a negative (Neg) control. **(c)** Sanger sequencing of the PCR fragment generated using primers flanking SNP rs851982 following GATA3 ChIP-qPCR. Primers are listed in **Supplementary Table 18**.



Supplementary Figure 15. Allele-specific chromatin looping between signal 4-PRE and *ESR1 and RMND1* promoters. (a) 3C followed by sequencing for the signal 4-PRE containing rs1361024 in ER$^+$ heterozygous MCF7 breast cancer cells shows allele-specific chromatin looping. Two of three independent 3C libraries are shown which were generated with *Bgl*II. **(b)** 3C followed by sequencing for the signal 3-PRE containing rs851983 in ER$^+$ heterozygous BT474 breast cancer cells. One representative 3C library is shown which was generated with *Hin*dIII.

Supplementary Table 1. SNPs associated with overall breast cancer risk in Europeans ($P<10^{-4}$).

SNP[1]	Position GRch37	Alleles	MAF	P value	OR (95%CIs)	beta_risk	se_risk	chi2_ risk	OR	LCI	UCI
6-151575957	151575957	CG	0.58	6.36E-04	1.03(1.01,1.05)	0.0339582	0.00994195	11.6676	1.03	1.01	1.05
6-151596083	151596083	GA	0.49	6.00E-04	0.97(0.95,0.99)	-0.033338	0.00971624	11.7746	0.97	0.95	0.99
6-151596175	151596175	AG	0.49	5.86E-04	0.97(0.95,0.99)	-0.0334252	0.00972313	11.8195	0.97	0.95	0.99
6-151596207	151596207	CT	0.49	6.93E-04	0.97(0.95,0.99)	-0.033018	0.0097337	11.5082	0.97	0.95	0.99
6-151605697	151605697	AG	0.45	5.69E-04	0.97(0.95,0.99)	-0.0338684	0.00982918	11.8743	0.97	0.95	0.99
6-151615204	151615204	CG	0.32	5.03E-04	0.96(0.94,0.98)	-0.0365906	0.0105172	12.1047	0.96	0.94	0.98
6-151816054	151816054	AC	0.02	1.63E-05	1.18(1.09,1.27)	0.163876	0.0380821	18.5846	1.18	1.09	1.27
6-151844694	151844694	AG	0.05	5.40E-04	1.08(1.03,1.13)	0.07821	0.0226191	11.9715	1.08	1.03	1.13
6-151846139	151846139	TC	0.05	2.59E-04	1.09(1.04,1.15)	0.0901844	0.0247039	13.3479	1.09	1.04	1.15
6-151860109	151860109	GA	0.03	7.34E-04	0.91(0.86,0.96)	-0.0950438	0.0281525	11.4023	0.91	0.86	0.96
6-151861507	151861507	AG	0.05	2.93E-04	1.11(1.05,1.18)	0.104793	0.0289619	13.113	1.11	1.05	1.18
rs7769700	151862142	TC	0.11	8.85E-04	1.05(1.02,1.09)	0.0519743	0.0156371	11.0548	1.05	1.02	1.09
6-151864968	151864968	CT	0.11	7.80E-04	1.05(1.02,1.09)	0.0531276	0.0158176	11.2892	1.05	1.02	1.09
6-151864991	151864991	TC	0.11	7.79E-04	1.05(1.02,1.09)	0.0531295	0.0158173	11.2903	1.05	1.02	1.09
6-151874544	151874544	GA	0.11	9.64E-04	1.05(1.02,1.09)	0.0515576	0.0156251	10.895	1.05	1.02	1.09
rs6915088	151896379	TG	0.11	6.44E-04	1.05(1.02,1.09)	0.0531283	0.0155749	11.644	1.05	1.02	1.09
rs9479077	151900070	TC	0.11	6.62E-04	1.05(1.02,1.09)	0.0530541	0.0155872	11.5931	1.05	1.02	1.09
6-151900232	151900232	CT	0.11	8.97E-04	1.05(1.02,1.09)	0.0522633	0.0157425	11.0291	1.05	1.02	1.09
rs6913493	151900811	TC	0.11	7.23E-04	1.05(1.02,1.09)	0.052671	0.0155857	11.4284	1.05	1.02	1.09
6-151912653	151912653	AG	0.13	3.41E-04	1.06(1.03,1.10)	0.0610726	0.0170558	12.8313	1.06	1.03	1.10
rs3757318	151914113	AG	0.07	7.55E-16	1.16(1.12,1.20)	0.148885	0.0185056	64.9852	1.16	1.12	1.20
rs9383930	151914421	GA	0.28	2.25E-05	1.05(1.02,1.07)	0.0458646	0.0108237	17.9638	1.05	1.02	1.07
rs58893329	151916064	AG	0.08	1.12E-17	1.17(1.13,1.21)	0.156954	0.0183744	73.2806	1.17	1.13	1.21
rs34430497	151917660	AG	0.06	2.38E-09	1.13(1.09,1.18)	0.123529	0.0207235	35.6319	1.13	1.09	1.18
6-151918021	151918021	GA	0.26	6.27E-06	1.05(1.03,1.07)	0.0497389	0.0110143	20.4033	1.05	1.03	1.07
rs12662670	151918856	GT	0.08	4.36E-18	1.17(1.13,1.21)	0.156694	0.0181142	75.1534	1.17	1.13	1.21
rs9397065	151919377	GA	0.26	1.42E-05	1.05(1.03,1.07)	0.0478064	0.0110153	18.8449	1.05	1.03	1.07
rs9383585	151919571	CG	0.14	7.18E-08	1.08(1.05,1.11)	0.0745709	0.0138528	29.0142	1.08	1.05	1.11
rs9383586	151919572	CG	0.14	7.45E-08	1.08(1.05,1.11)	0.0744848	0.0138536	28.944	1.08	1.05	1.11
rs9383931	151919706	CG	0.14	1.05E-07	1.08(1.05,1.11)	0.0740406	0.01393	28.2869	1.08	1.05	1.11
rs9383932	151919720	GA	0.14	7.85E-08	1.08(1.05,1.11)	0.0743507	0.0138532	28.8416	1.08	1.05	1.11
rs9397066	151919936	AG	0.26	1.03E-05	1.05(1.03,1.07)	0.0485313	0.0110032	19.4636	1.05	1.03	1.07
rs1158790	151920741	CA	0.26	9.70E-06	1.05(1.03,1.07)	0.0486576	0.011002	19.5694	1.05	1.03	1.07
rs1340874	151920772	AC	0.20	2.21E-09	1.08(1.05,1.10)	0.0725874	0.0121415	35.7804	1.08	1.05	1.10
rs9397067	151920851	AC	0.20	2.61E-09	1.07(1.05,1.10)	0.0722241	0.0121365	35.4515	1.07	1.05	1.10

rs9383587	151920913	AG	0.20	2.42E-09	1.08(1.05,1.10)	0.0724049	0.0121416	35.6	1.08	1.05	1.10
rs9383588	151920915	AG	0.20	2.35E-09	1.08(1.05,1.10)	0.0724676	0.0121421	35.6584	1.08	1.05	1.10
rs9383933	151920956	AG	0.20	2.34E-09	1.08(1.05,1.10)	0.0724776	0.0121421	35.6684	1.08	1.05	1.10
rs9478226	151921139	TG	0.20	2.76E-09	1.07(1.05,1.10)	0.0721683	0.0121451	35.3469	1.07	1.05	1.10
rs9383934	151921337	TA	0.20	2.49E-09	1.08(1.05,1.10)	0.0723569	0.0121424	35.548	1.08	1.05	1.10
rs9371543	151921471	AG	0.20	1.72E-09	1.08(1.05,1.10)	0.073539	0.0122178	36.2682	1.08	1.05	1.10
rs7349925	151922064	AG	0.58	7.96E-04	0.97(0.95,0.99)	-0.0329356	0.00981956	11.2516	0.97	0.95	0.99
6-151922622	151922622	TC	0.08	2.38E-17	1.17(1.13,1.21)	0.156471	0.0185058	71.8021	1.17	1.13	1.21
6-151923870	151923870	AC	0.58	7.24E-04	0.97(0.95,0.99)	-0.0332168	0.00982771	11.4256	0.97	0.95	0.99
6-151924379	151924379	GA	0.58	7.02E-04	0.97(0.95,0.99)	-0.0333172	0.00983286	11.4828	0.97	0.95	0.99
rs1110776	151924607	AT	0.08	1.02E-17	1.17(1.13,1.21)	0.154947	0.0181151	73.4731	1.17	1.13	1.21
6-151925377	151925377	TC	0.64	9.66E-06	0.96(0.94,0.98)	-0.0448144	0.0101303	19.5769	0.96	0.94	0.98
rs79416523	151925719	GT	0.08	1.45E-17	1.17(1.13,1.21)	0.156017	0.0183269	72.7817	1.17	1.13	1.21
rs17081488	151925783	AG	0.08	8.41E-18	1.17(1.13,1.21)	0.155412	0.0181226	73.8538	1.17	1.13	1.21
6-151925887	151925887	GC	0.58	9.76E-04	0.97(0.95,0.99)	-0.0325118	0.00986105	10.8719	0.97	0.95	0.99
6-151926133	151926133	CT	0.58	6.34E-04	0.97(0.95,0.99)	-0.0335996	0.0098344	11.6746	0.97	0.95	0.99
rs4324787	151926707	GT	0.64	1.20E-05	0.96(0.94,0.98)	-0.0443613	0.0101371	19.1574	0.96	0.94	0.98
6-151928164	151928164	CT	0.58	5.69E-04	0.97(0.95,0.99)	-0.0338709	0.00983006	11.8744	0.97	0.95	0.99
6-151928342	151928342	TC	0.58	6.64E-04	0.97(0.95,0.99)	-0.0334953	0.00984072	11.5873	0.97	0.95	0.99
rs77334499	151929669	AG	0.08	1.71E-17	1.17(1.13,1.21)	0.155576	0.0183158	72.4567	1.17	1.13	1.21
6-151929925	151929925	CG	0.08	1.08E-17	1.17(1.13,1.21)	0.156113	0.0182648	73.3686	1.17	1.13	1.21
rs12663827	151930249	AG	0.08	8.70E-18	1.17(1.13,1.21)	0.155363	0.0181252	73.7874	1.17	1.13	1.21
rs75988489	151932577	AG	0.05	9.44E-07	1.12(1.07,1.18)	0.116612	0.0238129	24.0399	1.12	1.07	1.18
rs1023940	151932778	GA	0.50	1.14E-07	1.05(1.03,1.07)	0.0514185	0.0096967	28.1275	1.05	1.03	1.07
rs1038304	151933175	GA	0.50	2.43E-07	1.05(1.03,1.07)	0.0500384	0.00969288	26.6585	1.05	1.03	1.07
6-151933895	151933895	AG	0.13	7.63E-05	0.94(0.90,0.97)	-0.0668491	0.0169	15.6473	0.94	0.90	0.97
6-151934085	151934085	T/TCTTTGTTTG	0.49	2.54E-08	1.06(1.04,1.08)	0.0547125	0.00982341	31.0314	1.06	1.04	1.08
rs75859313	151935539	CG	0.35	2.42E-14	1.08(1.06,1.10)	0.0786531	0.010319	58.1553	1.08	1.06	1.10
rs6929137	151936677	AG	0.32	2.59E-16	1.09(1.07,1.11)	0.0859428	0.0104986	67.0929	1.09	1.07	1.11
6-151938465	151938465	AG	0.24	9.68E-04	1.04(1.02,1.06)	0.0373323	0.0113163	10.8873	1.04	1.02	1.06
rs3734804	151939181	AG	0.51	1.75E-08	1.06(1.04,1.08)	0.054644	0.00969932	31.7507	1.06	1.04	1.08
rs3734805	151939350	CA	0.08	3.65E-19	1.17(1.13,1.22)	0.16077	0.0180099	80.0504	1.17	1.13	1.22
rs6932260	151939560	CT	0.51	1.57E-08	1.06(1.04,1.08)	0.0548032	0.00969468	31.9667	1.06	1.04	1.08
rs6932603	151939770	CT	0.51	1.68E-08	1.06(1.04,1.08)	0.0547144	0.00969891	31.8354	1.06	1.04	1.08
rs9383935	151939848	TC	0.08	1.79E-19	1.18(1.14,1.22)	0.162277	0.0180218	81.4558	1.18	1.14	1.22
rs6906130	151939873	TC	0.51	1.66E-08	1.06(1.04,1.08)	0.0547328	0.00969871	31.8581	1.06	1.04	1.08
rs11155801	151940073	TC	0.24	7.94E-04	1.04(1.02,1.06)	0.0381826	0.0113836	11.2549	1.04	1.02	1.06
rs9383589	151940260	GA	0.08	2.16E-19	1.18(1.13,1.22)	0.161888	0.018019	81.0902	1.18	1.13	1.22
6-151940847	151940847	TC	0.17	1.14E-05	0.94(0.91,0.96)	-0.0647904	0.0147644	19.2585	0.94	0.91	0.96
rs3734806	151941461	AG	0.33	7.49E-17	1.09(1.07,1.11)	0.0868691	0.0104235	69.5396	1.09	1.07	1.11

rs3757322	151942194	GT	0.33	8.15E-17	1.09(1.07,1.11)	0.0867489	0.0104216	69.3721	1.09	1.07	1.11
6-151943453	151943453	GC	0.51	1.69E-08	1.06(1.04,1.08)	0.0547356	0.00970475	31.8215	1.06	1.04	1.08
rs4591859	151943639	CT	0.51	2.49E-08	1.06(1.04,1.08)	0.0540306	0.00969516	31.0685	1.06	1.04	1.08
rs10872676	151943977	TC	0.51	2.63E-08	1.06(1.04,1.08)	0.0539307	0.00969353	30.9641	1.06	1.04	1.08
rs9383936	151944614	AG	0.08	2.30E-19	1.18(1.13,1.22)	0.161501	0.0179901	80.9593	1.18	1.13	1.22
rs11155802	151945470	TC	0.32	3.59E-17	1.09(1.07,1.12)	0.0886036	0.0105226	70.9918	1.09	1.07	1.12
6-151945666	151945666	TC	0.51	3.11E-08	1.06(1.04,1.08)	0.0537533	0.00971312	30.6367	1.06	1.04	1.08
rs11155803	151945669	CT	0.32	1.48E-16	1.09(1.07,1.11)	0.0862842	0.0104544	68.2016	1.09	1.07	1.11
rs11155804	151946152	AT	0.35	1.82E-14	1.08(1.06,1.10)	0.0785993	0.0102626	58.7164	1.08	1.06	1.10
6-151946173	151946173	G/GAA	0.51	2.01E-08	1.06(1.04,1.08)	0.0547988	0.00976817	31.4824	1.06	1.04	1.08
rs12665607	151946629	AT	0.08	2.02E-19	1.18(1.13,1.22)	0.161546	0.0179663	81.2208	1.18	1.13	1.22
rs7752591	151947068	AG	0.51	2.17E-08	1.06(1.04,1.08)	0.0543034	0.0097029	31.3331	1.06	1.04	1.08
rs11155805	151947326	GA	0.32	1.25E-16	1.09(1.07,1.11)	0.0864195	0.0104456	68.5309	1.09	1.07	1.11
6-151947539	151947539	TC	0.40	2.87E-08	0.95(0.93,0.96)	-0.0553473	0.00997465	30.7968	0.95	0.93	0.96
6-151947631	151947631	TC	0.38	7.06E-07	0.95(0.93,0.97)	-0.0501353	0.0101092	24.5996	0.95	0.93	0.97
6-151947736	151947736	GA	0.40	2.82E-08	0.95(0.93,0.96)	-0.0553508	0.00997057	30.8259	0.95	0.93	0.96
6-151947757	151947757	TC	0.08	1.51E-19	1.18(1.14,1.22)	0.162142	0.0179694	81.7949	1.18	1.14	1.22
rs7740686	151948173	TA	0.32	1.02E-16	1.09(1.07,1.11)	0.0866802	0.0104465	68.9335	1.09	1.07	1.11
rs2046210	151948366	AG	0.35	1.10E-14	1.08(1.06,1.10)	0.0792388	0.0102597	59.7106	1.08	1.06	1.10
rs7763637	151949312	AG	0.32	1.06E-16	1.09(1.07,1.11)	0.0866215	0.0104453	68.8556	1.09	1.07	1.11
rs6557160	151949582	CA	0.32	1.10E-16	1.09(1.07,1.11)	0.0865757	0.0104448	68.7889	1.09	1.07	1.11
rs6913578	151949806	CA	0.32	4.91E-17	1.09(1.07,1.11)	0.0881317	0.0105124	70.3738	1.09	1.07	1.11
rs6557161	151950235	GA	0.34	6.94E-15	1.08(1.06,1.11)	0.0802402	0.0103118	60.6144	1.08	1.06	1.11
rs7774781	151950723	TC	0.41	9.75E-08	0.95(0.93,0.97)	-0.0525478	0.00985757	28.4231	0.95	0.93	0.97
rs9397435	151951220	GA	0.07	1.02E-21	1.20(1.15,1.24)	0.180515	0.0189048	91.6858	1.20	1.15	1.24
rs9397436	151952002	GA	0.07	6.97E-22	1.20(1.16,1.24)	0.181573	0.0189392	92.4309	1.20	1.16	1.24
rs9397437	151952332	AG	0.07	4.03E-22	1.20(1.16,1.25)	0.182668	0.0189431	93.5157	1.20	1.16	1.25
rs58343273	151953180	GA	0.07	5.11E-22	1.20(1.16,1.24)	0.181556	0.018875	93.0453	1.20	1.16	1.24
rs9383590	151953765	CT	0.07	1.18E-21	1.20(1.16,1.25)	0.181945	0.019086	91.3878	1.20	1.16	1.25
rs9397068	151953859	AG	0.07	8.33E-22	1.20(1.16,1.25)	0.182686	0.0190922	92.0775	1.20	1.16	1.25
rs6900157	151954127	CT	0.34	5.20E-15	1.08(1.06,1.11)	0.0806407	0.0103151	61.1823	1.08	1.06	1.11
rs60954078	151955914	GA	0.07	3.24E-22	1.20(1.16,1.25)	0.182219	0.0188529	93.9469	1.20	1.16	1.25
6-151955985	151955985	GA	0.33	8.43E-15	1.08(1.06,1.11)	0.0806761	0.0104007	60.2332	1.08	1.06	1.11
6-151956201	151956201	GA	0.19	6.46E-10	1.10(1.06,1.13)	0.0910619	0.0147465	38.1768	1.10	1.06	1.13
6-151956257	151956257	AG	0.36	2.94E-08	0.94(0.92,0.96)	-0.0602213	0.0108618	30.7465	0.94	0.92	0.96
6-151956755	151956755	G/GCACATGCACA	0.40	6.69E-08	0.95(0.93,0.97)	-0.0551104	0.0102083	29.1519	0.95	0.93	0.97
rs9383937	151957119	CT	0.07	6.70E-22	1.20(1.16,1.24)	0.181355	0.0189084	92.5091	1.20	1.16	1.24
6-151957184	151957184	C/CCCT	0.46	2.53E-06	1.05(1.03,1.08)	0.0517906	0.011008	22.1415	1.05	1.03	1.08
6-151957189	151957189	C/TGC	0.53	1.83E-08	1.06(1.04,1.08)	0.0579859	0.0103053	31.6714	1.06	1.04	1.08
6-151957192	151957192	CT/C	0.30	1.87E-04	0.95(0.93,0.98)	-0.0498327	0.0133414	13.9526	0.95	0.93	0.98

6-151957257	151957257	TC	0.07	2.50E-22	1.21(1.16,1.26)	0.191152	0.0197263	94.4597	1.21	1.16	1.26
rs12173562	151957570	TC	0.07	1.47E-21	1.20(1.16,1.25)	0.181778	0.0191138	90.9542	1.20	1.16	1.25
rs12173570	151957714	TC	0.10	2.12E-15	1.14(1.10,1.18)	0.131593	0.0166115	62.9525	1.14	1.10	1.18
rs6930633	151958091	GA	0.33	5.90E-15	1.08(1.06,1.11)	0.0811338	0.0103994	60.934	1.08	1.06	1.11
rs6912323	151958612	TG	0.07	7.81E-22	1.20(1.15,1.24)	0.179159	0.0187093	92.2064	1.20	1.15	1.24
rs17081533	151958815	CT	0.10	4.00E-15	1.14(1.10,1.18)	0.129395	0.0164983	61.7013	1.14	1.10	1.18
rs852003	151962202	TC	0.58	2.14E-07	1.05(1.03,1.07)	0.0509046	0.00981608	26.8991	1.05	1.03	1.07
rs865898	151963697	TC	0.58	1.33E-07	1.05(1.03,1.07)	0.0517802	0.00981741	27.8251	1.05	1.03	1.07
6-151967175	151967175	TC	0.58	5.84E-07	1.05(1.03,1.07)	0.0493013	0.00986829	24.9645	1.05	1.03	1.07
rs77275268	151969198	TC	0.07	1.43E-19	1.19(1.14,1.23)	0.170609	0.0188996	81.897	1.19	1.14	1.23
rs9371545	151969740	AG	0.07	2.29E-18	1.19(1.14,1.23)	0.170818	0.0195899	76.419	1.19	1.14	1.23
6-151969912	151969912	CG	0.58	1.22E-06	1.05(1.03,1.07)	0.0479202	0.00987739	23.5416	1.05	1.03	1.07
6-151970639	151970639	GC	0.50	2.59E-05	0.96(0.94,0.98)	-0.0456687	0.0108564	17.6998	0.96	0.94	0.98
rs851974	151971687	AG	0.57	7.28E-06	1.04(1.02,1.07)	0.0438237	0.00977157	20.117	1.04	1.02	1.07
rs10484919	151974422	TC	0.09	8.86E-14	1.14(1.10,1.18)	0.129889	0.0174467	55.6043	1.14	1.10	1.18
6-151975773	151975773	AG	0.39	4.29E-04	1.04(1.02,1.06)	0.0348537	0.00989866	12.4003	1.04	1.02	1.06
rs6915267	151977085	AG	0.08	3.10E-13	1.14(1.10,1.18)	0.128569	0.0176636	53.1464	1.14	1.10	1.18
rs712219	151978439	CT	0.60	8.46E-05	1.04(1.02,1.06)	0.0388899	0.00989356	15.4529	1.04	1.02	1.06
rs9397440	151978802	CT	0.09	1.46E-13	1.14(1.10,1.18)	0.128723	0.0174451	54.618	1.14	1.10	1.18
rs851970	151979157	TC	0.61	1.23E-04	1.04(1.02,1.06)	0.0380318	0.00990538	14.7431	1.04	1.02	1.06
rs1771351	151980692	GA	0.60	7.51E-05	1.04(1.02,1.06)	0.0391465	0.00988716	15.6777	1.04	1.02	1.06
rs9397069	151980707	CT	0.09	1.54E-13	1.14(1.10,1.18)	0.12848	0.017428	54.5181	1.14	1.10	1.18
rs9371547	151982089	TC	0.08	3.04E-13	1.14(1.10,1.18)	0.128182	0.0176049	53.1799	1.14	1.10	1.18
rs9397441	151982315	CA	0.09	1.51E-13	1.14(1.10,1.18)	0.128568	0.0174337	54.5571	1.14	1.10	1.18
rs851997	151985550	AG	0.39	3.08E-04	1.04(1.02,1.06)	0.0357494	0.00990855	13.0199	1.04	1.02	1.06
6-151985574	151985574	CT	0.08	7.24E-15	1.15(1.11,1.19)	0.139938	0.0180187	60.5313	1.15	1.11	1.19
rs9397442	151986003	TC	0.11	1.35E-10	1.10(1.07,1.14)	0.0988182	0.0154031	41.2418	1.10	1.07	1.14
rs9371226	151986594	TG	0.08	2.98E-13	1.14(1.10,1.18)	0.127328	0.0174803	53.2217	1.14	1.10	1.18
rs9383938	151987357	TG	0.08	3.45E-15	1.15(1.11,1.19)	0.138058	0.0175655	61.9908	1.15	1.11	1.19
rs7745737	151987806	AC	0.14	1.76E-07	1.08(1.05,1.11)	0.0726301	0.0139135	27.2811	1.08	1.05	1.11
rs6913799	151988829	TC	0.09	1.32E-12	1.13(1.09,1.17)	0.121882	0.0172095	50.3016	1.13	1.09	1.17
rs9479090	151989300	CA	0.09	1.39E-12	1.13(1.09,1.17)	0.121746	0.017208	50.1982	1.13	1.09	1.17
6-151989609	151989609	AG	0.09	1.59E-12	1.13(1.09,1.17)	0.122278	0.0173283	49.9382	1.13	1.09	1.17
6-151990235	151990235	CT	0.39	3.27E-04	1.04(1.02,1.06)	0.0359146	0.00999642	12.9105	1.04	1.02	1.06
rs9479098	152004211	AC	0.07	2.95E-06	1.09(1.05,1.14)	0.0892052	0.0191017	21.8457	1.09	1.05	1.14
rs9383939	152006178	AG	0.07	2.23E-06	1.09(1.05,1.14)	0.0903034	0.019103	22.3847	1.09	1.05	1.14
6-152007816	152007816	TC	0.20	3.47E-04	0.95(0.93,0.98)	-0.0488046	0.013643	12.7967	0.95	0.93	0.98
6-152008780	152008780	TC	0.44	2.62E-04	1.04(1.02,1.06)	0.0360789	0.00988529	13.3234	1.04	1.02	1.06
6-152008982	152008982	AG	0.43	1.82E-04	1.04(1.02,1.06)	0.0366673	0.00979935	14.0041	1.04	1.02	1.06
6-152009638	152009638	GA	0.43	1.82E-04	1.04(1.02,1.06)	0.0366128	0.0097833	14.0084	1.04	1.02	1.06

6-152010370	152010370	A/AT	0.43	1.38E-04	1.04(1.02,1.06)	0.0373135	0.00979031	14.529	1.04	1.02	1.06
6-152010534	152010534	CT	0.43	2.12E-04	1.04(1.02,1.06)	0.0361722	0.00976754	13.7173	1.04	1.02	1.06
rs2982572	152010561	TC	0.43	1.97E-04	1.04(1.02,1.06)	0.0363511	0.00976477	13.8612	1.04	1.02	1.06
6-152012739	152012739	TA	0.43	1.99E-04	1.04(1.02,1.06)	0.0363282	0.00976695	13.8376	1.04	1.02	1.06
rs3020334	152012956	GA	0.43	2.17E-04	1.04(1.02,1.06)	0.0361118	0.00976429	13.6807	1.04	1.02	1.06
6-152012988	152012988	GA	0.43	1.96E-04	1.04(1.02,1.06)	0.0363683	0.0097657	13.8717	1.04	1.02	1.06
6-152013223	152013223	TG	0.43	1.83E-04	1.04(1.02,1.06)	0.0365663	0.00977465	13.9976	1.04	1.02	1.06
6-152013748	152013748	TC	0.43	1.06E-04	1.04(1.02,1.06)	0.0380836	0.00982832	15.0182	1.04	1.02	1.06
6-152013760	152013760	TG	0.43	1.06E-04	1.04(1.02,1.06)	0.0380922	0.00982854	15.0243	1.04	1.02	1.06
6-152014575	152014575	ATTC/A	0.42	3.29E-04	1.04(1.02,1.06)	0.0369768	0.010298	12.8955	1.04	1.02	1.06
rs862346	152016369	TA	0.44	2.53E-05	1.04(1.02,1.06)	0.041101	0.00975988	17.739	1.04	1.02	1.06
6-152016803	152016803	TC	0.44	2.30E-05	1.04(1.02,1.06)	0.0413737	0.00977434	17.9221	1.04	1.02	1.06
6-152017691	152017691	GT	0.45	1.37E-04	1.04(1.02,1.06)	0.0373886	0.00980686	14.5381	1.04	1.02	1.06
6-152017958	152017958	GC	0.44	2.74E-05	1.04(1.02,1.06)	0.0410011	0.00977699	17.591	1.04	1.02	1.06
rs851985	152020390	CA	0.41	2.31E-07	1.05(1.03,1.07)	0.0510053	0.00986323	26.7527	1.05	1.03	1.07
rs851984	152023191	AG	0.41	2.71E-07	1.05(1.03,1.07)	0.0506431	0.00984924	26.449	1.05	1.03	1.07
rs851983	152024415	GA	0.41	3.25E-07	1.05(1.03,1.07)	0.0503053	0.00984935	26.0966	1.05	1.03	1.07
rs851982	152024985	CT	0.41	3.29E-07	1.05(1.03,1.07)	0.0502716	0.00984763	26.0708	1.05	1.03	1.07
6-152027074	152027074	TA	0.27	4.58E-09	1.07(1.04,1.09)	0.0644991	0.0110079	34.3603	1.07	1.04	1.09
rs851980	152027955	CT	0.27	1.09E-08	1.06(1.04,1.09)	0.062522	0.0109436	32.6651	1.06	1.04	1.09
6-152029556	152029556	TG	0.28	1.15E-05	1.05(1.03,1.07)	0.0478051	0.010901	19.2409	1.05	1.03	1.07
6-152029608	152029608	CT	0.28	1.76E-05	1.05(1.03,1.07)	0.0461754	0.0107591	18.4276	1.05	1.03	1.07
6-152030008	152030008	CT	0.28	1.81E-05	1.05(1.03,1.07)	0.0461803	0.0107738	18.3813	1.05	1.03	1.07
rs851975	152031303	TC	0.26	5.46E-08	1.06(1.04,1.09)	0.0602937	0.0110966	29.5452	1.06	1.04	1.09
6-152032917	152032917	TC	0.28	1.85E-05	1.05(1.03,1.07)	0.0460916	0.0107666	18.3351	1.05	1.03	1.07
6-152033643	152033643	TG	0.28	1.61E-05	1.05(1.03,1.07)	0.0468434	0.0108626	18.6051	1.05	1.03	1.07
6-152034062	152034062	AG	0.25	5.54E-08	1.06(1.04,1.09)	0.0606405	0.0111656	29.518	1.06	1.04	1.09
6-152034386	152034386	TC	0.28	1.06E-05	1.05(1.03,1.07)	0.0481423	0.0109324	19.4014	1.05	1.03	1.07
6-152034624	152034624	AG	0.26	6.22E-08	1.06(1.04,1.09)	0.0602856	0.0111429	29.2924	1.06	1.04	1.09
6-152034758	152034758	TC	0.25	2.84E-08	1.07(1.04,1.09)	0.0629797	0.0113503	30.8127	1.07	1.04	1.09
6-152034820	152034820	CT	0.26	6.95E-08	1.06(1.04,1.09)	0.0598734	0.0111071	29.0795	1.06	1.04	1.09
6-152034856	152034856	TTC/T	0.23	1.45E-06	1.06(1.04,1.09)	0.0589898	0.0122486	23.2098	1.06	1.04	1.09
6-152034861	152034861	TC/T	0.16	5.09E-07	1.08(1.05,1.11)	0.0755407	0.015047	25.2293	1.08	1.05	1.11
6-152036607	152036607	TC/T	0.28	1.56E-05	1.05(1.03,1.07)	0.0464806	0.0107619	18.6624	1.05	1.03	1.07
6-152037555	152037555	GTA/G	0.23	4.65E-09	1.07(1.05,1.10)	0.0694357	0.0118561	34.33	1.07	1.05	1.10
6-152037556	152037556	TC	0.27	5.50E-06	1.05(1.03,1.07)	0.0502765	0.0110652	20.6553	1.05	1.03	1.07
6-152037557	152037557	AT	0.25	1.17E-08	1.07(1.04,1.09)	0.0653041	0.0114526	32.541	1.07	1.04	1.09
6-152038240	152038240	AG	0.26	5.66E-08	1.06(1.04,1.09)	0.0602405	0.0110997	29.4765	1.06	1.04	1.09
6-152039964	152039964	CT	0.28	1.61E-04	1.04(1.02,1.06)	0.0407957	0.0108143	14.2364	1.04	1.02	1.06
6-152040125	152040125	GA	0.26	5.39E-08	1.06(1.04,1.09)	0.0603549	0.011103	29.571	1.06	1.04	1.09

rs12525163	152040291	CT	0.28	1.16E-05	1.05(1.03,1.07)	0.0471323	0.0107521	19.2247	1.05	1.03	1.07
6-152040615	152040615	AG	0.25	1.30E-07	1.06(1.04,1.08)	0.059093	0.011197	27.8727	1.06	1.04	1.08
rs10484921	152042260	AC	0.26	8.76E-08	1.06(1.04,1.08)	0.0592073	0.0110691	28.6313	1.06	1.04	1.08
rs11756568	152042413	TA	0.28	1.47E-05	1.05(1.03,1.07)	0.0465135	0.0107353	18.7816	1.05	1.03	1.07
6-152042502	152042502	CA	0.29	1.96E-05	1.05(1.03,1.07)	0.0457508	0.0107183	18.2283	1.05	1.03	1.07
6-152043290	152043290	GA	0.29	1.81E-05	1.05(1.03,1.07)	0.0459857	0.0107294	18.3777	1.05	1.03	1.07
6-152044872	152044872	TA	0.28	1.64E-05	1.05(1.03,1.07)	0.0464783	0.0107893	18.5659	1.05	1.03	1.07
6-152044884	152044884	GA	0.26	5.11E-08	1.06(1.04,1.09)	0.0607312	0.0111528	29.6744	1.06	1.04	1.09
6-152047475	152047475	TG/T	0.20	3.54E-07	1.07(1.04,1.09)	0.0652628	0.0128218	25.9297	1.07	1.04	1.09
6-152047476	152047476	GT	0.25	8.85E-08	1.06(1.04,1.09)	0.0602228	0.0112633	28.6099	1.06	1.04	1.09
6-152047557	152047557	CG	0.27	1.01E-05	1.05(1.03,1.07)	0.0488314	0.0110629	19.493	1.05	1.03	1.07
6-152047753	152047753	GA	0.28	1.94E-05	1.05(1.03,1.07)	0.0462762	0.0108355	18.2483	1.05	1.03	1.07
6-152048022	152048022	TC	0.28	1.95E-05	1.05(1.03,1.07)	0.04626	0.0108347	18.2383	1.05	1.03	1.07
6-152048895	152048895	AC	0.05	3.03E-05	1.12(1.06,1.17)	0.108991	0.0261549	17.3983	1.12	1.06	1.17
rs35240111	152050523	CG	0.28	2.55E-05	1.05(1.02,1.07)	0.0455958	0.0108332	17.7232	1.05	1.02	1.07
rs6904031	152055978	TA	0.07	1.71E-11	1.14(1.10,1.18)	0.130553	0.0194341	45.2774	1.14	1.10	1.18
rs1361024	152070928	AG	0.08	8.13E-07	1.09(1.06,1.13)	0.0902842	0.0183223	24.3257	1.09	1.06	1.13
rs9918437	152072718	TG	0.08	5.63E-07	1.10(1.06,1.14)	0.0914285	0.0182898	25.0363	1.10	1.06	1.14
rs11155820	152204210	GA	0.31	1.77E-04	1.04(1.02,1.06)	0.0393919	0.0105074	14.0595	1.04	1.02	1.06
6-152224101	152224101	GA	0.31	8.87E-05	1.04(1.02,1.06)	0.0415095	0.0105925	15.3624	1.04	1.02	1.06
rs12199722	152234900	GA	0.31	1.70E-04	1.04(1.02,1.06)	0.0395525	0.0105221	14.1349	1.04	1.02	1.06
6-152248677	152248677	GT	0.05	1.51E-04	0.91(0.87,0.96)	-0.0945964	0.024969	14.3588	0.91	0.87	0.96
6-152333496	152333496	TC	0.02	3.59E-04	0.89(0.84,0.95)	-0.112871	0.031632	12.7361	0.89	0.84	0.95
6-152345025	152345025	TC	0.05	6.12E-04	0.93(0.89,0.97)	-0.0742985	0.0216843	11.7406	0.93	0.89	0.97
rs9478265	152348901	AG	0.05	4.95E-04	0.93(0.89,0.97)	-0.0755156	0.0216777	12.136	0.93	0.89	0.97
6-152351429	152351429	AC	0.05	5.36E-04	0.93(0.89,0.97)	-0.0756385	0.0218469	11.9876	0.93	0.89	0.97
6-152362526	152362526	GT	0.05	4.75E-04	0.93(0.89,0.97)	-0.0766939	0.0219469	12.2126	0.93	0.89	0.97
6-152363092	152363092	AG	0.05	4.75E-04	0.93(0.89,0.97)	-0.0766982	0.0219482	12.2125	0.93	0.89	0.97
6-152364192	152364192	AG	0.05	4.76E-04	0.93(0.89,0.97)	-0.0766916	0.0219506	12.2078	0.93	0.89	0.97
6-152368399	152368399	GCAA/G	0.05	7.20E-04	0.93(0.89,0.97)	-0.0741413	0.0219234	11.4374	0.93	0.89	0.97
6-152381998	152381998	CT	0.06	7.11E-04	0.93(0.90,0.97)	-0.0696886	0.020584	11.461	0.93	0.90	0.97
rs2813543	152424478	GA	0.78	1.77E-06	1.06(1.03,1.08)	0.0555356	0.0116233	22.8306	1.06	1.03	1.08
rs1543403	152428704	GC	0.49	1.58E-09	1.06(1.04,1.08)	0.0587185	0.00973004	36.4343	1.06	1.04	1.08
rs1543404	152428838	TC	0.49	1.16E-09	1.06(1.04,1.08)	0.0592111	0.00973136	37.0385	1.06	1.04	1.08
6-152429415	152429415	AG	0.06	2.00E-04	0.93(0.89,0.97)	-0.075086	0.020187	13.8355	0.93	0.89	0.97
6-152430326	152430326	CA	0.28	2.87E-06	1.05(1.03,1.07)	0.0506474	0.0108254	21.9013	1.05	1.03	1.07
6-152430638	152430638	TC	0.28	4.02E-06	1.05(1.03,1.08)	0.0509324	0.0110509	21.2536	1.05	1.03	1.08
rs910416	152432902	TC	0.54	4.39E-12	1.07(1.05,1.09)	0.0678282	0.00979871	47.9408	1.07	1.05	1.09
6-152434275	152434275	CA/C	0.54	3.69E-12	1.07(1.05,1.09)	0.0680012	0.00978866	48.2848	1.07	1.05	1.09
rs34133739	152434278	AC/A	0.54	3.78E-12	1.07(1.05,1.09)	0.0680994	0.00980805	48.2331	1.07	1.05	1.09

rs66485058	152434279	TC	0.46	9.66E-12	0.94(0.92,0.95)	-0.0665757	0.00977636	46.3972	0.94	0.92	0.95
rs9397485	152434828	GA	0.29	6.38E-06	1.05(1.03,1.07)	0.048372	0.0107205	20.3696	1.05	1.03	1.07
6-152435801	152435801	TC	0.16	8.23E-04	1.05(1.02,1.08)	0.0484035	0.014475	11.1884	1.05	1.02	1.08
6-152436158	152436158	CT	0.25	1.11E-04	1.04(1.02,1.07)	0.0434513	0.0112445	14.9392	1.04	1.02	1.07
rs2747652	152437016	CT	0.54	2.24E-12	1.07(1.05,1.09)	0.0685776	0.0097736	49.2588	1.07	1.05	1.09
rs7450824	152438103	CT	0.25	7.13E-05	1.05(1.02,1.07)	0.044543	0.0112173	15.776	1.05	1.02	1.07
6-152440519	152440519	TTC	0.16	5.85E-04	1.06(1.02,1.09)	0.0559227	0.0162693	11.8217	1.06	1.02	1.09
rs113345553	152440522	C/CA	0.53	9.40E-11	1.07(1.05,1.09)	0.0636911	0.00983673	41.9427	1.07	1.05	1.09
rs2813549	152441239	TC	0.77	1.80E-08	1.07(1.04,1.09)	0.0648042	0.0115102	31.7037	1.07	1.04	1.09
rs2813550	152441587	AC	0.77	1.82E-08	1.07(1.04,1.09)	0.0647875	0.0115115	31.6801	1.07	1.04	1.09
rs2747655	152447321	CT	0.77	4.10E-08	1.06(1.04,1.09)	0.0627815	0.0114441	30.0999	1.06	1.04	1.09
6-152448811	152448811	AC	0.20	3.94E-04	1.04(1.02,1.07)	0.0433507	0.0122345	12.5614	1.04	1.02	1.07
6-152448813	152448813	AC	0.20	3.94E-04	1.04(1.02,1.07)	0.0433528	0.0122345	12.5627	1.04	1.02	1.07
rs9322361	152459143	GA	0.17	2.42E-04	1.05(1.02,1.08)	0.0473744	0.0129088	13.4764	1.05	1.02	1.08
6-152459569	152459569	CA	0.89	2.57E-04	1.06(1.03,1.09)	0.0584898	0.0160021	13.3587	1.06	1.03	1.09
6-152461048	152461048	C/CTGTT	0.37	3.21E-04	0.96(0.95,0.98)	-0.0365186	0.0101497	12.9466	0.96	0.95	0.98
6-152462180	152462180	C/CA	0.12	5.20E-04	0.94(0.90,0.97)	-0.0658544	0.0189763	12.0433	0.94	0.90	0.97
6-152463745	152463745	CG	0.24	2.09E-04	1.04(1.02,1.07)	0.0424145	0.011443	13.7451	1.04	1.02	1.07
rs9371241	152468307	CG	0.24	1.72E-04	1.04(1.02,1.07)	0.0428634	0.0114129	14.112	1.04	1.02	1.07
6-152474790	152474790	CT	0.23	1.03E-05	1.05(1.03,1.08)	0.0515652	0.0116923	19.4617	1.05	1.03	1.08
rs17246069	152475745	GC	0.14	1.39E-04	1.06(1.03,1.09)	0.0539488	0.0141679	14.5104	1.06	1.03	1.09
rs2635475	152476648	AG	0.47	4.87E-04	0.97(0.95,0.99)	-0.0338478	0.00970567	12.1635	0.97	0.95	0.99

[1] Remaining candidate causal variants for signal 1 (red), signal 2 (dark blue), signal 3 (green), signal 4 (pink) and signal 5 (light blue). Minor Allele Frequency (MAF), Odds ratio (OR), 95% Lower confidence interval (LCI), 95% Upper Confidence Interval (UCI), standard error (se), chi squared value (chi2).

Supplementary Table 2. Correlation matrix for signal representative SNPs in European ancestry studies.

Europeans **SIGNAL**		**1**	**2**	**3**	**4**	**5**
Representative SNP		*rs3757322*	*rs9397437*	*rs851984*	*rs9918437*	*rs2747652*
1	*rs3757322*	1.00	0.16	0.07	0.00	0.00
2	*rs9397437*		1.00	0.19	0.00	0.00
3	*rs851984*			1.00	0.07	0.00
4	*rs9918437*				1.00	0.00
5	*rs2747652*					1.00

Supplementary Table 3. Association of each signal with the main tumor subtype combinations (case-control analysis).

SIGNAL		**ER+/PR+/HER2+ (1158 cases)**		**ER+/PR+/HER2- (9029 cases)**		**ER+/PR-/HER2+ (428 cases)**		**ER+/PR-/HER2- (1532 cases)**		**ER-/PR+/HER2- (268 cases)**		**ER-/PR-/HER2+ (858 cases)**		**ER-/PR-/HER2- (2840 cases)**	
Representative SNP		**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**
1	*rs3757322*	1.11(1.01-1.21)	2.90E-02	**1.07(1.03-1.11)**	**8.70E-04**	1.09(0.94-1.26)	2.67E-01	1.05(0.97-1.14)	2.10E-01	1.17(0.97-1.40)	9.00E-02	**1.19(1.07-1.32)**	**8.80E-04**	**1.20(1.12-1.28)**	**7.17E-08**
	conditional*	1.09 (0.98-1.20)	9.60E-02	**1.06(1.01-1.11)**	**7.00E-03**	1.03(0.87-1.22)	7.11E-01	1.03(0.94-1.12)	5.90E-01	1.26(1.03-1.55)	2.00E-02	**1.17(1.04-1.31)**	**9.11E-03**	**1.19(1.11-1.28)**	**3.48E-06**
2	*rs9397437*	1.21(1.04-1.42)	1.30E-02	1.12(1.05-1.20)	1.40E-03	1.32(1.04-1.69)	2.40E-02	1.17(1.01-1.35)	3.40E-02	1.14(0.83-1.58)	4.10E-01	1.25(1.04-1.5)	1.55E-02	1.25(1.11-1.40)	1.50E-04
	conditional*	1.17(0.98-1.4)	6.90E-02	1.9(1.01-1.17)	3.10E-02	1.32(1.01-1.73)	4.50E-02	1.15(0.98-1.35)	8.00E-02	1.07(0.76-1.52)	7.00E-01	1.13(0.93-1.38)	2.10E-01	1.13(0.996-1.28)	5.80E-02
3	*rs851984*	1.05(0.96-1.15)	2.53E-01	1.03(0.995-1.07)	8.30E-02	1.02(0.92-1.18)	7.27E-01	1.02(0.94-1.10)	6.70E-01	**1.30(1.10-1.55)**	**2.50E-03**	1(0.91-1.11)	9.40E-01	1.05(0.98-1.12)	1.40E-01
	conditional*	1.09(0.99-1.19)	7.10E-02	1.04(1-1.09)	3.00E-02	1.05(0.90-1.21)	5.38E-01	1.02(0.94-1.10)	6.70E-01	**1.40(1.16-1.68)**	**4.50E-04**	1.03(0.92-1.14)	6.30E-01	1.08(1.01-1.16)	2.00E-02
4	*rs9918437*	1.02(0.87-1.20)	7.97E-01	1.09(1.01-1.16)	1.70E-02	1.06(0.82-1.37)	6.59E-01	1.11(0.97-1.27)	1.30E-01	1.14(0.82-1.56)	4.40E-01	1.18(0.99-1.40)	6.80E-02	1.17(1.04-1.32)	7.00E-03
	conditional*	0.97(0.82-1.15)	7.54E-01	1.06(0.99-1.14)	1.11E-01	1.02(0.78-1.33)	8.78E-01	1.10(0.95-1.26)	2.00E-01	0.96(0.69-1.34)	8.00E-01	1.14(0.95-1.37)	1.60E-01	1.12(0.99-1.26)	7.20E-02
5	*rs2747652*	1.05(0.97-1.15)	2.49E-01	1.04(1.01-1.08)	2.10E-02	1.13(0.98-1.29)	9.10E-02	1.03(0.96-1.11)	3.90E-01	1.10(0.92-1.31)	2.90E-01	**1.24(1.12-1.37)**	**2.41E-05**	1.08(1.01-1.15)	1.65E-02
	conditional*	1.05(0.97-1.15)	2.28E-01	1.04(1.01-1.08)	2.00E-02	1.13(0.99-1.30)	7.90E-02	1.03(0.96-1.12)	3.70E-01	1.10(0.92-1.30)	2.90E-01	**1.24(1.12-1.37)**	**2.38E-05**	1.08(1.01-1.15)	1.72E-02

* conditional results of fitting the model with the five representative SNPs. Odds ratio (OR), confidence interval (CI).

Supplementary Table 4. Association of each signal with tumor grade - shown separately for ER^+ and ER^- tumors

		ER+												ER-											
SIGNAL		**Grade 1 vs controls**				**Grade2 vs controls**				**Grade3 vs controls**				**Grade1 vs controls**				**Grade2 vs controls**				**Grade3 vs controls**			
Representative SNP		**OR**	**LCI**	**UCI**	**p-value**	**OR**	**LCI**	**UCI**	**p-value**	**OR**	**LCI**	**UCI**	**p-value**	**OR**	**LCI**	**UCI**	**p-value**	**OR**	**LCI**	**UCI**	**p-value**	**OR**	**LCI**	**UCI**	**p-value**
1	*rs3757322*	1.048	1.002	1.096	4.04E-02	1.077	1.042	1.112	8.77E-06	1.062	1.012	1.114	1.37E-02	1.231	1.006	1.507	4.36E-02	0.003	1.046	1.243	2.88E-03	1.195	1.133	1.260	6.10E-11
	conditional*	1.047	0.996	1.100	7.15E-02	1.069	1.031	1.109	3.49E-04	1.059	1.004	1.118	3.67E-02	1.158	0.924	1.453	2.03E-01	1.144	1.039	1.261	6.29E-03	1.173	1.105	1.245	1.75E-07
2	*rs9397437*	1.044	0.960	1.136	3.17E-01	1.157	1.090	1.227	1.48E-06	1.174	1.078	1.279	2.22E-04	1.353	0.958	1.910	8.60E-02	1.189	1.021	1.386	2.63E-02	1.304	1.189	1.430	1.88E-08
	conditional*	1.009	0.921	1.106	8.43E-01	1.122	1.052	1.197	4.76E-04	1.162	1.058	1.276	1.62E-03	1.200	0.823	1.751	3.43E-01	1.106	0.936	1.307	2.37E-01	1.189	1.074	1.315	8.21E-04
3	*rs851984*	1.003	0.962	1.046	8.79E-01	1.047	1.015	1.080	3.51E-03	1.109	1.061	1.161	6.30E-06	0.868	0.714	1.056	1.57E-01	1.085	0.999	1.178	5.30E-02	1.048	0.995	1.103	7.49E-02
	conditional*	1.005	0.960	1.051	8.47E-01	1.066	1.031	1.102	1.80E-04	1.121	1.067	1.177	4.67E-06	0.925	0.748	1.143	4.68E-01	1.098	1.004	1.201	4.09E-02	1.079	1.021	1.141	7.08E-03
4	*rs9918437*	1.072	0.993	1.156	7.54E-02	1.081	1.022	1.144	6.57E-03	1.164	1.074	1.261	2.17E-04	0.870	0.600	1.262	4.64E-01	1.257	1.089	1.451	1.79E-03	1.194	1.090	1.307	1.24E-04
	conditional*	1.069	0.987	1.157	1.03E-01	1.042	0.982	1.105	1.73E-01	1.089	1.001	1.185	4.61E-02	0.904	0.613	1.334	6.11E-01	1.190	1.023	1.383	2.41E-02	1.138	1.034	1.251	7.82E-03
5	*rs2747652*	0.987	0.946	1.029	5.30E-01	1.064	1.032	1.097	7.91E-05	1.121	1.072	1.173	6.11E-07	1.013	0.836	1.228	8.96E-01	1.123	1.034	1.219	5.93E-03	1.112	1.057	1.170	4.36E-05
	conditional*	0.986	0.946	1.028	5.12E-01	1.065	1.033	1.098	6.05E-05	1.121	1.072	1.173	6.31E-07	1.014	0.837	1.230	8.85E-01	1.121	1.032	1.217	6.72E-03	1.112	1.057	1.170	4.33E-05

* conditional results of fitting the model with the five representative SNPs. Odds ratio (OR), 95% Lower confidence interval (LCI), 95% Upper Confidence Interval (UCI).

Supplementary Table 5. Association of each signal with tumor subtype combinations and tumor grade* (case-only analysis)
*grade adjusted for ER status.

ER+/ER- case-only			
SIGNAL	***Representative SNP***	**p-value**	**conditional model**
1	rs3757322	5.30E-05	0.002
2	rs9397437	0.00318	0.15
3	rs851984	0.7	0.96
4	rs9918437	0.00359	0.0085
5	rs2747652	0.00076	0.0008

HER2+/HER2- case only			
SIGNAL	***Representative SNP***	**p-value**	**conditional model**
1	rs3757322	0.18	0.36
2	rs9397437	0.14	0.29
3	rs851984	0.89	0.64
4	rs9918437	0.72	0.89
5	rs2747652	0.025	0.02

HER2+/HER2- in ER-disease case-only	
p-value	**conditional model**
0.777	0.744
0.489	0.603
0.159	0.114
0.626	0.354
0.020	0.018

PR+/PR- case-only			
SIGNAL	***Representative SNP***	**p-value**	**conditional model**
1	rs3757322	4.57E-05	1.79E-03
2	rs9397437	7.78E-03	2.54E-01
3	rs851984	5.42E-01	7.78E-01
4	rs9918437	5.50E-03	9.43E-03
5	rs2747652	1.80E-03	1.91E-03

Grade case-only			
SIGNAL	***Representative SNP***	**p-value**	**conditional model**
1	rs3757322	7.90E-01	9.18E-01
2	rs9397437	1.47E-02	6.42E-03
3	rs851984	2.35E-04	5.43E-04
4	rs9918437	2.10E-02	2.96E-01
5	rs2747652	2.27E-05	1.82E-05

Supplementary Table 6. Haplotype Analysis using the five signal representative SNPs - signal 1:rs3757322, signal 2:rs9397437, signal 3:rs851984, signal 4: rs9918437, signal 5rs2747652.

		BCAC ER+				BCAC ER-				CIMBA BRCA1				CAC ER-_CiMBA BRCA1 Meta-analys			BCAC HER2-				BCAC HER2+				Mammographic Dense Area*			
Haplotype	**hap.freq.BCAC**	**OR**	**LCI**	**UCI**	**pvalue**	**OR**	**LCI**	**UCI**	**pvalue**	**OR**	**LCI**	**UCI**	**pvalue**	**ma_beta**	**ma_var**	**ma_p**	**OR**	**LCI**	**UCI**	**pvalue**	**OR**	**LCI**	**UCI**	**pvalue**	**beta**	**LCI**	**UCI**	**pvalue**
11112	0.1485	0.917	0.869	0.967	0.001	0.930	0.850	1.019	0.119	1.018	0.942	1.101	0.646	-0.021	0.000	0.117	0.918	0.853	0.989	0.024	1.018	0.882	1.175	0.804	0.077	-0.060	0.215	0.270
11121	0.0036	0.808	0.597	1.093	0.166	1.316	0.864	2.004	0.201	1.273	0.895	1.810	0.179	0.145	0.007	0.040	0.913	0.609	1.367	0.658	1.406	0.713	2.773	0.326	0.088	-0.592	0.768	0.799
11122	0.0056	0.995	0.803	1.233	0.962	0.773	0.500	1.195	0.247	1.185	0.902	1.557	0.224	-0.021	0.006	0.397	0.917	0.680	1.237	0.570	1.047	0.552	1.989	0.888	0.143	-0.344	0.631	0.565
11211	0.1531	1.058	1.006	1.113	0.028	1.145	1.053	1.245	0.002	1.147	1.063	1.238	0.000	0.073	0.000	0.000	1.030	0.961	1.105	0.405	1.204	1.054	1.375	0.006	0.042	-0.090	0.174	0.533
11212	0.1387	1.027	0.982	1.075	0.243	0.923	0.853	1.000	0.049	1.079	1.008	1.155	0.028	-0.012	0.000	0.225	1.001	0.940	1.065	0.987	0.972	0.858	1.102	0.662	0.100	-0.014	0.214	0.085
11221	0.0267	1.110	1.004	1.227	0.042	1.131	0.953	1.341	0.158	1.158	0.993	1.350	0.061	0.071	0.001	0.019	1.169	1.017	1.344	0.028	0.958	0.710	1.292	0.777	0.162	-0.099	0.423	0.223
11222	0.0162	1.077	0.941	1.233	0.283	1.443	1.180	1.764	0.000	1.144	0.924	1.417	0.216	0.156	0.002	0.000	1.254	1.048	1.501	0.014	1.240	0.861	1.785	0.248	-0.037	-0.400	0.326	0.841
21111	0.1034	1.069	1.009	1.132	0.023	1.169	1.063	1.285	0.001	1.168	1.072	1.273	0.000	0.084	0.000	0.000	1.080	0.996	1.170	0.061	1.314	1.135	1.521	0.000	0.165	0.019	0.312	0.027
21112	0.0887	1.008	0.954	1.064	0.782	1.077	0.984	1.178	0.108	1.120	1.038	1.208	0.004	0.049	0.000	0.003	1.049	0.973	1.130	0.210	0.943	0.807	1.101	0.456	0.137	-0.001	0.274	0.051
21211	0.0221	1.012	0.901	1.137	0.841	1.274	1.072	1.515	0.006	1.154	0.985	1.352	0.077	0.112	0.001	0.001	1.076	0.923	1.255	0.351	1.041	0.777	1.395	0.786	0.098	-0.175	0.371	0.482
21212	0.0209	1.046	0.924	1.184	0.475	1.113	0.911	1.360	0.294	1.113	0.956	1.295	0.167	0.062	0.001	0.055	1.020	0.860	1.211	0.816	1.279	0.957	1.710	0.096	0.080	-0.219	0.379	0.599
21221	0.0105	1.190	1.013	1.399	0.034	1.222	0.935	1.596	0.143	1.386	1.106	1.736	0.005	0.137	0.003	0.005	1.128	0.900	1.413	0.296	0.982	0.594	1.622	0.943	0.246	-0.226	0.718	0.308
21222	0.0068	1.167	0.942	1.446	0.158	1.112	0.772	1.602	0.568	1.423	1.078	1.878	0.013	0.122	0.005	0.042	1.002	0.727	1.380	0.992	1.753	1.090	2.819	0.021	0.045	-0.499	0.589	0.872
22111	0.0262	1.152	1.047	1.266	0.004	1.364	1.180	1.577	0.000	1.165	1.021	1.330	0.023	0.138	0.001	0.000	1.124	0.990	1.276	0.071	**1.500**	**1.206**	**1.865**	**0.000**	**0.445**	**0.203**	**0.687**	**0.000**
22112	0.0302	1.135	1.043	1.235	0.003	1.237	1.082	1.414	0.002	**1.341**	**1.210**	**1.486**	**0.000**	0.141	0.001	0.000	1.175	1.051	1.313	0.004	0.959	0.749	1.227	0.739	0.285	0.069	0.501	0.010
22211	0.0022	1.558	1.028	2.360	0.036	0.882	0.397	1.956	0.757	0.745	0.451	1.230	0.249	-0.132	0.021	0.182	1.500	0.848	2.654	0.163	1.761	0.701	4.428	0.229				
22212	0.0026	0.990	0.668	1.467	0.960	1.276	0.769	2.118	0.345	2.232	1.497	3.327	0.000	0.268	0.010	0.003	1.221	0.754	1.976	0.417	1.697	0.771	3.736	0.189				
22221	0.0047	**1.379**	**1.113**	**1.708**	**0.003**	**2.337**	**1.763**	**3.097**	**0.000**	1.279	0.910	1.797	0.156	**0.355**	**0.003**	**0.000**	1.437	1.056	1.957	0.021	1.455	0.804	2.631	0.215	0.177	-0.289	0.643	0.457
22222	0.0015	1.201	0.729	1.978	0.473	0.900	0.317	2.553	0.842	1.310	0.764	2.246	0.326	0.085	0.031	0.316	0.963	0.467	1.989	0.920	2.561	1.134	5.786	0.024				
haplo.rare	0.0016	0.981	0.981	0.981	0.000	1.447	1.447	1.447	0.000	1.666	1.144	2.426	0.008	0.161	0.000	0.000	0.892	0.892	0.892	0.000	2.656	2.656	2.656	0.000				
11111	0.1863																											

* Mammographic dense area (DA) was square-root transformed and adjusted for age, body mass index (BMI), menopausal status, study and relevant principal components. Odds ratio (OR), 95% Lower confidence interval (LCI), 95% Upper Confidence Interval (UCI).

Supplementary Table 7. Association of each signal-representative SNP with breast cancer phenotypes in the 9 Asian-ancestry studies.

SIGNAL		**Overall Breast Cancer**				**ER-positive (3372 cases)**				**ER-negative (1623 cases)**			
	Representative SNP	**OR**	**LCI**	**UCI**	**p-value**	**OR**	**LCI**	**UCI**	**p-value**	**OR**	**LCI**	**UCI**	**p-value**
1	**rs3757322**	**1.18**	**1.04**	**1.34**	**0.012116**	**1.15**	**0.99**	**1.35**	**0.075087**	**1.22**	**1.00**	**1.48**	**0.049361**
2	rs9397437	1.10	0.97	1.26	0.146399	1.08	0.91	1.27	0.378725	1.21	0.99	1.48	0.065793
3	**rs851984**	**1.14**	**1.04**	**1.26**	**0.007119**	**1.15**	**1.02**	**1.29**	**0.020445**	**1.17**	**1.00**	**1.36**	**0.046067**
4	rs9918437	1.03	0.92	1.16	0.573472	1.04	0.91	1.20	0.568669	1.10	0.92	1.32	0.282621
5	**rs2747652**	**1.05**	**1.00**	**1.11**	**0.048313**	1.01	0.95	1.07	0.800233	**1.09**	**1.01**	**1.19**	**0.032038**

Conditional results of fitting the model with the five representative SNPs. Odds ratio (OR), 95% Lower confidence interval (LCI), 95% Upper Confidence Interval (UCI).

Supplementary Table 8. Associations of signal-representative SNPs with *ESR1* expression (determined by microarray) in *ER*$^-$ and *ER*$^+$ breast tumors and their adjacent (Adj) normal tissue from the METABRIC study.

SIGNAL 1 (rs2046210)							
ER-				**ER+**			
Allele status	**Adj Normal**	**Tumor**	**N**	**Allele status**	**Adj Normal**	**Tumor**	**N**
Reference genotype (AA)	9.5	5.8	8	Reference genotype (AA)	8.7	9.9	41
1 or 2 risk alleles (AG, GG)	8.3	6.0	12	1 or 2 risk alleles (AG, GG)	8.9	9.9	50
Change*	-1.2	0.2		Change*	0.2	0	

SIGNAL 2 (rs12173570)							
ER-				**ER+**			
Allele status	**Adj Normal**	**Tumor**	**N**	**Allele status**	**Adj Normal**	**Tumor**	**N**
Reference genotype (TT)	8.5	6.0	15	Reference genotype (TT)	8.7	9.9	71
1 or 2 risk alleles (TC, CC)	8.8	5.8	5	1 or 2 risk alleles (TC, CC)	8.5	9.7	20
Change*	0.3	-0.2		Change*	-0.2	-0.2	

SIGNAL 3 (rs851985)							
ER-				**ER+**			
Allele status	**Adj Normal**	**Tumor**	**N**	**Allele status**	**Adj Normal**	**Tumor**	**N**
Reference genotype (CC)	7.4	5.9	3	Reference genotype (CC)	8.4	10.0	28
1 or 2 risk alleles (CA, AA)	8.8	5.9	17	1 or 2 risk alleles (CA, AA)	9.0	9.9	63
Change*	1.4	0		Change*	0.6	-0.1	

SIGNAL 4 (rs9918437)							
ER-				**ER+**			
Allele status	**Adj Normal**	**Tumor**	**N**	**Allele status**	**Adj Normal**	**Tumor**	**N**
Reference genotype (GG)	8.7	5.8	15	Reference genotype (GG)	8.8	9.9	82
1 or 2 risk alleles (GT, TT)	8.1	6.1	5	1 or 2 risk alleles (GT, TT)	8.2	8.9	9
Change*	-0.6	0.3		Change*	-0.6	-1.0	

SIGNAL 5 (rs2747652)							
ER-				**ER+**			
Allele status	**Adj Normal**	**Tumor**	**N**	**Allele status**	**Adj Normal**	**Tumor**	**N**
Reference genotype (TT)	8.6	5.9	12	Reference genotype (TT)	8.7	9.9	71
1 or 2 risk alleles (TC, CC)	8.5	5.9	8	1 or 2 risk alleles (TC, CC)	9.2	9.6	20
Change*	-0.1	0		Change*	0.5	-0.3	

* Change is the measured expression difference between alleles.

Supplementary Table 9. Allelic imbalance identified from 742 TGCA[5] breast tumor cases between risk/proxy SNPs and *ESR1*, *RMND1*, *C6orf211* and *CCDC170* transcripts. Three Signal 1 SNPs, a proxy SNP for signal 2 ($r^2 = 0.85$) and two signal 2 SNPs were on the Affymetrix SNP Array 6.0. For each risk SNP, allelic imbalance for the target transcripts was compared between heterozygote (AB) and homozygote (AA and BB) samples. For rs7740686/signal 1 and rs9397437/signal 2, Levene's Test (equality of variances) and, for rs851985/signal 3, two-tailed t-Test (equality of means) was used to calculate *P*-values.

Risk/Proxy SNP	Signal	Target gene	# samples (AA,AB,BB)	*P*-value
rs7740686	1	***ESR1***	21, 142, 136	**0.041***
rs7740686	1	*RMND1*	19, 102, 97	0.725
rs7740686	1	*C6orf211*	11, 80, 68	0.334
rs7740686	1	*CCDC170*	16, 154, 109	0.671
rs2046210	1	*ESR1*	32, 140, 127	0.103
rs2046210	1	*RMND1*	24, 103, 91	0.778
rs2046210	1	*C6orf211*	18, 80, 61	0.715
rs2046210	1	*CCDC170*	25, 152, 102	0.807
rs7763637	1	*ESR1*	138, 135, 23	0.055
rs7763637	1	*RMND1*	97, 101, 19	0.708
rs7763637	1	*C6orf211*	70, 77, 11	0.202
rs7763637	1	*CCDC170*	113, 143, 20	0.425
rs9397437	2	***ESR1***	250, 47, 2	**0.039***
rs9397437	2	*RMND1*	185, 31, 2	0.479
rs9397437	2	*C6orf211*	136, 22, 1	0.369
rs9397437	2	***CCDC170***	222, 55, 2	**0.010***
rs851985	3	***ESR1***	55, 139, 105	**0.032***
rs851985	3	*RMND1*	37, 98, 83	0.087
rs851985	3	*C6orf211*	26, 65, 68	0.276
rs851985	3	*CCDC170*	44, 128, 107	0.610
rs851983	3	*ESR1*	106, 140, 53	0.058
rs851983	3	***RMND1***	84, 97, 37	**0.016***
rs851983	3	*C6orf211*	68, 64, 27	0.128
rs851983	3	*CCDC170*	108, 128, 43	0.230

*$P<0.05$

Supplementary Table 10. Associations of signal representative SNPs with expression of target genes in 183 normal breast samples from the GTEx database[6].

Risk SNP	Signal	Target gene	# samples (AA,AB,BB)	*P*-value
rs3757322	1	*ESR1*	89, 73, 21	0.12
		RMND1		0.79
		CCDC170		0.17
rs9397437	2	*ESR1*	160, 22, 1	0.32
		RMND1		0.61
		CCDC170		0.057
rs851984	3	*ESR1*	64, 95, 24	0.54
		RMND1		0.65
		CCDC170		**0.039***
rs9918437	4	*ESR1*	148, 35, 0	0.36
		RMND1		0.45
		CCDC170		0.23
rs2747652	5	*ESR1*	46, 90, 47	0.88
		RMND1		0.60
		CCDC170		0.81

*$P<0.05$

Supplementary Table 11. Associations of signal-representative SNPs with expression of 12 local genes in 135 normal breast samples from the METABRIC study.

SIGNAL	*Representative SNP*	**Chr Position (GRch37)**	**Alleles**	**MAF**	**Imp r^2**	**Overall Breast Cancer Risk**	**Normal breast eQTL (n=135)**											
							AKAP12	*C6ORF211*	*CCDC170*	*ESR1*	*FBXO5*	*MTHFD1L*	*MTRF1L*	*MYCT1*	*PLEKHG1*	*RMND1*	*SYNE1*	*ZBTB2*
							Per-allele *P*-trend											
1	rs3757322	1.52E+08	G/T	0.33	1.00	8.15E-17	0.554	0.575	0.460	0.473	0.031	0.921	0.524	0.599	0.604	0.221	0.315	0.840
2	rs9397437	1.52E+08	G/A	0.07	1.00	4.03E-22	0.223	0.882	0.791	0.085	0.207	0.115	0.149	0.789	0.831	0.915	0.479	0.296
3	rs851984	1.52E+08	G/A	0.41	1.00	2.71E-07	0.616	0.780	0.052	0.597	0.580	0.519	0.342	0.662	0.813	0.097	0.234	0.408
4	rs9918437	1.52E+08	G/T	0.07	1.00	5.63E-07	0.408	**0.008**	0.099	0.233	0.074	0.011	0.692	0.958	0.286	0.179	0.213	0.160
5	rs2747652	1.52E+08	T/C	0.54	1.00	2.24E-12	0.764	0.712	0.469	0.627	0.789	0.454	0.514	0.626	0.251	0.131	0.512	0.921
*****	6-151580765	1.52E+08	A/G	0.44	0.97	0.28	0.217	0.076	0.683	0.447	0.541	0.311	**3.53E-05**	0.586	0.870	0.902	0.025	0.606
	6-151591385	1.52E+08	G/A	0.11	0.98	0.60	0.210	0.087	0.993	0.311	0.902	0.537	0.857	0.129	0.004	0.480	**3.37E-04**	0.140
	c6_pos1516424	1.52E+08	G/A	0.04	0.99	0.17	0.103	0.479	**6.36E-03**	0.568	0.515	0.664	0.046	0.034	0.245	0.864	0.691	0.238
	6-151702442	1.52E+08	G/C	0.33	0.97	0.06	0.002	0.001	0.583	0.469	0.022	0.005	0.223	**1.15E-04**	0.031	0.728	0.069	0.371
	6-151712279	1.52E+08	T/C	0.27	0.91	0.01	0.003	**2.49E-04**	0.064	0.164	0.019	0.004	0.205	0.007	0.045	0.719	0.142	0.281
	6-151729581	1.52E+08	G/C	0.20	0.93	0.01	0.000	0.003	0.186	0.533	0.001	**5.76E-04**	0.138	0.016	0.117	0.999	0.258	0.144
	6-152020999	1.52E+08	C/T	0.02	0.68	0.98	**1.68E-06**	0.291	0.744	0.433	0.660	0.736	0.002	0.781	0.368	0.232	0.382	0.111
	rs4365941	1.52E+08	G/A	0.96	1.00	0.91	0.238	0.000	0.493	**1.04E-04**	0.141	0.340	0.265	0.822	0.123	0.479	0.039	0.796
	rs2763031	1.52E+08	T/G	0.35	1.00	0.75	0.007	0.168	0.617	0.528	0.546	0.057	0.337	0.189	**1.20E-03**	0.373	0.084	0.463
	c6_pos1526064	1.53E+08	A/G	0.08	1.00	0.91	0.037	0.540	0.035	0.410	0.136	0.004	0.011	0.057	0.285	**3.62E-04**	0.148	0.266
	6-152569070	1.53E+08	A/G	0.04	0.97	0.45	0.011	0.322	0.395	0.152	**2.00E-04**	0.289	0.513	0.130	0.917	0.594	0.014	0.923
	6-152573028	1.53E+08	A/AT	0.94	0.36	0.27	0.406	0.005	0.155	0.563	0.040	0.998	0.382	0.198	0.657	0.534	0.064	**2.32E-03**

* The strongest associations of each gene probe with any of the 3872 SNPs in the locus. Bolded values are positive controls.

Supplementary Table 12. Summary of functional evidence for the seven prioritized candidate causal SNPs across the signals.

Signal	Candidate SNP	PRE[1]	Target genes identified by 3C[2] experiments				Luciferase activities		*In vitro* TF binding (EMSA)[4]	*In vivo* TF binding (ChIP)[5]
			MCF7 (ER+)	T47D (ER+)	Bre-80 (ER-)	MCF10A (ER-)	Individual SNP[3]	Haplotype		
1	rs7763637	enhancer	*ESR1A* *ESR1B* *RMND1* *C6orf211* *CCDC170*	*ESR1A* *ESR1B* *RMND1* *C6orf211* *CCDC170*	*ESR1A* - *RMND1* *C6orf211* -	*ESR1A* - *RMND1* *C6orf211* *CCDC170*	No effect ↓ prom activity No effect No effect No effect	↓ prom activity No effect ↓ prom activity No effect ↓ prom activity	Not identified	-
1	rs6557160	enhancer	*ESR1A* *ESR1B* *RMND1* *C6orf211* *CCDC170*	*ESR1A* *ESR1B* *RMND1* *C6orf211* *CCDC170*	*ESR1A* - *RMND1* *C6orf211* -	- - *RMND1* *C6orf211* *CCDC170*	↓ prom activity No effect ↓ prom activity No effect No effect	↓ prom activity No effect ↓ prom activity No effect ↓ prom activity	Not identified	-
2	rs17081533	enhancer	*ESR1A* *ESR1B* *RMND1* *C6orf211* *CCDC170*	*ESR1A* *ESR1B* *RMND1* *C6orf211* *CCDC170*	*ESR1A* - *RMND1* *C6orf211* -	- *RMND1* *C6orf211* *CCDC170*	↓ prom activity No effect ↓ prom activity No effect No effect	- - - - -	Not identified	-
3	rs851983	silencer	*ESR1B* *RMND1* *C6orf211*	*ESR1B* *RMND1* *C6orf211*	*RMND1* *C6orf211* -	- - -	No effect No effect No effect	↑ prom activity ↑ prom activity No effect	CTCF	enriched (BT474)
3	rs851982	silencer	*ESR1B* *RMND1* *C6orf211*	*ESR1B* *RMND1* *C6orf211*	*RMND1* *C6orf211* -	- - -	↑ prom activity ↑ prom activity No effect	↑ prom activity ↑ prom activity No effect	GATA3	enriched (BT474)
4	rs1361024	enhancer	*ESR1A* *RMND1* *C6orf211*	- - -	*RMND1* *C6orf211* -	- - -	No effect No effect No effect	- - -	CTCF	enriched (BT474)
5	rs910416	enhancer	*ESR1A*	*ESR1A*	-	-	↓ prom activity	-	C-MYC	Not detected

[1]PRE=putative regulatory element, [2]3C=chromosome conformation capture, [3]prom=promoter, [4]EMSA=electrophoretic mobility shift assay, [5]ChIP=chromatin immunoprecipitation.

Supplementary Table 13. Predicted effects of candidate casual variants on transcription factor binding motifs.

rsID	Position	Signal	TFBS[a]	Motif change[b]	Expression[c] HMEC	Expression[c] MCF7
rs6557160	151949582	1	SIX5	++	░	
rs6557160	151949582	1	SMAD3	++	░	▒
rs6557160	151949582	1	CEBPα	-		░
rs851983	152024415	3	NR1D1	++	░	░
rs910416	152432902	5	ARNT	--	░	▒
rs910416	152432902	5	FOXA1	+		█
rs910416	152432902	5	MXI1	--	░	░
rs910416	152432902	5	MYC	-	█	▓
rs910416	152432902	5	OCT1	+	░	░
rs910416	152432902	5	AP2	-	▒	▓

[a] Altered transcription factor binding site (TFBS) determined by HaploReg[3] v3 or AliBaba2[7] (TRANSFAC and JASPAR matrices).

[b] Degree of change to motif for minor allele: + increased agreement with consensus, - decreased.

[c] Expression levels measured by ENCODE RNA-seq accessed via EBI Expression Atlas[8], where darker colour represents higher expression.

Supplementary Table 14. MODE consortium study details.

Study	Country	Design	Number of Cases/Controls	Mean Age (SD), years	Mean Body Mass Index (SD), kg/m2	% Pre-menopausal women	% Current HRT user	Mammogram view	MD measurement software
Australian Breast Cancer Family Study	Australia	Population-based case-control study	104/0	39.5 (6.3)	23.7 (3.8)	71.2	3.8	CC	Cumulus
Bavarian Breast Cancer Cases and Controls	Germany	Hospital based cases; population based controls	510/361	59.5 (11.6)	26.3 (5.1)	25.7	11.2	CC	Cumulus
EPIC-NORFOLK	UK	Population-based cohort study	86/957	66.0 (6.1)	27.8 (4.9)	24.1	20.4	MLO	Cumulus
Mayo Clinic Breast Cancer Study	USA	Clinic-based breast cancer case-control study	671/860	60.0 (11.5)	28.0 (5.6)	24.1	13.5	CC	Cumulus
Melbourne Collaborative Cohort Study	Australia	Population-based prospective cohort study	68/28	59.1 (7.1)	27.3 (4.9)	21.9	13.8	CC	Cumulus
Multi-ethnic Cohort	USA	Prospective cohort study: nested case-control	110/101	58.5 (8.9)	25.6 (5.9)	17.5	54.0	CC	Cumulus
Mayo Mammography Health Study	USA	Nested breast cancer case-control study	455/1166	60.9 (11.0)	28.2 (6.4)	24.9	23.3	CC	Cumulus
Norwegian Breast Cancer Study	Norway	Hospital-based case-control study	0/40	64.5 (5.5)	27.1 (4.8)	12.5	-	CC	Cumulus
Ontario Familial Breast Cancer Registry	Canada	Population-based familial case-control study	86/0	54.5 (7.0)	26.6 (4.8)	18.6	1.2	CC	Cumulus
Singapore and Sweden Breast Cancer Study	Sweden	Retrospective breast cancer case control study	865/773	62.5 (6.4)	25.6 (4.0)	2.4	23.3	MLO	Cumulus
Sisters in Breast Screening	UK	Population-based cohort study	0/1359	59.5 (6.2)	27.0 (5.1)	13.0	13.8	MLO	Cumulus
			2955/5645	60.9 (9.6)	27.1 (5.4)	18.8	18.7		

Supplementary Table 15. Oligonucleotides used in 3C assays.

3C Primers (*Eco*RI)	3C Fragment (hg19 coord)	Sequence (5' to 3')
C6orf211 prom bait	151,768,128	AAGGAGCCATGCCACACAGTTTTCTATCTTCC
CCDC170 prom bait	151,809,872	GTGGGCAGAATCAGAGCAGCTCTGTGC
ESR1A prom bait	152,010,205	CCAGAATGGGTGAAGTATGCTTTTCAAACAGC
ESR1B prom bait	152,124,412	CATAACCAACCTGTGGAAGGCATGAACACC
Signal 1/2 Fragment 1	151,930,241	GCAACCAACACTCATCTCTACCCCAAAGAAGG
Signal 1/2 Fragment 2	151,936,490	TGGCACACAATTCCCAATTTCACAAATTCC
Signal 1/2 Fragment 3	151,939,509	GTTAATGTTTCAGCAGGGCTGGTCTCAGTCC
Signal 1/2 Fragment 4	151,940,487	GGCTTGCTTGAAAGATTCAGGGGTAGACTAGC
Signal 1/2 Fragment 5	151,943,670	GATGGACTAATGGACGATAACTGGCAGTTTGG
Signal 1/2 Fragment 6	151,948,649	GTGCCAAATAGTACACCAAGCATTTCCATGC
Signal 1/2 Fragment 7	151,949,449	ATGGGCAGCTGAAGGACCCATTAGAAGG
Signal 1/2 Fragment 8	151,959,562	GCATGTGGCTATCTAGTTGCTCCAGCACC
Signal 1/2 Fragment 9	151,962,081	CCAAATACCTTGCATTAGGCCCAACCTCC
Signal 1/2 Fragment 10	151,966,431	GCTACCCCTACTCACTTTTGGTGTCCATTTGC
Signal 1/2 Fragment 11	151,968,435	GAAGGAGGAGTTGAGGAGATATCGGTCAAAGC
Signal 3/4 Fragment 1	152,012,876	TTCCCACTGGACCCAACAGCAAAAGC
Signal 3/4 Fragment 2	152,014,089	TGCCTCTAAATTGCACAGCTAGAGAGTGGTGG
Signal 3/4 Fragment 3	152,021,922	TTTACTGTGGGTCATCAGCCTAAGCTGTTGG
Signal 3/4 Fragment 4	152,034,576	CCATTAATATTGGCTGACCCCGGTGGTAGG
Signal 3/4 Fragment 5	152,039,012	CAACACCAACAAAGAGCTCCTCCACACTCC
Signal 3/4 Fragment 6	152,041,581	TCCCAAAGGCTTTAATGTGCTAATCTGCACTG
Signal 3/4 Fragment 7	152,045,149	TGAGCATTTTCTACATGAAGGGCATTACCAGG
Signal 3/4 Fragment 8	152,047,035	TGCATACATCAAACACCCCTGTGGTTTTCC
Signal 3/4 Fragment 9	152,048,904	AGATGGCAAAGGAGTAGCCAAGGCACG
Signal 3/4 Fragment 10	152,057,853	TGACATCCCTCCAGCTCCACATATTCTATAAGAGC
Signal 3/4 Fragment 11	152,059,922	CTGCCAGTTCCTAACTGCGGAAACTTGG
Signal 3/4 Fragment 12	152,064,247	TGGTGGCATCTCTCATTAGAACAGGTAGTCACC
Signal 3/4 Fragment 13	152,065,381	CAATGGCAAAATGGACGCACTCTGAAATG
Signal 3/4 Fragment 14	152,073,572	GACTATGATGATGCAGAATGAAGACCTGGAGAGG
Signal 3/4 Fragment 15	152,075,281	GTGTGCTTCTAAACAGAGGCCATTTCGAGG
Signal 5 Fragment 1	152,417,744	AGAATGCCATTTGCCTACATTTCCCTCTGC
Signal 5 Fragment 2	152,418,967	GCAGGCTCAGCCTTCCTCTTTCACACC
Signal 5 Fragment 3	152,428,613	GCCAAGGGATTTGCAGAACCTTCTGAGC
Signal 5 Fragment 4	152,434,065	TGTCTGCTCGCAATGGAATGGAGAAGG
Signal 5 Fragment 5	152,442,590	GGTAGATTGTACGACACTGACATGGTGCTTGG
Signal 5 Fragment 6	152,443,277	GTGGGAAGGACCAAATGAAATAGCCAGTCC
Signal 5 Fragment 7	152,450,932	CGGAGCCTGTTTTCATTCCAGTCCCTAGC
Signal 5 Fragment 8	152,451,478	TGGCACCACTGCCATTTGATTCATGG

*Hin*dIII *ESR1A* prom	152,011,388	CCAGGCCCGAATCTAACTTTCTTAGCACTTCC
*Hin*dIII *RMND1* prom	152,127,909	CATGCCTTCCACAGGTTGGTTATGCAACC
Signal 3-PRE allele specific 3C	152,023,473	AACCTAAGTGACACAGTTACCCAGGCAGATGC
Signal 3-PRE allele specific seq	152,023,473	GTATGGATCTCATACCATTTTCAGC
*Bgl*II *ESR1B* prom	152,007,472	TCAGGACTTGTGATCATGGCAATGGTTCC
*Bgl*II *RMND1* prom	151,767,593	GGAATGTTCATGTGTGTATCTGACATGCCTCG
Signal 4-PRE allele specific 3C	152,066,960	GTTGATCAACCTCTCCCCATAGCCATTTCC
Signal 4-PRE allele specific seq	152,066,960	CTAACTGGGTGACCCTGTGC

Supplementary Table 16. Oligonucleotides used in EMSAs.

Signal	SNP	allele[a]	Sequence (5’ to 3’)[b]
1	rs7763637	com	$^{\text{BIO}}$CCAAGCATTTCCAT**G**CACAATCACTCGTG
		min	$^{\text{BIO}}$CCAAGCATTTCCAT**A**CACAATCACTCGTG
	rs6557160	com	$^{\text{BIO}}$CAAACTTTATTAGC**A**AGACGGTAATTTTT
		min	$^{\text{BIO}}$CAAACTTTATTAGC**C**AGACGGTAATTTTT
	rs6900157	com	$^{\text{BIO}}$GAATTATTAAATTA**T**TGATGCTTTAACAA
		min	$^{\text{BIO}}$GAATTATTAAATTA**C**TGATGCTTTAACAA
2	rs1217357	com	$^{\text{BIO}}$CAGGTGTGAGCCAC**C**GTGTCCTGCTTGAG
		min	$^{\text{BIO}}$CAGGTGTGAGCCAC**T**GTGTCCTGCTTGAG
	rs1708153	com	$^{\text{BIO}}$TTTTTGTAAGATTC**T**TTTGTGAAGTTCAG
		min	$^{\text{BIO}}$TTTTTGTAAGATTC**C**TTTGTGAAGTTCAG
3	rs851984	com	$^{\text{BIO}}$CTGACTTTGTCCGT**G**AATTGATAAGATCT
		min	$^{\text{BIO}}$CTGACTTTGTCCGT**A**AATTGATAAGATCT
	rs851983	com	$^{\text{BIO}}$TAAATAAAGTCACC**A**CTTCCAGGCTTAGC
		min	$^{\text{BIO}}$TAAATAAAGTCACC**G**CTTCCAGGCTTAGC
	rs851982	com	$^{\text{BIO}}$TTAGATCCAAAACT**T**TGATTCCAGAAAGG
		min	$^{\text{BIO}}$TTAGATCCAAAACT**C**TGATTCCAGAAAGG
4	rs1361024	com	$^{\text{BIO}}$ATATTTTTAGCTCC**G**TGGGGGAAAAAGAA
		min	$^{\text{BIO}}$ATATTTTTAGCTCC**A**TGGGGGAAAAAGAA
	rs9918437	com	$^{\text{BIO}}$AGGGAGAAATTTAG**G**GGGGAAAAATCCCA
		min	$^{\text{BIO}}$AGGGAGAAATTTAG**T**GGGGAAAAATCCCA
5	rs910416	com	$^{\text{BIO}}$GTAGCTGCTTTACA**C**GTGGTCTCAGTGCC
		min	$^{\text{BIO}}$GTAGCTGCTTTACA**T**GTGGTCTCAGTGCC

[a] com: common allele, min: minor allele

[b] BIO: 5’ biotinylation (present on both the sense and antisense strands of the duplex)

Supplementary Table 17. EMSA competitor duplexes and their target DNA binding proteins.

Competition Target	**Sequence (5' to 3')**
AP1	CGCTTGATGACTCAGCCGGAA
AP2	GATCGAACTGACCGCCCGCGGCCCGT
CEBP	TGCAGATTGCGCAATCTGCA
CTCF	AAGAAACCGCTAGGGGGCCTACT
EGR1	CTCGCGGGGGTGGGGGGCGGAG
FOXA1	CTGGTCTTAAAGGTGTTTACCTTGTCTGAT
ER	GGATCTAGGTCACTGTGACCCCGGATC
FOXM1	CTCTTCAAGATGGAGTCGCTCTGGTTC
GABP	TCGAGCAGGAAGAGGAAGTCTCGA
GATA3	CACTTGATAACAGAAAGTGATAACTCT
MYC	TCAGACCACGTGGTCGGG
NFkB	AGTTGAGGGGACTTTCCCAGGC
NRSF	GCAAAGCCATTCAGCACCACGGAGAGTGCCTCTGC
OCT	TGTCGAATGCAAATCACTAGAA
TCF4	ATAAATCACTATCAAAGGATAGAATTT

Supplementary Table 18. Oligonucleotides used for ChIP analyses.

Primer name	**Sequence (5' to 3')**
ChIP negcontrol FOR1	CTAAGGACGAGATGCACATGG
ChIP negcontrol REV1	TCAAGTTTCCAACTCCAACAGG
ChIP Signal 3 rs851982 FOR	CTACACATGTCAGTCCCTGAGTAGTC
ChIP Signal 3 rs851982 REV	GCGCAATAGCGTCTAGAATCC
ChIP Signal 3 rs851983 FOR	CCCTACTGCATAAGAAATGAAGG
ChIP Signal 3 rs851983 REV	CTCCAGCCTCAGAAGACTGG
ChIP Signal 4 rs1361024 FOR	TGTGCCTCCACATTATTCTGG
ChIP Signal 4 rs1361024 REV	GGTCTCTGTAACTTGTTTCTGAATGAG
ChIP Signal 5 rs910416 FOR	CTGAGTATTTCCACATTTCCAACC
ChIP Signal 5 rs910416 REV	GAAATGCTTCCCTTGCTGG

SUPPLEMENTARY NOTE

Intra-genomic replicates (IGR)

The IGR computational method[4] estimates the modulation in transcription factor affinity produced by a variant or mutation. More generally, it computes the difference in any genomic annotation between the alleles of a variant based on the underlying k-mer composition of the region. In this study, the method makes use of transcription factor ChIP-seq data. The core operation in IGR is to obtain an estimate of the affinity between a sequence of length k (a k-mer) and a transcription factor. This is done in the following manner: (1) all instances of the k-mer are searched across the genome, (2) the binding information at each of the instances of the k-mer is retrieved from the ChIP-seq data, and (3) the signal from the ChIP-seq data set is averaged over all instances to obtain an affinity profile for that k-mer. This process is repeated for all possible k-mers, and the collection of affinity profiles is stored in a lookup table that is indexed by the k-mers. In order to estimate the change in affinity between alleles, we slide a window of size k over the location of the variant for each allele. In doing so we obtain a collection of k-mers for each allele based on the genomic context of the variant. The affinity profile for each k-mer is then obtained from the lookup table. Each of these profiles is derived from a different number of instances depending on the frequency of the k-mer in the genome. We define the collection of affinity profiles for all k-mers associated with an allele and its sequence context as the affinity lattice for that allele. In this study we use seven and eight as values of k when constructing the affinity lattices. Similarly, we define the lookup table of affinity profiles over all possible k-mers as the affinity model for that ChIP-seq data set. We can now compare the affinity lattices between alleles to infer their impact on transcription factor binding affinity. For each value of k the maximum affinity profiles are compared between the alleles. The comparison between maxima represents the highest possible affinity for each allele given its genomic context. Note that if a binding motif of high affinity is altered by a variant allele, the binding factor can possibly find a higher affinity configuration than the altered motif sequence by moving a few bases or reversing its orientation. The selection of maxima in the comparison of alleles allows IGR to account for such displacements. Statistical significance of the affinity modulation between the two alleles is assessed with a t test. Results are Bonferroni corrected based on the total number of tests, which is the number of variants times the number of affinity models times the number of values for k. The basic application of IGR is further expanded through the use of two types of filters: k-mer filters and result filters.

IGR k-mer filters. The k-mer filters restrict the k-mer search for the affinity profiles to chromatin regions that are capable of binding the factor under study. For instance, only k-mer matches that fall within H3K4me2 or DNase I hypersensitive regions are considered for the FOXA1 pioneer factor. However, some factors do not require any known marks or open chromatin. In this case, no k-mer filters will be applied, as any region in the genome can bind the factor if the sequence is favourable. Because the SNPs studied as part of this study are from individuals that develop cancer, where elements that are regularly repressed in breast tissue can become aberrantly activated, we used all k-mer instances that occurred within any known DNaseI hypersensitive region across all profiled ENCODE cell types as our k-mer filter.

IGR results filters. A number of results filters (*completeness*, *complexity*, *shuffle* and *fold change*) are imposed on the Bonferroni-corrected significant results to attempt to lower the rate of false positives. The *completeness* filter keeps results where at least ¾ of the k-mer entries in the lattice in both alleles have at least 683 instances genome wide. We chose 683 instances as the cut-off because in the clustered ENCODE DNaseI hypersensitive regions 95% of k-mers have at least that many instances. Lattice entries with few instances are noisy and confound the comparison of k-mers within and between lattices. The *complexity* filter removes results where the SNP dramatically changes the complexity of the surrounding sequence. In order to find sequences with similar uniqueness properties, the number of possible permutations for each of the reference and alternate alleles is computed from the nucleotide composition. Then results in which the ratio of possible permutations was greater than 3:1 were excluded, as these cases were deemed more likely to have problematic mapping properties which could interfere with proper estimation. The *shuffle* filter forces the affinity profile of at least one of the two allele's highest affinity k-mer in the lattice to be higher that what we observe in a set of shuffled versions of that same k-mer. This indicates that the affinity for that k-mer is driven by the actual sequence and not just its composition, under the assumption that certain factors might be biased towards specific nucleotide distributions without binding directly to a given k-mer sequence (for instance, due to differences in major and minor groove width). We generate 10,000 shuffled versions of each the highest affinity k-mers, we keep the results where either the reference or alternate allele was higher than at least 95% of all shuffled k-mers. The *fold change* filter restricts results to fold changes greater than 4/3 or smaller than ¾ in order to enrich for changes in binding that are more likely to be biologically significant and amenable to experimental validation. Results that are removed by any of these filters may still alter transcription factor binding in such a way that is biologically relevant, but with the filters we intend to highlight the results that are the most biologically interpretable and, hopefully, reproducible.

IGR analysis. We built affinity models using IGR for the following transcription factors: FOXA1 (in MCF7, T47D, LNCaP and VCAP), GATA3 (in MCF7 and T47D), CTCF (in MCF7, HMEC, LNCaP and PrEC), and EGR1, ELF1, FOXM1, GABP, GATA3, JUND, MAX, NR2F2, NRSF, PML, RAD21, STAG1, C-MYC (in MCF7). These affinity models are then used to score each of the SNPs in the study for affinity modulation.

Supplementary References

1. Corradin, O. et al. Combinatorial effects of multiple enhancer variants in linkage disequilibrium dictate levels of gene expression to confer susceptibility to common traits. Genome Res 24, 1-13 (2014).
2. Hnisz, D. et al. Super-enhancers in the control of cell identity and disease. Cell 155, 934-47 (2013).
3. Ward, L.D. & Kellis, M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. Nucleic Acids Res 40, D930-4 (2012).
4. Cowper-Sal lari, R. et al. Breast cancer risk-associated SNPs modulate the affinity of chromatin for FOXA1 and alter gene expression. Nat Genet 44, 1191-8 (2012).
5. The Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. Nature 490, 61-70 (2012).
6. Lonsdale, J. et al. The Genotype-Tissue Expression (GTEx) project. Nat Genet 45, 580-585 (2013).
7. Grabe, N. AliBaba2: context specific identification of transcription factor binding sites. In Silico Biol 2, S1-15 (2002).
8. Petryszak, R. et al. Expression atlas update-a database of gene and transcript expression from microarray- and sequencing-based functional genomics experiments. Nucleic Acids Res 42, D926-324 (2013).

Supplementary Acknowledgements

M.D. and E.L.-K. were funded through NIHR BRC at the Royal Marsden Hospital and Breast Cancer Now. D.F.E. is a Principal Research Fellow of CR-UK. G.C.-T. is an NHMRC Senior Principal Research Fellow. S.L.E., J.D.F. and K.-A.P. are supported by Fellowships from the National Breast Cancer Foundation (NBCF) Australia. The QIMR Berghofer groups were supported by a NHMRC project grant (1058415 to S.L.E. and J.D.F).

BCAC studies. BCAC is funded by Cancer Research UK [C1287/A10118, C1287/A12014] and by the European Community´s Seventh Framework Programme under grant agreement number 223175 (grant number HEALTH-F2-2009-223175) (COGS). ABCFS: Maggie Angelakos, Judi Maskiell, Gillian Dite. The Australian Breast Cancer Family Study (ABCFS) was supported by grant UM1 CA164920 from the National Cancer Institute (USA). The content of this manuscript does not necessarily reflect the views or policies of the National Cancer Institute or any of the collaborating centers in the Breast Cancer Family Registry (BCFR), nor does mention of trade names, commercial products, or organizations imply endorsement by the USA Government or the BCFR. The ABCFS was also supported by the National Health and Medical Research Council of Australia, the New South Wales Cancer Council, the Victorian Health Promotion Foundation (Australia) and the Victorian Breast Cancer Research Consortium. J.L.H. is a National Health and Medical Research Council (NHMRC) Australia Fellow and a Victorian Breast Cancer Research Consortium Group Leader. M.C.S. is a NHMRC Senior Research Fellow and a Victorian Breast Cancer Research Consortium Group Leader. ABCS: Sten Cornelissen, Richard van Hien, Linde Braaf, Frans Hogervorst, Senno Verhoef, Laura van 't Veer, Emiel Rutgers, C Ellen van der Schoot, Femke Atsma. The ABCS study was supported by the Dutch Cancer Society [grants NKI 2007-3839; 2009 4363]; BBMRI-NL, which is a Research Infrastructure financed by the Dutch government (NWO 184.021.007); and the Dutch National Genomics Initiative. ACP: The ACP study wishes to thank the participants in the Thai Breast Cancer study. Special Thanks also go to the Thai Ministry of Public Health (MOPH), doctors and nurses who helped with the data collection process. Finally, the study would like to thank Dr Prat Boonyawongviroj, the former Permanent Secretary of MOPH and Dr Pornthep Siriwanarungsan, the Department Director-General of Disease Control who have supported the study throughout. The ACP study is funded by the Breast Cancer Research Trust, UK. BBCC: The work of the BBCC was partly funded by ELAN-Fond of the University Hospital of Erlangen. BBCS: Eileen Williams, Elaine Ryder-Mills, Kara Sargus. The BBCS is funded by Cancer Research UK and Breakthrough Breast Cancer and acknowledges NHS funding to the NIHR Biomedical Research Centre, and the National Cancer Research Network (NCRN). BIGGS: Niall McInerney, Gabrielle Colleran, Andrew Rowan, Angela Jones. ES is supported by NIHR Comprehensive Biomedical Research Centre, Guy's & St. Thomas' NHS Foundation Trust in partnership with King's College London, United Kingdom. IT is supported by the Oxford Biomedical Research Centre. BSUCH: Peter Bugert, Medical Faculty Mannheim. The BSUCH study was supported by the Dietmar-Hopp Foundation, the Helmholtz Society and the German Cancer Research Center (DKFZ). CCGCRN: Patients were recruited for study from the City of Hope Clinical Cancer Genomics Community

Research Network, supported in part by Award Number RC4CA153828 (PI: J. Weitzel) from the National Cancer Institute and the Office of the Director, National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. CECILE: The CECILE study was funded by Fondation de France, Institut National du Cancer (INCa), Ligue Nationale contre le Cancer, Ligue contre le Cancer Grand Ouest, Agence Nationale de Sécurité Sanitaire (ANSES), Agence Nationale de la Recherche (ANR). CGPS: Staff and participants of the Copenhagen General Population Study. For the excellent technical assistance: Dorthe Uldall Andersen, Maria Birna Arnadottir, Anne Bank, Dorthe Kjeldgård Hansen. The CGPS was supported by the Chief Physician Johan Boserup and Lise Boserup Fund, the Danish Medical Research Council and Herlev Hospital. CNIO-BCS: Guillermo Pita, Charo Alonso, Daniel Herrero, Nuria Álvarez, Pilar Zamora, Primitiva Menendez, the Human Genotyping-CEGEN Unit (CNIO). The CNIO-BCS was supported by the Genome Spain Foundation, the Red Temática de Investigación Cooperativa en Cáncer and grants from the Asociación Española Contra el Cáncer and the Fondo de Investigación Sanitario (PI11/00923 and PI081120). The Human Genotyping-CEGEN Unit (CNIO) is supported by the Instituto de Salud Carlos III. CTS: The CTS Steering Committee includes Leslie Bernstein, Susan Neuhausen, James Lacey, Sophia Wang, Huiyan Ma, Yani Lu, and Jessica Clague DeHart at the Beckman Research Institute of City of Hope, Dennis Deapen, Rich Pinder, Eunjung Lee, and Fred Schumacher at the University of Southern California, Pam Horn-Ross, Peggy Reynolds, Christina Clarke Dur and David Nelson at the Cancer Prevention Institute of California, and Hoda Anton-Culver, Argyrios Ziogas, and Hannah Park at the University of California Irvine. The CTS was initially supported by the California Breast Cancer Act of 1993 and the California Breast Cancer Research Fund (contract 97-10500) and is currently funded through the National Institutes of Health (R01 CA77398). Collection of cancer incidence data was supported by the California Department of Public Health as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885. HAC receives support from the Lon V Smith Foundation (LVS39420). ESTHER: Hartwig Ziegler, Sonja Wolf, Volker Hermann. The ESTHER study was supported by a grant from the Baden Württemberg Ministry of Science, Research and Arts. Additional cases were recruited in the context of the VERDI study, which was supported by a grant from the German Cancer Aid (Deutsche Krebshilfe). GC-HBOC: Heide Hellebrand, Stefanie Engert and GC-HBOC (Supported by Deutsche Krebshilfe). The GC-HBOC was supported by Deutsche Krebshilfe (107 352). b: The GENICA Network: Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, and University of Tübingen, Germany [HB, Wing-Yee Lo, Christina Justenhoven], German Cancer Consortium (DKTK) and German Cancer Research Center (DKFZ) [HB], Department of Internal Medicine, Evangelische Kliniken Bonn gGmbH, Johanniter Krankenhaus, Bonn, Germany [Yon-Dschun Ko, Christian Baisch], Institute of Pathology, University of Bonn, Germany [Hans-Peter Fischer], Molecular Genetics of Breast Cancer, Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany [UH], Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr University Bochum (IPA), Bochum, Germany [Thomas Bruening, Beate Pesch, Sylvia Rabstein, Anne Lotz]; and Institute of Occupational Medicine and Maritime Medicine, University Medical Center Hamburg-Eppendorf, Germany [Volker Harth]. The GENICA was funded by the Federal Ministry of Education and Research (BMBF) Germany grants 01KW9975/5, 01KW9976/8, 01KW9977/0 and 01KW0114, the Robert Bosch Foundation, Stuttgart, Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, the Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr University Bochum (IPA), Bochum, as well as the Department of Internal Medicine, Evangelische Kliniken Bonn gGmbH, Johanniter Krankenhaus, Bonn, Germany. HEBCS: Kirsimari Aaltonen, Karl von Smitten, Sofia Khan, Tuomas Heikkinen, Irja Erkkilä. The HEBCS was financially supported by the Helsinki University Central Hospital Research Fund, Academy of Finland (266528), the Finnish Cancer Society, The Nordic Cancer Union and the Sigrid Juselius Foundation. HERPACC: The HERPACC was supported by a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science, Sports, Culture and Technology of Japan, by a Grant-in-Aid for the Third Term Comprehensive 10-Year Strategy for Cancer Control from Ministry Health, Labour and Welfare of Japan, by Health and Labour Sciences Research Grants for Research on Applying Health Technology from Ministry Health, Labour and Welfare of Japan, National Cancer Center Research and Development Fund and Grant form Takeda Health Foundation. HMBCS: Peter Hillemanns, Hans Christiansen and Johann H. Karstens. The HMBCS was supported by a grant from the Friends of Hannover Medical School and by the Rudolf Bartling Foundation. KARBAC: Financial support for KARBAC was provided through the regional agreement on medical training and clinical research (ALF) between Stockholm County Council and Karolinska Institutet, the Swedish Cancer Society, The Gustav V Jubilee foundation and Bert von Kantzows foundation. KBCP: Eija Myöhänen, Helena Kemiläinen. The KBCP was financially supported by the special Government Funding (EVO) of Kuopio University Hospital grants, Cancer Fund of North Savo, the Finnish Cancer Organizations, and by the strategic funding of the University of Eastern Finland. kConFab/AOCS: We wish to thank Heather Thorne, Eveline Niedermayr, all the kConFab research nurses and staff, the heads and staff of the Family Cancer Clinics, and the Clinical Follow Up Study (which has received funding from the NHMRC, the National Breast Cancer Foundation, Cancer Australia, and the National Institute of Health (USA)) for their contributions to this resource, and the many families who contribute to kConFab. kConFab is supported by a grant from the National Breast Cancer Foundation, and previously by the National Health and Medical Research Council (NHMRC), the Queensland Cancer Fund, the Cancer Councils of New South Wales, Victoria, Tasmania and South Australia, and the Cancer Foundation of Western Australia. Financial support for the AOCS was provided by the United States Army Medical Research and Materiel Command [DAMD17-01-1-0729], Cancer Council Victoria, Queensland Cancer Fund, Cancer Council New South Wales, Cancer Council South Australia, The Cancer Foundation of Western Australia, Cancer Council Tasmania and the National Health and Medical Research Council of Australia (NHMRC; 400413, 400281, 199600). G.C.T. and P.W. are supported by the NHMRC. RB was a Cancer Institute NSW Clinical Research Fellow. LAABC: We thank all the study participants and the entire data collection team, especially Annie Fung and June Yashiki. LAABC is supported by grants (1RB-0287, 3PB-0102, 5PB-0018, 10PB-0098) from the California Breast Cancer Research Program. Incident breast cancer cases were collected by the USC Cancer Surveillance Program (CSP) which is supported under subcontract by the California Department of Health. The CSP is also part of the National Cancer Institute's Division of Cancer Prevention and Control Surveillance, Epidemiology, and End Results Program, under contract number N01CN25403. LMBC: Gilian Peuteman, Dominiek Smeets, Thomas Van Brussel and Kathleen Corthouts. LMBC is supported by the 'Stichting tegen Kanker' (232-2008 and 196-2010). Diether Lambrechts is supported by the FWO and the KULPFV/10/016-SymBioSysII. MARIE: Petra Seibold, Judith Heinz, Nadia Obi, Alina Vrieling, Sabine Behrens, Ursula Eilber, Muhabbet Celik, Til Olchers, Stefan Nickels, Dieter Flesch-Janys. The MARIE study was supported by the Deutsche Krebshilfe e.V. [70-2892-BR I, 106332, 108253, 108419], the Hamburg Cancer Society, the German Cancer Research Center and the Federal Ministry of Education and Research (BMBF) Germany [01KH0402]. MBCSG: Siranoush Manoukian, Bernard Peissel and Daniela Zaffaroni of the Fondazione IRCCS Istituto Nazionale dei Tumori (INT); Monica Barile and Irene Feroce of the Istituto Europeo di Oncologia (IEO) and the personnel of the Cogentech Cancer Genetic Test Laboratory. MBCSG is supported by grants from the Italian Association for Cancer Research (AIRC) and by funds from the Italian citizens who allocated the 5/1000 share of their tax payment in support of the Fondazione IRCCS Istituto Nazionale Tumori, according to Italian laws (INT-Institutional strategic projects “5x1000”). MCBCS: The MCBCS was supported by the NIH grants CA128978, CA116167, CA176785 an NIH Specialized Program of Research Excellence (SPORE) in Breast Cancer [CA116201], and the Breast Cancer Research Foundation and a generous gift from the David F. and Margaret T. Grohne Family Foundation and the Ting Tsung and Wei Fong Chao Foundation. MCCS: MCCS cohort recruitment was funded by VicHealth and Cancer Council Victoria. The MCCS was further supported by Australian NHMRC grants 209057, 251553 and 504711 and by infrastructure provided by Cancer Council Victoria. MEC: The MEC was support by NIH grants CA63464, CA54281, CA098758 and CA132839. MTLGEBCS: We would like to thank Martine Tranchant (CHU de Québec Research Center), Marie-France Valois, Annie Turgeon and Lea Heguy (McGill University Health Center, Royal Victoria Hospital; McGill University) for DNA extraction, sample management and skillful technical assistance. J.S. is Chairholder of the Canada Research Chair in Oncogenetics. The work of MTLGEBCS was supported by the Quebec Breast Cancer Foundation, the Canadian Institutes of Health Research for the “CIHR Team in Familial Risks of Breast Cancer” program – grant # CRN-87521 and the Ministry of Economic Development, Innovation and Export Trade – grant # PSR-SIIRI-701. MYBRCA: Phuah Sze Yee, Peter Kang, Kang In Nee, Kavitta Sivanandan, Shivaani Mariapun, Yoon Sook-Yee, Daphne Lee, Teh Yew Ching and Nur Aishah Mohd Taib for DNA Extraction and patient recruitment. MYBRCA is funded by research grants from the Malaysian Ministry of Science, Technology and Innovation (MOSTI), Malaysian Ministry of Higher Education (UM.C/HIR/MOHE/06) and Cancer Research Initiatives Foundation (CARIF). Additional controls were recruited by the Singapore Eye Research Institute, which was supported by a grant from the Biomedical Research Council (BMRC08/1/35/19/550), Singapore and the National medical Research Council, Singapore (NMRC/CG/SERI/2010). NBCS: NBCS includes the following clinical collaborators: Prof. Per Eystein Lønning, MD (Section of Oncology, Institute of Medicine, University of Bergen and Department of Oncology, Haukeland University Hospital, Bergen, Norway), Prof. Em. Sophie D. Fosså, MD (National Resource Centre for Long-term Studies after Cancer, Rikshospitalet-Radiumhospitalet Cancer Clinic Montebello, Oslo, Norway), Head physician Tone Ikdahl, MD (Department of Oncology, Oslo University Hospital, Oslo, Norway), Dr. Lars Ottestad, MD (Department of Genetics and Department of Oncology, Oslo University Hospital Radiumhospitalet), Dr. Marit Muri Holmen, MD (Department of Radiology, Oslo University Hospital Radiumhospitalet, Oslo, Norway), Dr. Vilde Haakensen, MD (Department of Genetics and Department of Oncology, Oslo University

Hospital Radiumhospitalet and Institute for Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway), Prof. Bjørn Naume, MD (Division of Cancer Medicine and Radiotherapy, Department of Oncology, Oslo University Hospital Radiumhospitalet, Oslo, Norway), Prof. Eiliv Lund (Department of Community Medicine, Faculty of Health Sciences, University of Tromsø - The Arctic University of Norway, Tromsø, Norway) , Assoc. Prof. Åslaug Helland, MD (Department of Genetics, Institute for Cancer Research and Department of Oncology, Oslo University Hospital Radiumhospitalet, Oslo, Norway and Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway), Prof. Inger Torhild Gram, MD (Department of Community Medicine, Faculty of Health Sciences, University of Tromsø and Norwegian Centre for Integrated Care and Telemedicine, University Hospital of North Norway, Tromsø, Norway), Prof. Em. Rolf Kåresen, MD (Department of Breast and Endocrine Surgery, Institute for Clinical Medicine, Ullevaal Hospital, Oslo University Hospital and Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway), Dr. Ellen Schlichting, MD (Department for Breast and Endocrine Surgery, Oslo University Hospital Ullevaal, Oslo, Norway), Prof. Toril Sauer, MD (Department of Pathology at Akershus University hospital, Lørenskog, Norway), Dr. Olav Engebråten, MD (Institute for Clinical Medicine, Faculty of Medicine, University of Oslo and Department of Oncology, Oslo University Hospital, Oslo, Norway), Dr. Margit Riis, MD (Department of Surgery, Akershus University Hospital and Department of Clinical Molecular Biology (EpiGen), Institute of Clinical Medicine, Akershus University Hospital, University of Oslo, Lørenskog, Norway). The NBCS has received funding from the K.G. Jebsen Centre for Breast Cancer Research; the Research Council of Norway grant 193387/V50 (to A-L Børresen-Dale and V.N. Kristensen) and grant 193387/H10 (to A-L Børresen-Dale and V.N. Kristensen), South Eastern Norway Health Authority (grant 39346 to A-L Børresen-Dale) and the Norwegian Cancer Society (to A-L Børresen-Dale and V.N. Kristensen). NBHS: We thank study participants and research staff for their contributions and commitment to this study. The NBHS was supported by NIH grant R01CA100374. Biological sample preparation was conducted the Survey and Biospecimen Shared Resource, which is supported by P30 CA68485. OBCS: Meeri Otsukka, Kari Mononen. The OBCS was supported by research grants from the Finnish Cancer Foundation, the Academy of Finland (grant number 250083, 122715 and Center of Excellence grant number 251314), the Finnish Cancer Foundation, the Sigrid Juselius Foundation, the University of Oulu, the University of Oulu Support Foundation and the special Governmental EVO funds for Oulu University Hospital-based research activities. OFBCR: Teresa Selander, Nayana Weerasooriya. The Ontario Familial Breast Cancer Registry (OFBCR) was supported by grant UM1 CA164920 from the National Cancer Institute (USA). The content of this manuscript does not necessarily reflect the views or policies of the National Cancer Institute or any of the collaborating centers in the Breast Cancer Family Registry (BCFR), nor does mention of trade names, commercial products, or organizations imply endorsement by the USA Government or the BCFR. ORIGO: We thank E. Krol-Warmerdam, and J. Blom for patient accrual, administering questionnaires, and managing clinical information. The LUMC survival data were retrieved from the Leiden hospital-based cancer registry system (ONCDOC) with the help of Dr. J. Molenaar. The ORIGO study was supported by the Dutch Cancer Society (RUL 1997-1505) and the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI-NL CP16). PBCS: Louise Brinton, Mark Sherman, Neonila Szeszenia-Dabrowska, Beata Peplonska, Witold Zatonski, Pei Chao, Michael Stagner. The PBCS was funded by Intramural Research Funds of the

National Cancer Institute, Department of Health and Human Services, USA. pKARMA: The Swedish Medical Research Counsel. The pKARMA study was supported by Märit and Hans Rausings Initiative Against Breast Cancer. RBCS: Petra Bos, Jannet Blom, Ellen Crepin, Elisabeth Huijskens, Annette Heemskerk, the Erasmus MC Family Cancer Clinic The RBCS was funded by the Dutch Cancer Society (DDHK 2004-3124, DDHK 2009-4318). SASBAC: The Swedish Medical Research Counsel. The SASBAC study was supported by funding from the Agency for Science, Technology and Research of Singapore (A*STAR), the US National Institute of Health (NIH) and the Susan G. Komen Breast Cancer Foundation. SBCGS: We thank study participants and research staff for their contributions and commitment to this study. The SBCGS was supported primarily by NIH grants R01CA64277, R01CA148667, and R37CA70867. Biological sample preparation was conducted the Survey and Biospecimen Shared Resource, which is supported by P30 CA68485. The scientific development and funding of this project were, in part, supported by the Genetic Associations and Mechanisms in Oncology (GAME-ON) Network U19 CA148065. SBCS: Sue Higham, Helen Cramp, Ian Brock, Sabapathy Balasubramanian and Dan Connley. The SBCS was supported by Yorkshire Cancer Research S295, S299, S305PA and Sheffield Experimental Cancer Medicine Centre. SCCS: The SCCS is supported by a grant from the National Institutes of Health (R01 CA092447). Data on SCCS cancer cases used in this publication were provided by the Alabama Statewide Cancer Registry; Kentucky Cancer Registry, Lexington, KY; Tennessee Department of Health, Office of Cancer Surveillance; Florida Cancer Data System; North Carolina Central Cancer Registry, North Carolina Division of Public Health; Georgia Comprehensive Cancer Registry; Louisiana Tumor Registry; Mississippi Cancer Registry; South Carolina Central Cancer Registry; Virginia Department of Health, Virginia Cancer Registry; Arkansas Department of Health, Cancer Registry, 4815 W. Markham, Little Rock, AR 72205. The Arkansas Central Cancer Registry is fully funded by a grant from National Program of Cancer Registries, Centers for Disease Control and Prevention (CDC). Data on SCCS cancer cases from Mississippi were collected by the Mississippi Cancer Registry which participates in the National Program of Cancer Registries (NPCR) of the Centers for Disease Control and Prevention (CDC). The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the CDC or the Mississippi Cancer Registry. SEARCH: The SEARCH and EPIC teams. SEARCH is funded by a programme grant from Cancer Research UK [C490/A10124] and supported by the UK National Institute for Health Research Biomedical Research Centre at the University of Cambridge. SEBCS: SEBCS was supported by the BRL (Basic Research Laboratory) program through the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology (2012-0000347). SGBCC: We thank the participants and research coordinator Kimberley Chua. "SGBCC is funded by the NUS start-up Grant, National University Cancer Institute Singapore (NCIS) Centre Grant and the NMRC Clinician Scientist Award. Additional controls were recruited by the Singapore Consortium of Cohort Studies-Multi-ethnic cohort (SCCS-MEC), which was funded by the Biomedical Research Council, grant number: 05/1/21/19/425." SKKDKFZS: We thank all study participants, clinicians, family doctors, researchers and technicians for their contributions and commitment to this study. SKKDKFZS is supported by the DKFZ. SZBCS: The SZBCS was supported by Grant PBZ_KBN_122/P05/2004. TBCS: The TBCS was funded by The National Cancer Institute Thailand. TNBCC: Robert Pilarski and Charles Shapiro were instrumental in the formation of the OSU

Breast Cancer Tissue Bank. We thank the Human Genetics Sample Bank for processing of samples and providing OSU Columbus area control samples. The TNBCC was supported by: a Specialized Program of Research Excellence (SPORE) in Breast Cancer (CA116201), a grant from the Breast Cancer Research Foundation, a generous gift from the David F. and Margaret T. Grohne Family Foundation, the Stefanie Spielman Breast Cancer fund and the OSU Comprehensive Cancer Center, the Hellenic Cooperative Oncology Group research grant (HR R_BG/04) and the Greek General Secretary for Research and Technology (GSRT) Program, Research Excellence II, the European Union (European Social Fund – ESF), and Greek national funds through the Operational Program "Education and Lifelong Learning" of the National Strategic Reference Framework (NSRF) - ARISTEIA. TWBCS: The TWBCS is supported by the Taiwan Biobank project of the Institute of Biomedical Sciences, Academia Sinica, Taiwan. UKBGS: We thank Breakthrough Breast Cancer and the Institute of Cancer Research for support and funding of the Breakthrough Generations Study, and the study participants, study staff, and the doctors, nurses and other health care providers and health information sources who have contributed to the study. We acknowledge NHS funding to the Royal Marsden/ICR NIHR Biomedical Research Centre. The UKBGS is funded by Breakthrough Breast Cancer and the Institute of Cancer Research (ICR), London. ICR acknowledges NHS funding to the NIHR Biomedical Research Centre.

CIMBA studies. BCFR-AU: Maggie Angelakos, Judi Maskiell, Gillian Dite, Helen Tsimiklis. BCFR-NY: We wish to thank members and participants in the New York site of the Breast Cancer Family Registry for their contributions to the study. BCFR-ON: We wish to thank members and participants in the Ontario Familial Breast Cancer Registry for their contributions to the study. BFBOCC-LT: We acknowledge Vilius Rudaitis, Laimonas Griškevičius. BFBOCC-LV: Acknowledge Drs Janis Eglitis, Anna Krilova and Aivars Stengrevics. BMBSA: We wish to thank the families who contribute to the BMBSA study. BRICOH: We wish to thank Yuan Chun Ding and Linda Steele for their work in participant enrolment and biospecimen and data management. CNIO: We thank Alicia Barroso, Rosario Alonso and Guillermo Pita for their assistance. CONSIT TEAM: Alessandra Viel of the CRO Aviano National Cancer Institute, Aviano (PN), Italy; Laura Ottini of the "Sapienza" University, Rome, Italy; Liliana Varesco of the IRCCS AOU San Martino - IST Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy; Maria Grazia Tibiletti of the Ospedale di Circolo-Università dell'Insubria, Varese, Italy; Antonella Savarese of the Istituto Nazionale Tumori Regina Elena, Rome, Italy; Stefania Tommasi of the Istituto Nazionale Tumori "Giovanni Paolo II" - Bari, Italy. EMBRACE: Epidemiological study of BRCA1 & BRCA2 mutation carriers (EMBRACE): Douglas F. Easton is the PI of the study. EMBRACE Collaborating Centres are: Coordinating Centre, Cambridge: Debra Frost, Steve Ellis, Elena Fineberg, Radka Platte. North of Scotland Regional Genetics Service, Aberdeen: Zosia Miedzybrodzka, Helen Gregory. Northern Ireland Regional Genetics Service, Belfast: Patrick Morrison, Lisa Jeffers. West Midlands Regional Clinical Genetics Service, Birmingham: Trevor Cole, Kai-ren Ong, Jonathan Hoffman. South West Regional Genetics Service, Bristol: Alan Donaldson, Margaret James. East Anglian Regional Genetics Service, Cambridge: Marc Tischkowitz, Joan Paterson, Amy Taylor. Medical Genetics Services for Wales, Cardiff: Alexandra Murray, Mark T. Rogers, Emma McCann. St James's Hospital, Dublin & National Centre for Medical Genetics, Dublin: M. John Kennedy, David Barton. South East of Scotland

Regional Genetics Service, Edinburgh: Mary Porteous, Sarah Drummond. Peninsula Clinical Genetics Service, Exeter: Carole Brewer, Emma Kivuva, Anne Searle, Selina Goodman, Kathryn Hill. West of Scotland Regional Genetics Service, Glasgow: Rosemarie Davidson, Victoria Murday, Nicola Bradshaw, Lesley Snadden, Mark Longmuir, Catherine Watt, Sarah Gibson, Eshika Haque, Ed Tobias, Alexis Duncan. South East Thames Regional Genetics Service, Guy's Hospital London: Louise Izatt, Chris Jacobs, Caroline Langman. North West Thames Regional Genetics Service, Harrow: Huw Dorkins. Leicestershire Clinical Genetics Service, Leicester: Julian Barwell. Yorkshire Regional Genetics Service, Leeds: Julian Adlard, Gemma Serra-Feliu. Cheshire & Merseyside Clinical Genetics Service, Liverpool: Ian Ellis, Catherine Houghton. Manchester Regional Genetics Service, Manchester: D Gareth Evans, Fiona Lalloo, Jane Taylor. North East Thames Regional Genetics Service, NE Thames, London: Lucy Side, Alison Male, Cheryl Berlin. Nottingham Centre for Medical Genetics, Nottingham: Jacqueline Eason, Rebecca Collier. Northern Clinical Genetics Service, Newcastle: Fiona Douglas, Oonagh Claber, Irene Jobson. Oxford Regional Genetics Service, Oxford: Lisa Walker, Diane McLeod, Dorothy Halliday, Sarah Durell, Barbara Stayner. The Institute of Cancer Research and Royal Marsden NHS Foundation Trust: Ros Eeles, Susan Shanley, Nazneen Rahman, Richard Houlston, Elizabeth Bancroft, Elizabeth Page, Audrey Ardern-Jones, Kelly Kohut, Jennifer Wiggins, Elena Castro, Emma Killick, Sue Martin, Gillian Rea, Anjana Kulkarni. North Trent Clinical Genetics Service, Sheffield: Jackie Cook, Oliver Quarrell, Cathryn Bardsley. South West Thames Regional Genetics Service, London: Shirley Hodgson, Sheila Goff, Glen Brice, Lizzie Winchester, Charlotte Eddy, Vishakha Tripathi, Virginia Attard, Anna Lehmann. Wessex Clinical Genetics Service, Princess Anne Hospital, Southampton: Diana Eccles, Anneke Lucassen, Gillian Crawford, Donna McBride, Sarah Smalley. FCCC: We thank Ms. JoEllen Weaver and Dr. Betsy Bove for their technical support. GEMO: Genetic Modifiers of Cancer Risk in BRCA1/2 Mutation Carriers (GEMO) study: National Cancer Genetics Network «UNICANCER Genetic Group», France. We wish to thank all the GEMO collaborating groups for their contribution to this study. GEMO Collaborating Centers are: Coordinating Centres, Unité Mixte de Génétique Constitutionnelle des Cancers Fréquents, Hospices Civils de Lyon - Centre Léon Bérard, & Equipe «Génétique du cancer du sein», Centre de Recherche en Cancérologie de Lyon: Olga Sinilnikova, Sylvie Mazoyer, Francesca Damiola, Laure Barjhoux, Carole Verny-Pierre, Alain Calender, Sophie Giraud, Mélanie Léone; and Service de Génétique Oncologique, Institut Curie, Paris: Dominique Stoppa-Lyonnet, Marion Gauthier-Villars, Bruno Buecher, Claude Houdayer, Virginie Moncoutier, Muriel Belotti, Carole Tirapo, Antoine de Pauw. Institut Gustave Roussy, Villejuif: Brigitte Bressac-de-Paillerets, Olivier Caron. Centre Jean Perrin, Clermont–Ferrand: Yves-Jean Bignon, Nancy Uhrhammer. Centre Léon Bérard, Lyon: Christine Lasset, Valérie Bonadona, Sandrine Handallou. Centre François Baclesse, Caen: Agnès Hardouin, Pascaline Berthet. Institut Paoli Calmettes, Marseille: Hagay Sobol, Violaine Bourdon, Tetsuro Noguchi, Audrey Remenieras, François Eisinger. CHU Arnaud-de-Villeneuve, Montpellier: Isabelle Coupier, Pascal Pujol. Centre Oscar Lambret, Lille: Jean-Philippe Peyrat, Joëlle Fournier, Françoise Révillion, Philippe Vennin, Claude Adenis. Hôpital René Huguenin/Institut Curie, St Cloud: Etienne Rouleau, Rosette Lidereau, Liliane Demange, Catherine Nogues. Centre Paul Strauss, Strasbourg: Danièle Muller, Jean-Pierre Fricker. Institut Bergonié, Bordeaux: Emmanuelle Barouk-Simonet, Françoise Bonnet, Virginie Bubien, Nicolas Sevenet, Michel Longy. Institut Claudius Regaud, Toulouse: Christine Toulas, Rosine Guimbaud, Laurence Gladieff, Viviane Feillel. CHU Grenoble: Dominique Leroux, Hélène Dreyfus, Christine Rebischung, Magalie Peysselon. CHU Dijon: Fanny Coron, Laurence Faivre. CHU St-Etienne: Fabienne Prieur, Marine Lebrun, Caroline Kientz. Hôtel Dieu Centre Hospitalier, Chambéry: Sandra Fert Ferrer. Centre Antoine Lacassagne, Nice: Marc Frénay. CHU Limoges: Laurence Vénat-Bouvet. CHU Nantes: Capucine Delnatte. CHU Bretonneau, Tours: Isabelle Mortemousque. Groupe Hospitalier Pitié-Salpétrière, Paris: Florence Coulet, Chrystelle Colas, Florent Soubrier. CHU Vandoeuvre-les-Nancy : Johanna Sokolowska, Myriam Bronner. CHU Besançon: Marie-Agnès Collonge-Rame, Alexandre Damette. Creighton University, Omaha, USA: Henry T.Lynch, Carrie L.Snyder. G-FAST: We wish to thank the technical support of Ilse Coene en Brecht Crombez. HCSC: We acknowledge Alicia Tosar for her technical assistance. HEBCS: HEBCS would like to thank Dr. Kristiina Aittomäki, Taru A. Muranen, Drs. Carl Blomqvist and Kirsimari Aaltonen and RNs Irja Erkkilä and Virpi Palola for their help with the HEBCS data and samples. HEBON: The Hereditary Breast and Ovarian Cancer Research Group Netherlands (HEBON) consists of the following Collaborating Centers: Coordinating center: Netherlands Cancer Institute, Amsterdam, NL: M.A. Rookus, F.B.L. Hogervorst, F.E. van Leeuwen, S. Verhoef, M.K. Schmidt, N.S. Russell, J.L. de Lange, R. Wijnands; Erasmus Medical Center, Rotterdam, NL: J.M. Collée, A.M.W. van den Ouweland, M.J. Hooning, C. Seynaeve, C.H.M. van Deurzen, I.M. Obdeijn; Leiden University Medical Center, NL: C.J. van Asperen, J.T. Wijnen, R.A.E.M. Tollenaar, P. Devilee, T.C.T.E.F. van Cronenburg; Radboud University Nijmegen Medical Center, NL: C.M. Kets, A.R. Mensenkamp; University Medical Center Utrecht, NL: M.G.E.M. Ausems, R.B. van der Luijt, C.C. van der Pol; Amsterdam Medical Center, NL: C.M. Aalfs, T.A.M. van Os; VU University Medical Center, Amsterdam, NL: J.J.P. Gille, Q. Waisfisz, H.E.J. Meijers-Heijboer; University Hospital Maastricht, NL: E.B. Gómez-Garcia, M.J. Blok; University Medical Center Groningen, NL: J.C. Oosterwijk, A.H. van der Hout, M.J. Mourits, G.H. de Bock; The Netherlands Foundation for the detection of hereditary tumours, Leiden, NL: H.F. Vasen; The Netherlands Comprehensive Cancer Organization (IKNL): S. Siesling, J. Verloop; The Dutch Pathology Registry (PALGA): L.I.H. Overbeek. HRBCP: We wish to thank Hong Kong Sanatoriuma and Hospital for their continual support. HUNBOCS: We wish to thank the Hungarian Breast and Ovarian Cancer Study Group members (Janos Papp, Tibor Vaszko, Aniko Bozsik, Timea Pocza, Judit Franko, Maria Balogh, Gabriella Domokos, Judit Ferenczi, Department of Molecular Genetics, National Institute of Oncology, Budapest, Hungary) and the clinicians and patients for their contributions to this study. HVH: We wish to thank the Oncogenetics Group (VHIO), and the High Risk and Cancer Prevention Unit of the University Hospital Vall d'Hebron. ICO: We wish to thank the ICO Hereditary Cancer Program team led by Dr. Gabriel Capella. INHERIT: We would like to thank Dr Martine Dumont, Martine Tranchant for sample management and skillful technical assistance. J.S. is Chair holder of the Canada Research Chair in Oncogenetics. J.S. and P.S. were part of the QC and Genotyping coordinating group of iCOGS (BCAC and CIMBA). IPOBCS: We wish to thank Drs. Ana Peixoto, Catarina Santos, Patrícia Rocha and Pedro Pinto for their skillful contribution to the study. KCONFAB: We wish to thank Heather Thorne, Eveline Niedermayr, all the kConFab research nurses and staff, the heads and staff of the Family Cancer Clinics, and the Clinical Follow Up Study (which has received funding from the NHMRC, the National Breast Cancer Foundation, Cancer Australia, and the National Institute of Health (USA)) for their contributions to this resource, and the many families who contribute to kConFab. MODSQUAD: Modifier Study of Quantitative

Effects on Disease (MODSQUAD): MODSQUAD acknowledges ModSQuaD members Csilla Szabo (National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA); Lenka Foretova and Eva Machackova (Department of Cancer Epidemiology and Genetics, Masaryk Memorial Cancer Institute and MF MU, Brno, Czech Republic); and Michal Zikan, Petr Pohlreich and Zdenek Kleibl (Oncogynecologic Center and Department of Biochemistry and Experimental Oncology, First Faculty of Medicine, Charles University, Prague, Czech Republic). MSKCC: Anne Lincoln, Lauren Jacobs. NICCC: We wish to thank the NICCC National Familial Cancer Consultation Service team led by Sara Dishon, the lab team led by Dr. Flavio Lejbkowicz, and the research field operations team led by Dr. Mila Pinchev. NRG Oncology: We thank the investigators of the Australia New Zealand NRG Oncology group. OCGN: We wish to thank members and participants in the Ontario Cancer Genetics Network for their contributions to the study. OSU CCG: Leigha Senter, Kevin Sweet, Caroline Craven, and Michelle O'Conor were instrumental in accrual of study participants, ascertainment of medical records and database management. Samples were processed by the OSU Human Genetics Sample Bank. SEABASS: We would like to thank Yip Cheng Har, Nur Aishah Mohd Taib, Phuah Sze Yee, Norhashimah Hassan and all the research nurses, research assistants and doctors involved in the MyBrCa Study for assistance in patient recruitment, data collection and sample preparation. In addition, we thank Philip Iau, Sng Jen-Hwei and Sharifah Nor Akmal for contributing samples from the Singapore Breast Cancer Study and the HUKM-HKL Study, respectively. The Malaysian Breast Cancer Genetic Study is funded by research grants from the Malaysian Ministry of Science, Technology and Innovation, Ministry of Higher Education (UM.C/HIR/MOHE/06) and charitable funding from Cancer Research Initiatives Foundation. SMC: SMC team wishes to acknowledge the assistance of the Meirav Comprehensive breast cancer center team at the Sheba Medical Center for assistance in this study. SWE-BRCA: Swedish scientists participating as SWE-BRCA collaborators are: from Lund University and University Hospital: Åke Borg, Håkan Olsson, Helena Jernström, Karin Henriksson, Katja Harbst, Maria Soller, Ulf Kristoffersson; from Gothenburg Sahlgrenska University Hospital: Anna Öfverholm, Margareta Nordling, Per Karlsson, Zakaria Einbeigi; from Stockholm and Karolinska University Hospital: Anna von Wachenfeldt, Annelie Liljegren, Annika Lindblom, Brita Arver, Gisela Barbany Bustinza, Johanna Rantala; from Umeå University Hospital: Beatrice Melin, Christina Edwinsdotter Ardnor, Monica Emanuelsson; from Uppsala University: Hans Ehrencrona, Maritta Hellström Pigg, Richard Rosenquist; from Linköping University Hospital: Marie Stenmark-Askmalm, Sigrun Liedgren. UCHICAGO: We wish to thank Cecilia Zvocec, Qun Niu, physicians, genetic counsellors, research nurses and staff of the Cancer Risk Clinic for their contributions to this resource, and the many families who contribute to our program. UCLA: We thank Joyce Seldon MSGC and Lorna Kwan, MPH for assembling the data for this study. UCSF: We would like to thank Dr. Robert Nussbaum and the following genetic counsellors for participant recruitment: Beth Crawford, Kate Loranger, Julie Mak, Nicola Stewart, Robin Lee, Amie Blanco and Peggy Conrad. And thanks to Ms. Salina Chan for her data management. UKFOCR: We thank Paul Pharoah, Simon Gayther, Susan Ramus, Carole Pye, Patricia Harrington and Eva Wozniak for their contributions towards the UKFOCR. VFCTG: Geoffrey Lindeman, Marion Harris, Martin Delatycki of the Victorian Familial Cancer Trials Group. We thank Sarah Sawyer and Rebecca Driessen for assembling this data and Ella Thompson for performing all DNA amplification.

MODE studies. ABCFS: The Australian Breast Cancer Family Registry (ABCFR; 1992-1995) was supported by the Australian NHMRC, the New South Wales Cancer Council, and the Victorian Health Promotion Foundation (Australia), and by grant UM1CA164920 from the USA National Cancer Institute. The Genetic Epidemiology Laboratory at the University of Melbourne has also received generous support from Mr B. Hovey and Dr and Mrs R.W. Brown to whom we are most grateful. The content of this manuscript does not necessarily reflect the views or policies of the National Cancer Institute or any of the collaborating centers in the Breast Cancer Family Registry (BCFR), nor does mention of trade names, commercial products, or organizations imply endorsement by the USA Government or the BCFR. BBCC: This study was funded in part by the ELAN-Program of the University Hospital Erlangen; Katharina Heusinger was funded by the ELAN program of the University Hospital Erlangen. BBCC was supported in part by the ELAN program of the Medical Faculty, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nuremberg. EPIC-Norfolk: This study was funded by research programme grant funding from Cancer Research UK and the Medical Research Council with additional support from the Stroke Association, British Heart Foundation, Department of Health, Research into Ageing and Academy of Medical Sciences. MCBCS: This study was supported by Public Health Service Grants P50 CA 116201, R01 CA 128931, R01 CA 128931-S01, R01 CA 122340, CCSG P30 CA15083, from the National Cancer Institute, National Institutes of Health, and Department of Health and Human Services. MCCS: Melissa C. Southey is a National Health and Medical Research Council Senior Research Fellow and a Victorian Breast Cancer Research Consortium Group Leader. The study was supported by the Cancer Council of Victoria and by the Victorian Breast Cancer Research Consortium. MEC: National Cancer Institute: R37CA054281, R01CA063464, R01CA085265, R25CA090956, R01CA132839. MMHS: This work was supported by grants from the National Cancer Institute, National Institutes of Health, and Department of Health and Human Services (R01 CA128931, R01 CA 128931-S01, R01 CA97396, P50 CA116201, and Cancer Center Support Grant P30 CA15083). NBCS: This study has been supported with grants from Norwegian Research Council (#183621/S10 and #175240/S10), The Norwegian Cancer Society (PK80108002, PK60287003), and The Radium Hospital Foundation as well as S-02036 from South Eastern Norway Regional Health Authority. OFBCR: This work was supported by grant UM1 CA164920 from the USA National Cancer Institute. The content of this manuscript does not necessarily reflect the views or policies of the National Cancer Institute or any of the collaborating centers in the Breast Cancer Family Registry (BCFR), nor does mention of trade names, commercial products, or organizations imply endorsement by the USA Government or the BCFR. SASBAC: The SASBAC study was supported by Märit and Hans Rausing's Initiative against Breast Cancer, National Institutes of Health, Susan Komen Foundation and Agency for Science, Technology and Research of Singapore (A*STAR). SIBS: SIBS was supported by program grant C1287/A10118 and project grants from Cancer Research UK (grant numbers C1287/8459).

Full membership lists of participating study groups

Epidemiological study of BRCA1 & BRCA2 mutation carriers (EMBRACE):

Douglas F. Easton is the PI of the study. EMBRACE Collaborating Centres are: Coordinating Centre, Cambridge: Debra Frost, Steve Ellis, Radka Platte, Jo Perkins. North of Scotland Regional Genetics Service, Aberdeen: Zosia Miedzybrodzka, Helen Gregory. Northern Ireland Regional Genetics Service, Belfast: Patrick Morrison, Lisa Jeffers. West Midlands Regional Clinical Genetics Service, Birmingham: Kai-ren Ong, Jonathan Hoffman. South West Regional Genetics Service, Bristol: Alan Donaldson, Margaret James. East Anglian Regional Genetics Service, Cambridge: Joan Paterson, Marc Tischkowitz, Sarah Downing, Amy Taylor. Medical Genetics Services for Wales, Cardiff: Alexandra Murray, Mark T. Rogers, Emma McCann. St James's Hospital, Dublin & National Centre for Medical Genetics, Dublin: M. John Kennedy, David Barton. South East of Scotland Regional Genetics Service, Edinburgh: Mary Porteous, Sarah Drummond. Peninsula Clinical Genetics Service, Exeter: Carole Brewer, Emma Kivuva, Anne Searle, Selina Goodman, Kathryn Hill. West of Scotland Regional Genetics Service, Glasgow: Rosemarie Davidson, Victoria Murday, Nicola Bradshaw, Lesley Snadden, Mark Longmuir, Catherine Watt, Sarah Gibson, Eshika Haque, Ed Tobias, Alexis Duncan. South East Thames Regional Genetics Service, Guy's Hospital London: Louise Izatt, Chris Jacobs, Caroline Langman. North West Thames Regional Genetics Service, Harrow: Huw Dorkins. Leicestershire Clinical Genetics Service, Leicester: Julian Barwell. Yorkshire Regional Genetics Service, Leeds: Julian Adlard, Gemma Serra-Feliu. Cheshire & Merseyside Clinical Genetics Service, Liverpool: Ian Ellis, Claire Foo. Manchester Regional Genetics Service, Manchester: D Gareth Evans, Fiona Lalloo, Jane Taylor. North East Thames Regional Genetics Service, NE Thames, London: Lucy Side, Alison Male, Cheryl Berlin. Nottingham Centre for Medical Genetics, Nottingham: Jacqueline Eason, Rebecca Collier. Northern Clinical Genetics Service, Newcastle: Alex Henderson, Oonagh Claber, Irene Jobson. Oxford Regional Genetics Service, Oxford: Lisa Walker, Diane McLeod, Dorothy Halliday, Sarah Durell, Barbara Stayner. The Institute of Cancer Research and Royal Marsden NHS Foundation Trust: Ros Eeles, Nazneen Rahman, Elizabeth Bancroft, Elizabeth Page, Audrey Ardern-Jones, Kelly Kohut, Jennifer Wiggins, Jenny Pope, Sibel Saya, Natalie Taylor, Zoe Kemp and Angela George North Trent Clinical Genetics Service, Sheffield: Jackie Cook, Oliver Quarrell, Cathryn Bardsley. South West Thames Regional Genetics Service, London: Shirley Hodgson, Sheila Goff, Glen Brice, Lizzie Winchester, Charlotte Eddy, Vishakha Tripathi, Virginia Attard. Wessex Clinical Genetics Service, Princess Anne Hospital, Southampton: Diana Eccles, Anneke Lucassen, Gillian Crawford, Donna McBride, Sarah Smalley.

Genetic Modifiers of Cancer Risk in BRCA1/2 Mutation Carriers (GEMO) on behalf the National Cancer Genetics Network, UNICANCER Genetic Group, France:

GEMO Collaborating Centers are: Coordinating Centres, Unité Mixte de Génétique Constitutionnelle des Cancers Fréquents, Hospices Civils de Lyon - Centre Léon Bérard, & Equipe «Génétique du cancer du sein», Centre de Recherche en Cancérologie de Lyon: Olga Sinilnikova (dec.), Sylvie Mazoyer, Francesca Damiola, Laure Barjhoux, Carole Verny- Pierre, Sophie Giraud, Mélanie

Léone; Nadia Boutry-Kryza, and Service de Génétique Oncologique, InstitutCurie, Paris: Dominique Stoppa-Lyonnet, Marion Gauthier-Villars, Bruno Buecher, Claude Houdayer, Etienne Rouleau, Lisa Golmard, Agnès Collet, Virginie Moncoutier, Cédrick Lefol, Muriel Belotti, Antoine de Pauw, Camille Elan, Catherine Nogues, Emmanuelle Fourme, Anne-Marie BirotInstitutGustave Roussy, Villejuif: Brigitte Bressac-dePaillerets, Olivier Caron, Marine Guillaud-Bataille Centre Jean Perrin, Clermont–Ferrand: Yves-Jean Bignon, Nancy Uhrhammer. Centre Léon Bérard, Lyon: Christine Lasset, Valérie Bonadona, Sandrine Handallou. Centre François Baclesse, Caen: Agnès Hardouin, Pascaline Berthet, Dominique Vaur, Laurent Castera. Institut Paoli Calmettes, Marseille: Hagay, Sobol, Violaine Bourdon, Tetsuro Noguchi, Audrey Remenieras, François Eisinger. CHU Arnaud-de-Villeneuve, Montpellier: Isabelle Coupier, Pascal Pujol, Centre Oscar Lambret, Lille: Jean-Philippe Peyrat Joëlle Fournier, Françoise Révillion, Philippe Vennin (dec.), Claude Adenis. Centre Paul Strauss, Strasbourg: Danièle Muller, Jean-Pierre Fricker. Institut Bergonié, Bordeaux: Emmanuelle Barouk-Simonet, Françoise Bonnet, Virginie Bubien, Nicolas Sevenet, Michel Longy. Institut Claudius Regaud, Toulouse: Christine Toulas, Rosine Guimbaud, Laurence Gladieff, Viviane Feillel. CHU Grenoble: Dominique Leroux, Hélène Dreyfus, Christine Rebischung, Magalie Peysselon. CHU Dijon: Fanny Coron, Laurence Faivre. CHU St-Etienne: Fabienne Prieur, Marine Lebrun, Caroline Kientz. Hôtel Dieu Centre Hospitalier, Chambéry: Sandra Fert Ferrer. Centre Antoine Lacassagne, Nice: Marc Frénay. CHU Limoges: Laurence Vénat-Bouvet. CHU Nantes: Capucine Delnatte. CHU Bretonneau, Tours: Isabelle Mortemousque. Groupe Hospitalier Pitié-Salpétrière, Paris: Florence Coulet, Chrystelle Colas, Florent Soubrier, Mathilde Warcoin. CHU Vandoeuvre-les-Nancy: Johanna Sokolowska, Myriam Bronner. Creighton University, Omaha, USA: Henry T.Lynch, Carrie L.Snyder.

The Hereditary Breast and Ovarian Cancer Research Group Netherlands (HEBON):
HEBON consists of the following Collaborating Centers: Coordinating center: Netherlands Cancer Institute, Amsterdam, NL: M.A. Rookus, F.B.L. Hogervorst, F.E. van Leeuwen, S. Verhoef, M.K. Schmidt, N.S. Russell, J.L. de Lange, R. Wijnands; Erasmus Medical Center, Rotterdam, NL: J.M. Collée, A.M.W. van den Ouweland, M.J. Hooning, C. Seynaeve, C.H.M. van Deurzen, I.M. Obdeijn; Leiden University Medical Center, NL: C.J. van Asperen, J.T. Wijnen, R.A.E.M. Tollenaar, P. Devilee, T.C.T.E.F. van Cronenburg; Radboud University Nijmegen Medical Center, NL: C.M. Kets, A.R. Mensenkamp; University Medical Center Utrecht, NL: M.G.E.M. Ausems, R.B. van der Luijt, C.C. van der Pol; Amsterdam Medical Center, NL: C.M. Aalfs, T.A.M. van Os; VU University Medical Center, Amsterdam, NL: J.J.P. Gille, Q. Waisfisz, H.E.J. Meijers-Heijboer; University Hospital Maastricht, NL: E.B. Gómez-Garcia, M.J. Blok; University Medical Center Groningen, NL: J.C. Oosterwijk, A.H. van der Hout, M.J. Mourits, G.H. de Bock; The Netherlands Foundation for the detection of hereditary tumours, Leiden, NL: H.F. Vasen; The Netherlands Comprehensive Cancer Organization (IKNL): S. Siesling, J.Verloop; The Dutch Pathology Registry (PALGA): L.I.H. Overbeek.

Kathleen Cuningham Foundation Consortium for research into Familial Breast cancer (kConFab):
Morteza Aghmesheh, David Amor, Lesley Andrews, Yoland Antill, Shane Armitage, Leanne Arnold, Rosemary Balleine, Agnes Bankier, Patti Bastick, Jonathan Beesley, John Beilby, Barbara Bennett, Ian Bennett, Geoffrey Berry, Anneke Blackburn, Michael Bogwitz, Meagan Brennan, Melissa Brown, Michael Buckley, Matthew Burgess, Jo Burke, Phyllis Butow, Keith Byron, David Callen, Ian Campbell, Deepa Chauhan, Manisha Chauhan, Georgia Chenevix-Trench, Alice Christian, Christine Clarke, Alison Colley, Dick Cotton, Ashley Crook, James Cui, Bronwyn Culling, Margaret Cummings, Sarah-Jane Dawson, Anna deFazio, Martin Delatycki, Rebecca Dickson, Joanne Dixon, Alexander Dobrovic, Tracy Dudding, Ted Edkins, Stacey Edwards, Maurice Eisenbruch, Gelareh Farshid, Susan Fawcett, Andrew Fellows, Georgina Fenton, Michael Field, Frank Firgaira, James Flanagan, Jean Fleming, Peter Fong, John Forbes, Stephen Fox, Juliet French, Michael Friedlander, Clara Gaff, Mac Gardner, Mike Gattas, Peter George, Graham Giles, Grantley Gill, Jack Goldblatt, Sian Greening, Scott Grist, Eric Haan, Kate Hardie, Marion Harris, Stewart Hart, Nick Hayward, Sue Healey, Louise Heiniger, John Hopper, Evelyn Humphrey, Clare Hunt, Paul James, Mark Jenkins, Alison Jones, Rick Kefford, Alexa Kidd, Belinda Kiely, Judy Kirk, Jessica Koehler, James Kollias, Serguei Kovalenko, Sunil Lakhani, Amanda Leaming, Jennifer Leary, Jacqueline Lim, Geoff Lindeman, Lara Lipton, Liz Lobb, Graham Mann, Deborah Marsh, Sue Anne McLachlan, Bettina Meiser, Cliff Meldrum, Roger Milne, Gillian Mitchell, Beth Newman, Eveline Niedermayr, Sophie Nightingale, Shona O'Connell, Imelda O'Loughlin, Richard Osborne, Nick Pachter, Briony Patterson, Lester Peters, Kelly Phillips, Melanie Price, Lynne Purser, Tony Reeve, Jeanne Reeve, Robert Richards, Edwina Rickard, Bridget Robinson, Barney Rudzki, Mona Saleh, Elizabeth Salisbury, Joe Sambrook, Christobel Saunders, Jodi Saunus, Robyn Sayer, Elizabeth Scott, Rodney Scott, Clare Scott, Ram Seshadri, Adrienne Sexton, Raghwa Sharma, Andrew Shelling, Peter Simpson, Melissa Southey, Amanda Spurdle, Graeme Suthers, Pamela Sykes, Margaret Tassell, Donna Taylor, Jessica Taylor, Benjamin Thierry, Susan Thomas, Ella Thompson, Heather Thorne, Sharron Townshend, Alison Trainer, Lan Tran, Kathy Tucker, Janet Tyler, Jane Visvader, Logan Walker, Ian Walpole, Robin Ward, Paul Waring, Bev Warner, Graham Warren, Rachael Williams, Judy Wilson, Ingrid Winship, Kathy Wu, Mary Ann Young.