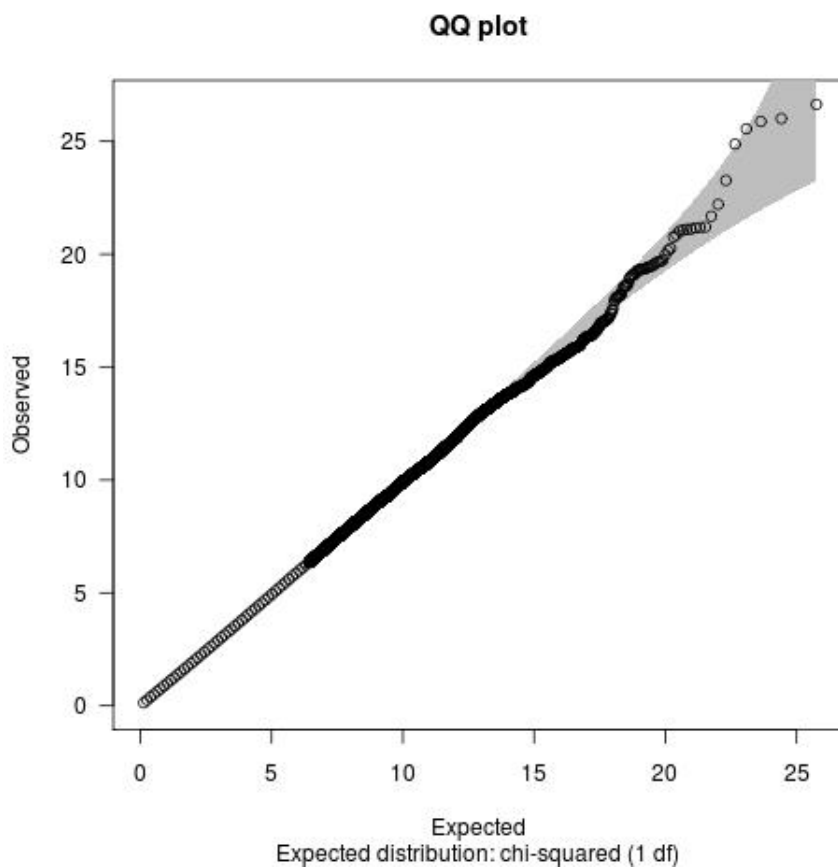
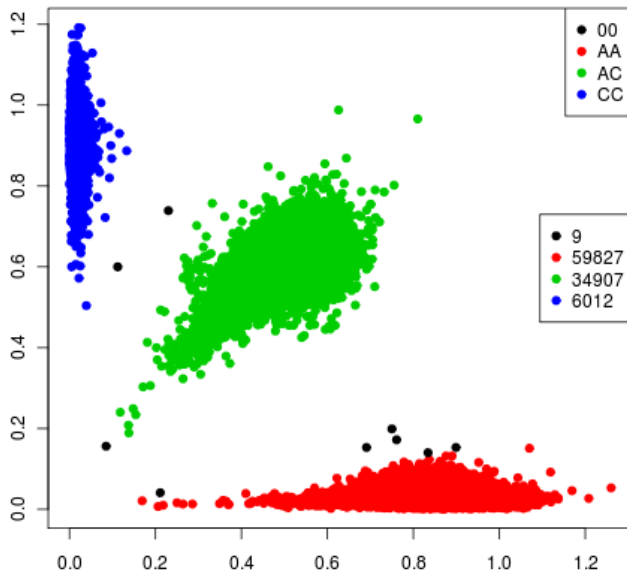


Supplementary Figure 1: QQ Plot of Association Statistics for the C-BCAC ER- GWAS. The observed versus expected score test statistics are shown for ~2.6M autosomal loci after QC exclusions and imputation to HapMap2 ($\lambda=0.98$).

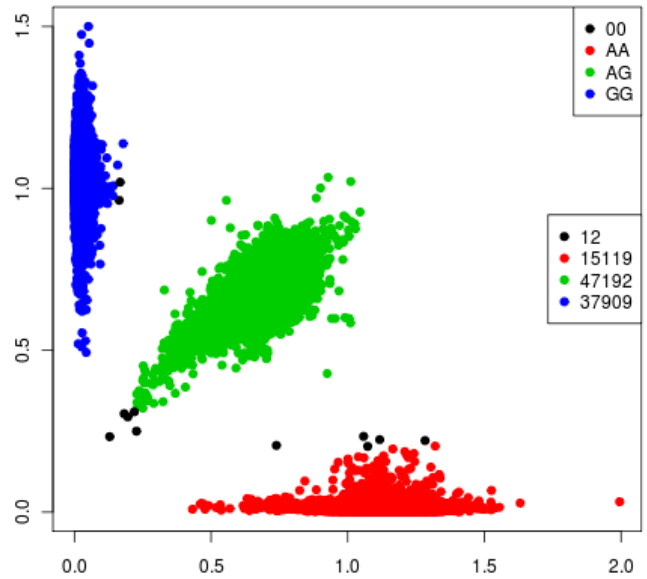


Supplementary Figure 2: Cluster plots for the normalized intensities of the two alleles, over all BCAC studies, for four SNPs achieving genome-wide significance.

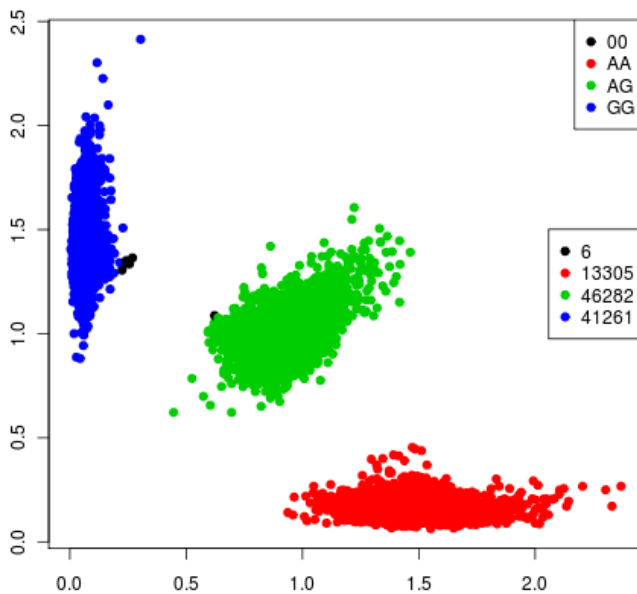
A. rs4245739 1q32.1/*MDM4*



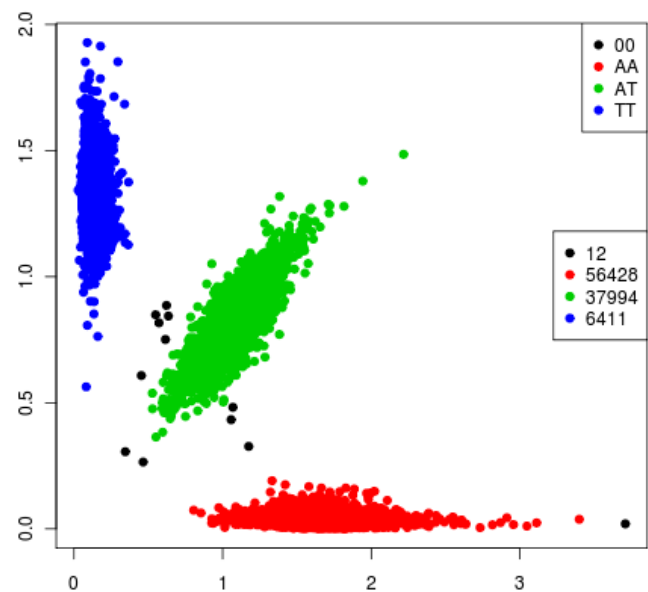
B. rs6678914 1q32.1/*LGR6*



C. rs12710696 2p24

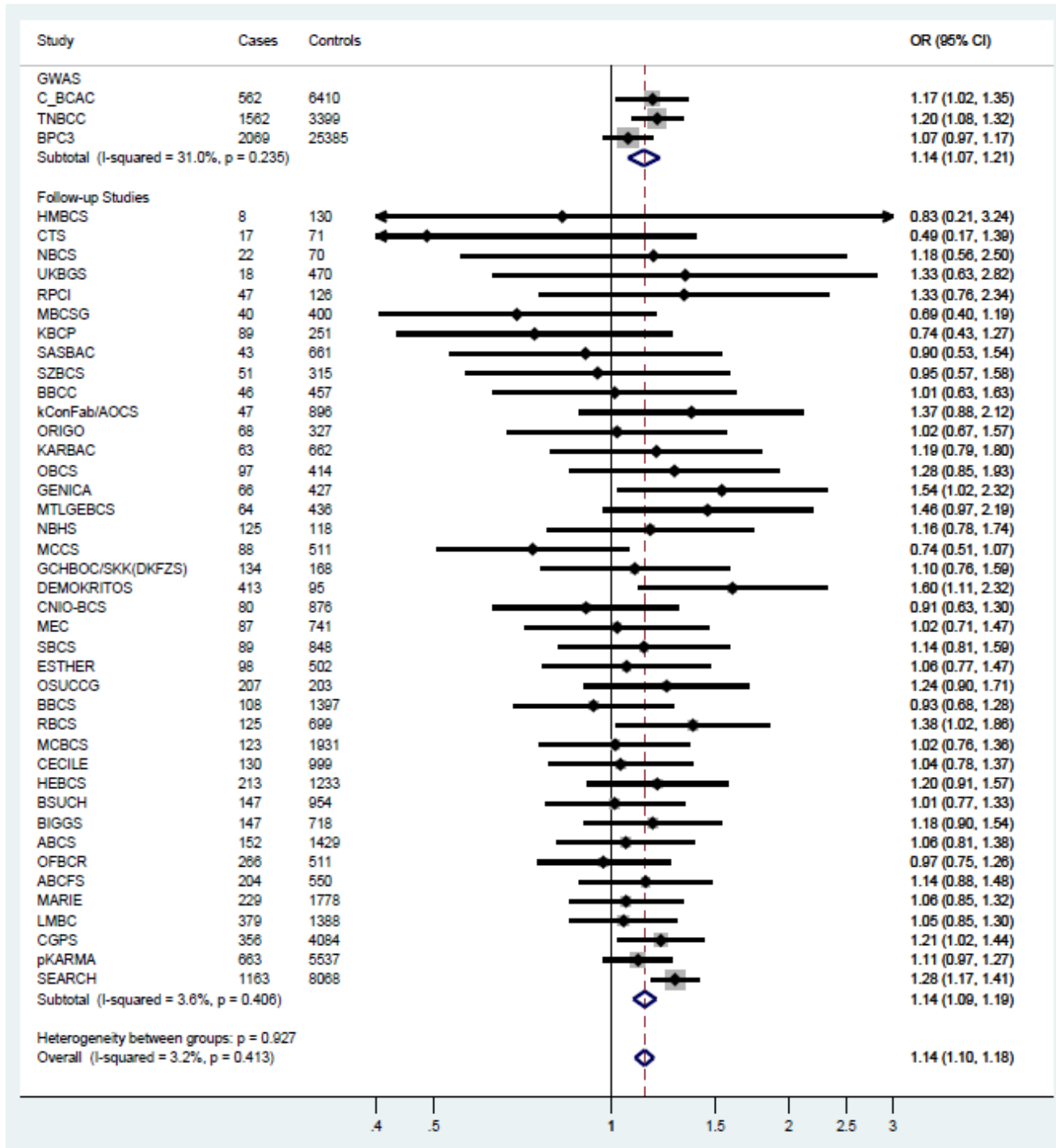


D. rs11075995 6q12/*FTO*

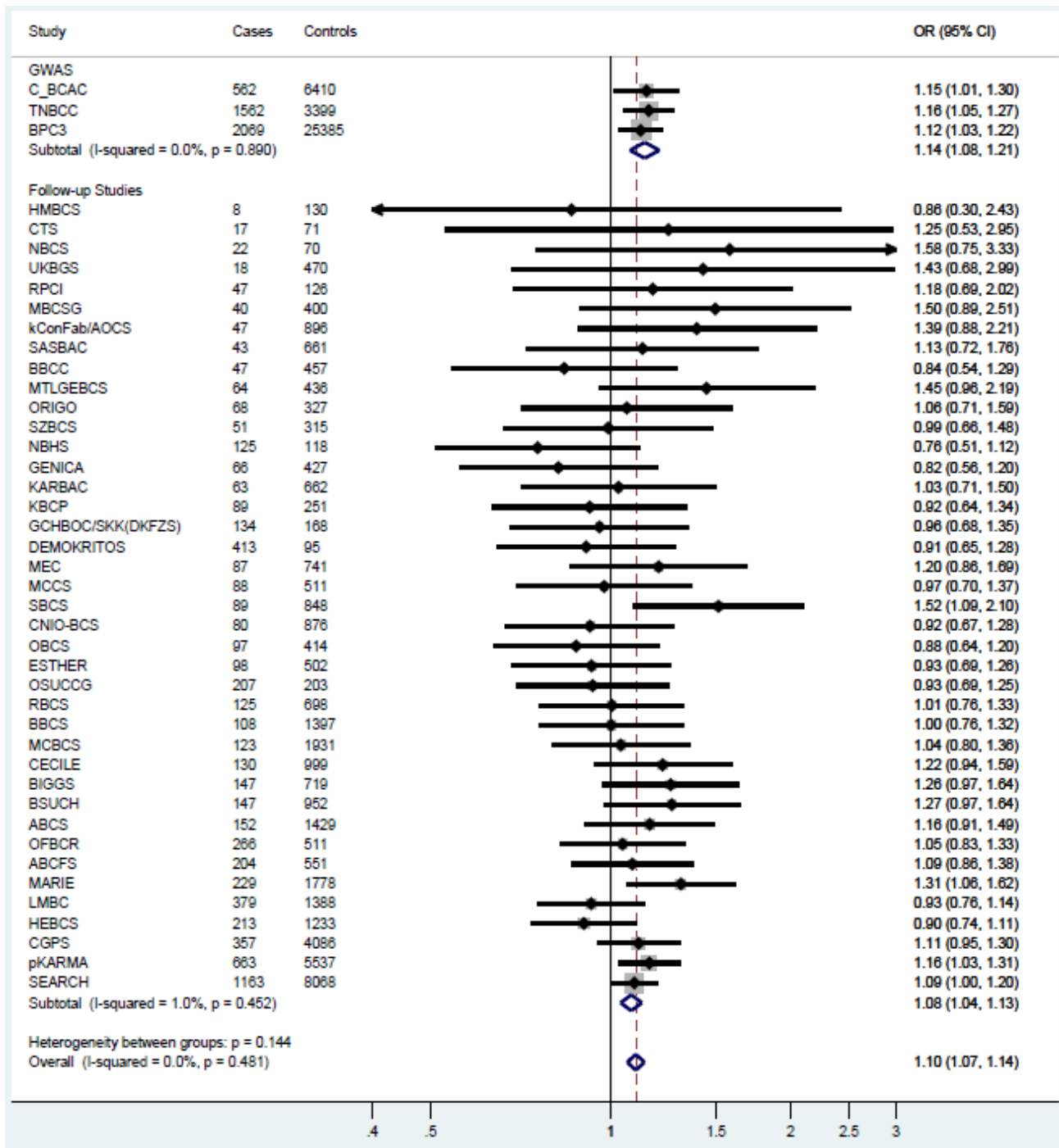


Supplementary Figure 3: Forest plots showing study-specific estimates and meta-analysis of ER-disease for 1q32.1/MDM4, 1q32.1/LGR6, 2p24 and 6q12.2/FTO loci in women of European ancestry. Black circles denote the estimated per-allele OR for the risk allele in Europeans. The horizontal lines denote 95% confidence limits. The area of the grey squares is inversely proportional to the variance of the estimate. The diamond denotes the estimated per-allele OR and overall CI from the combined analyses. Estimates from combined analyses differ slightly from those shown in Table 1 because of different software used.

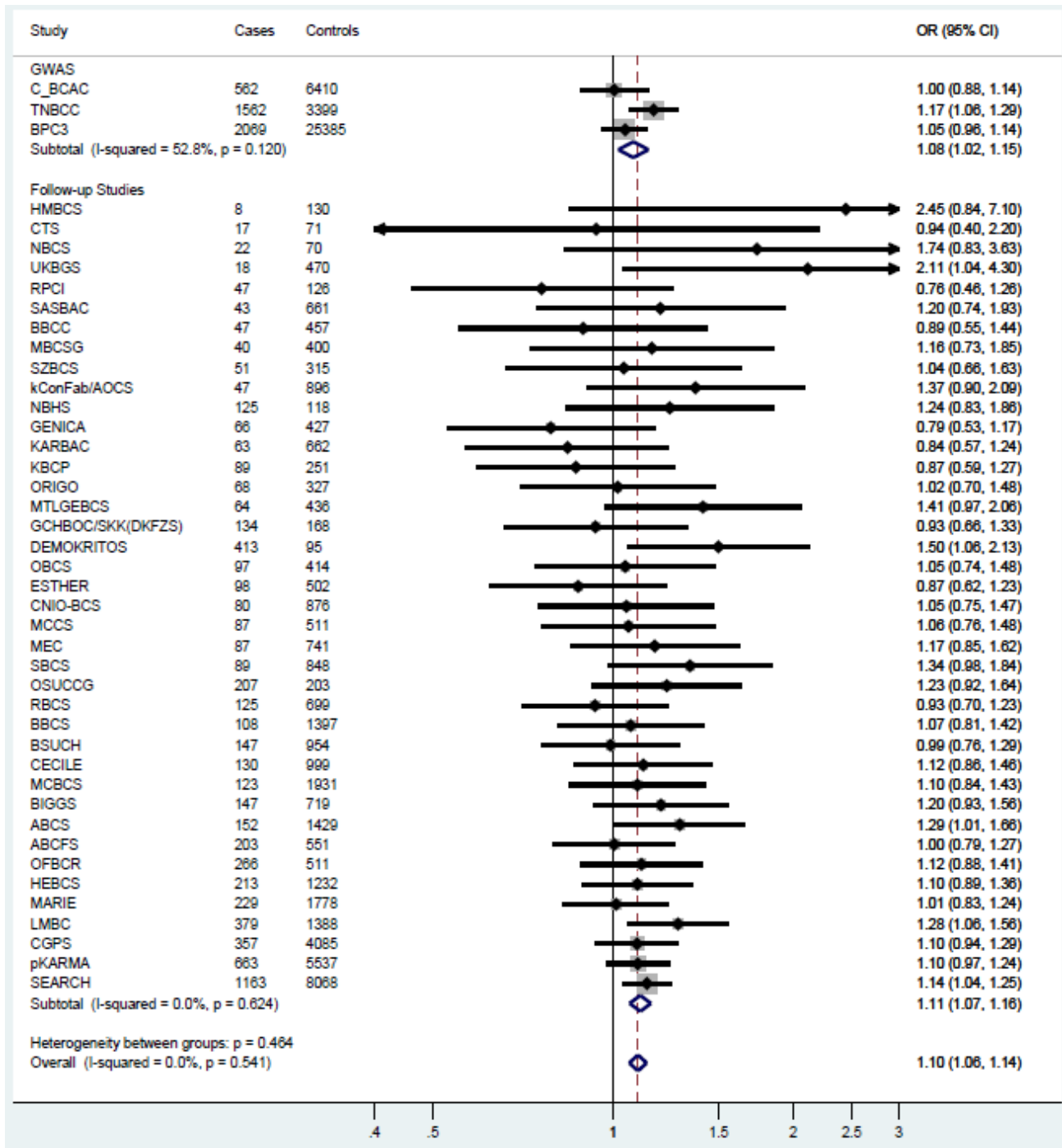
A. rs4245739 in 1q32.1/MDM4



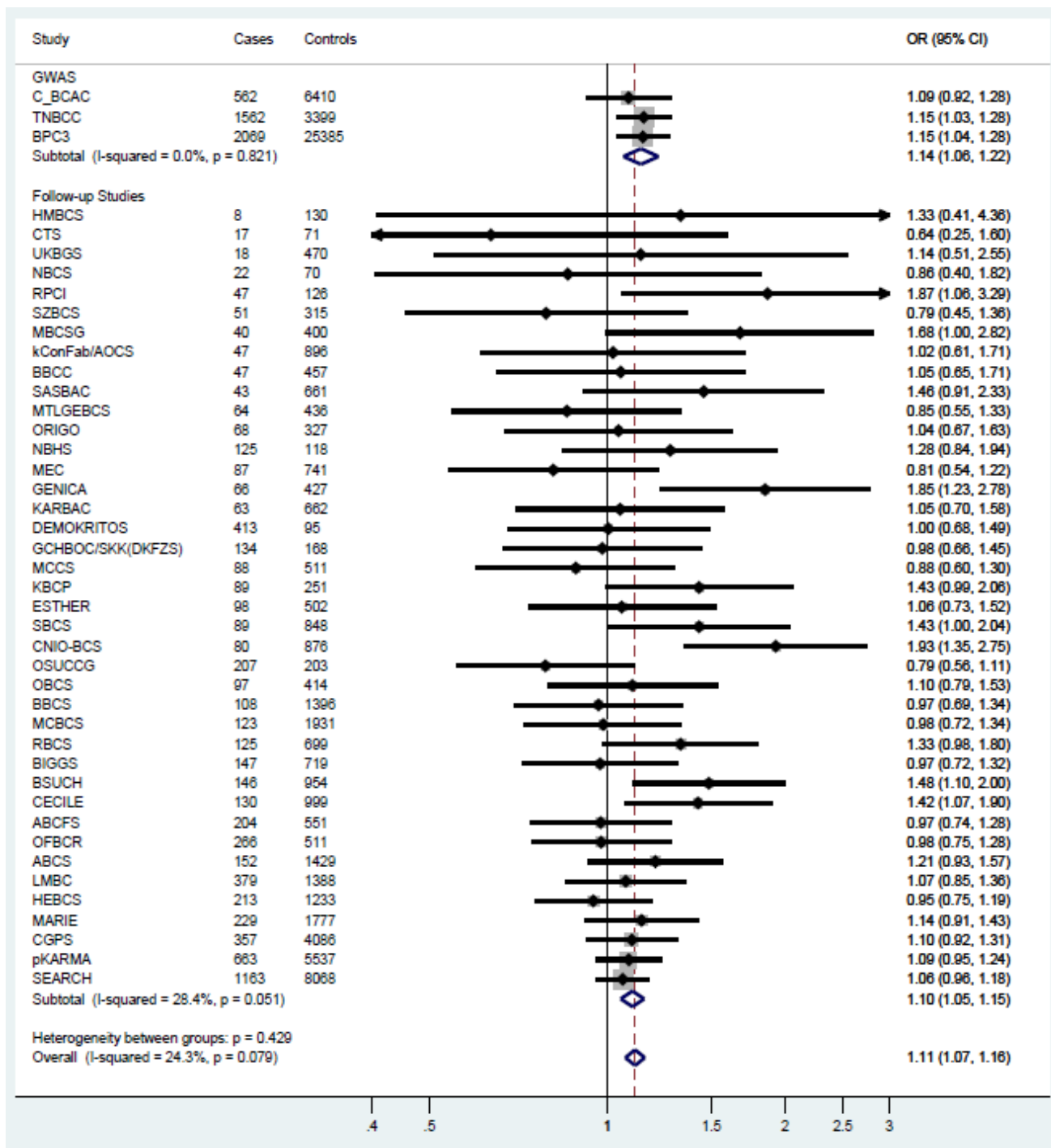
B. rs6678914 in 1q32.1/LGR6



C. rs12710696 in 2p24

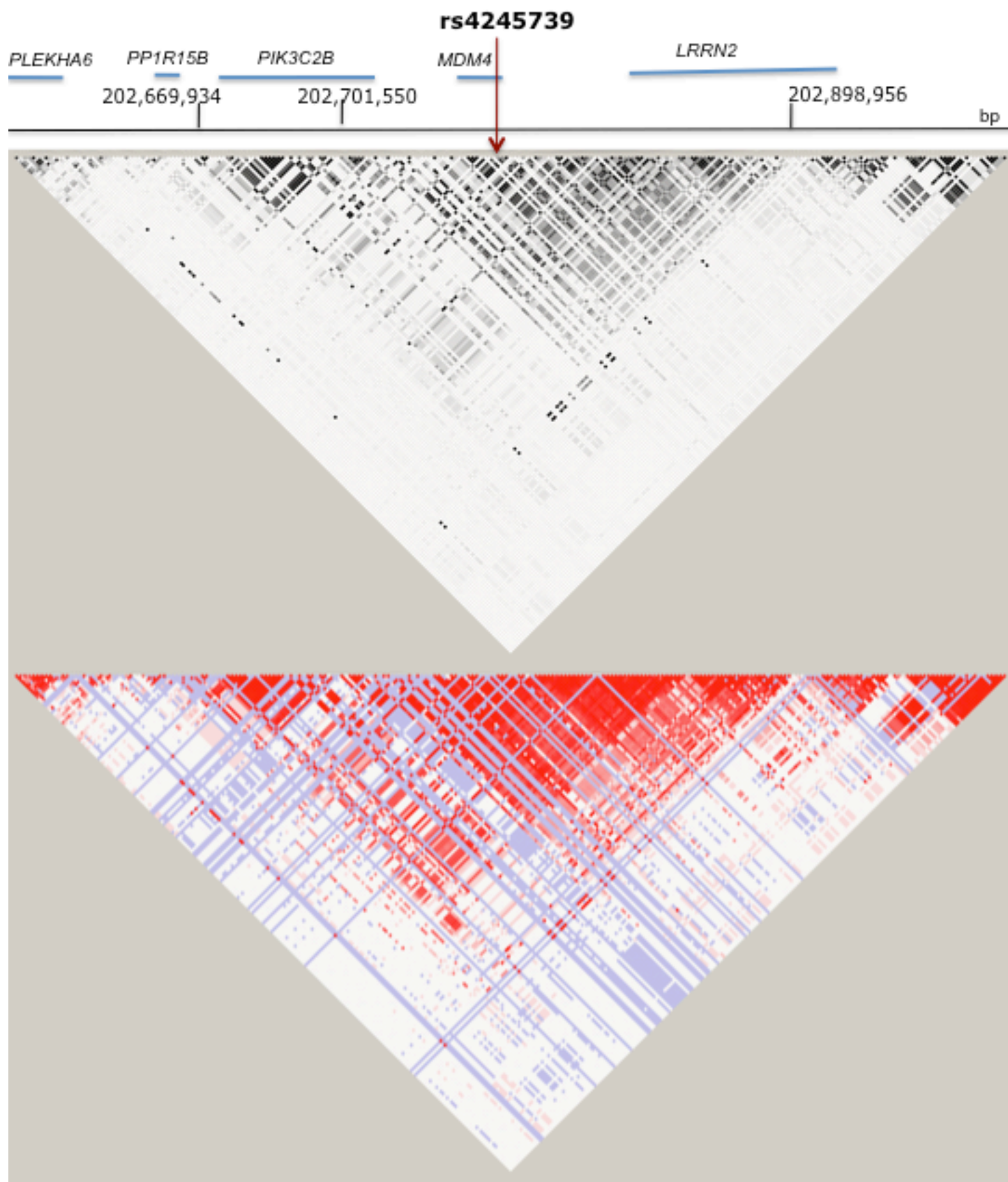


D. rs11075995 in 6q12.2/FTO

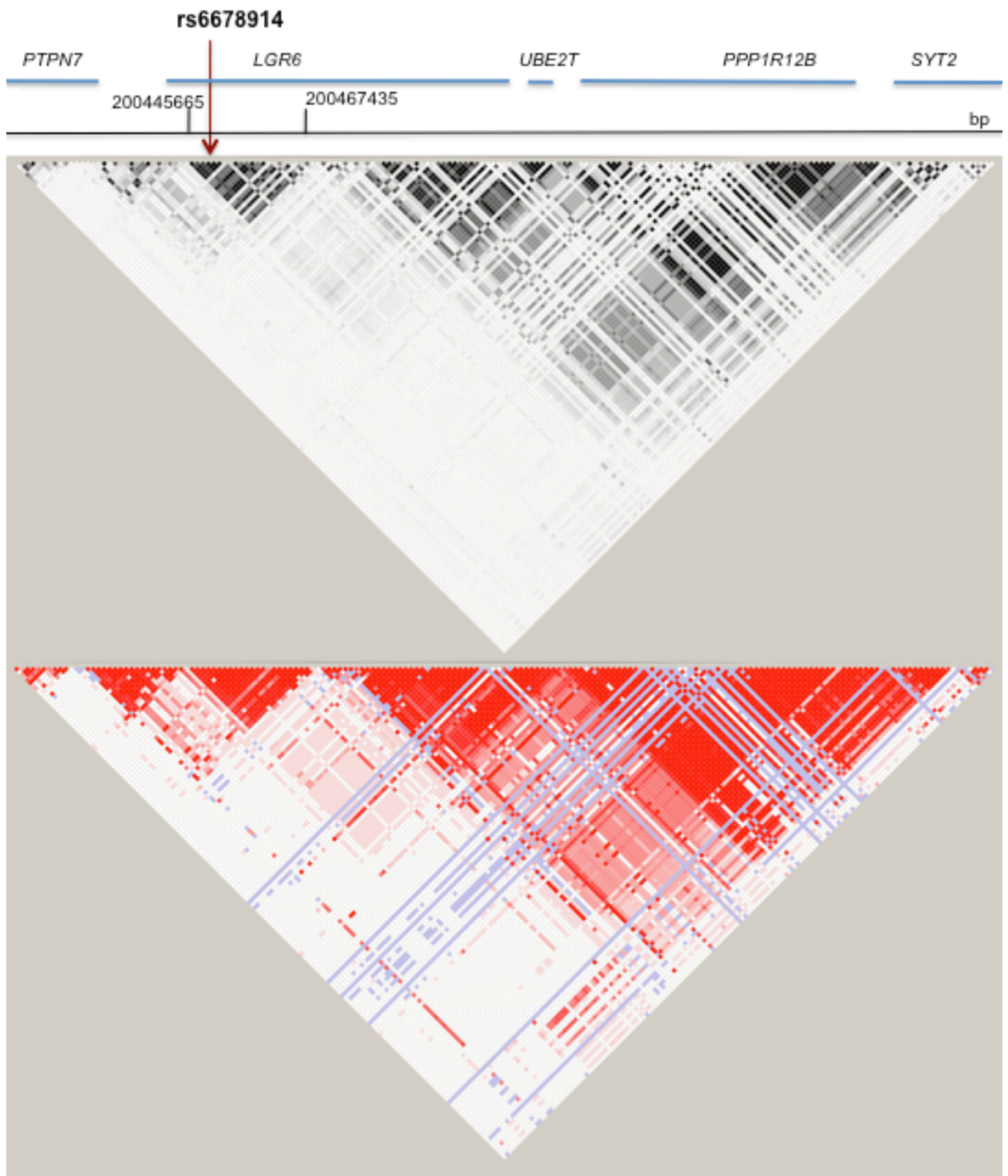


Supplementary Figure 4: Linkage Disequilibrium (LD) Structure at the 1q32.1/*MDM4*, 1q32.1/*LGR6*, 2p24 and 16q12.2/*FTO* loci. rs3751812 is used as a surrogate for the obesity-related SNP rs9939609¹⁴. rs17817449 is ~5Kb from rs3751812 and has been associated with ER-positive and ER-negative disease¹⁵. Pairwise LD plots generated using data from the HapMap CEU population and estimated by r^2 (top panel) and D' (bottom panel). The positions of rs4245739, rs6678914 and rs6678914 are indicated. Gene positions are approximate. Genomic coordinates are from NCBI build 36.

A. 1q32 (*MDM4*) from 202,585kb to 202,885kb



B. 1q32.1 (*LGR6*) from 200380kb to 200880kb



C.

2p24 from 18984kb to 19284kb

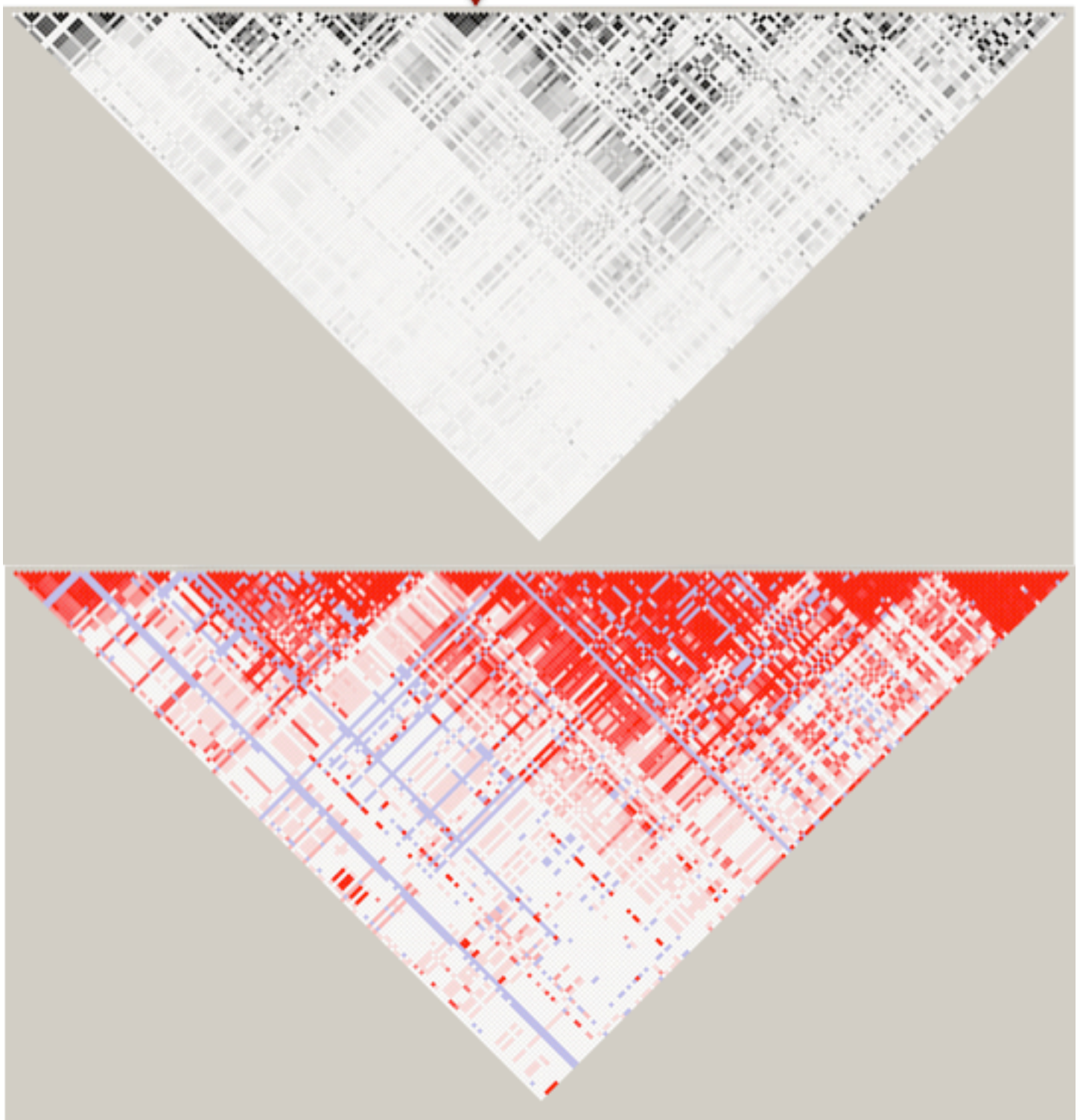
rs12710696

19,173,704

19,325,619

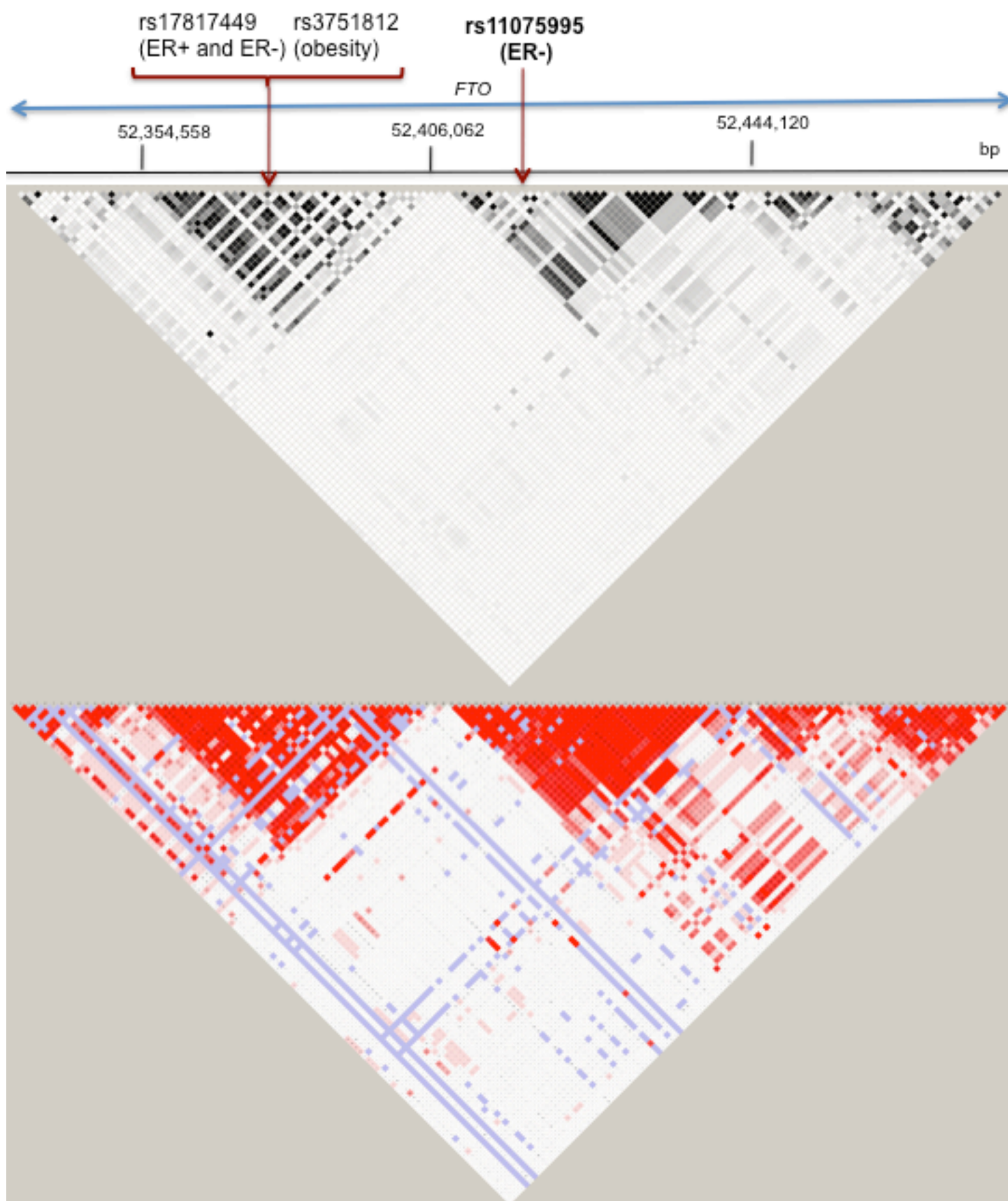
19,351,987

bp



D.

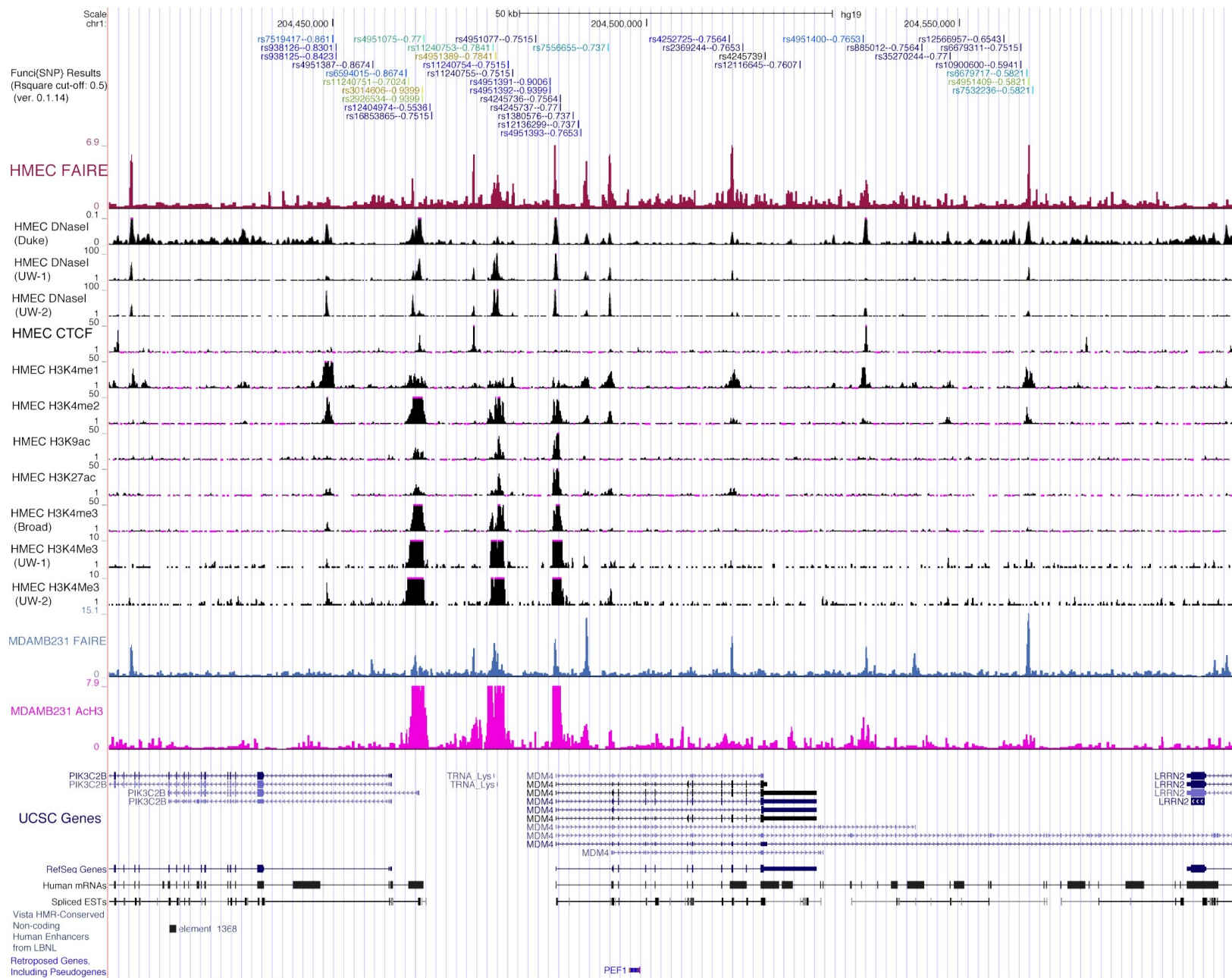
16q12.2 from 52310kb to 52509kb



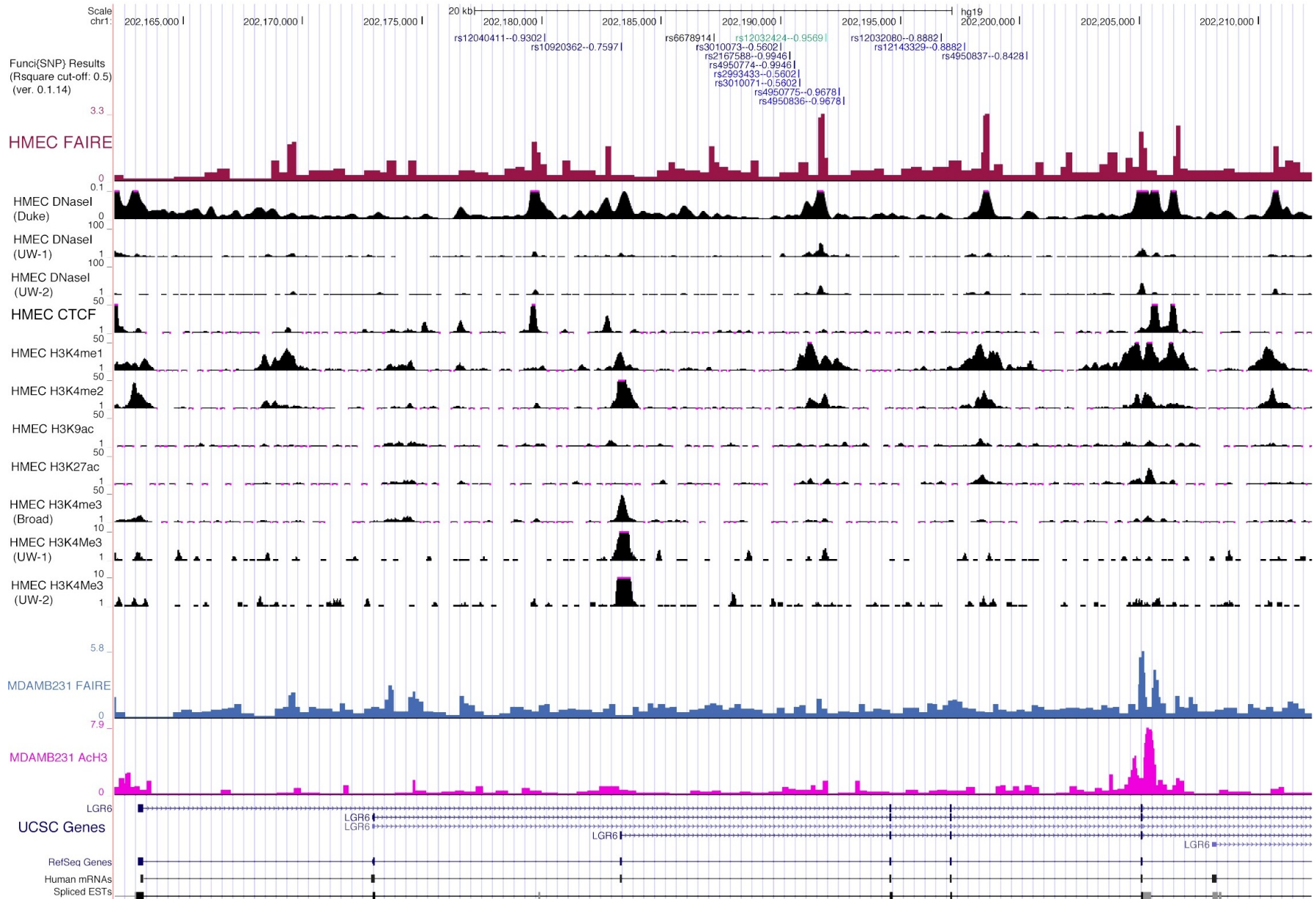
Supplementary Figure 5: Chromatin features for 1q32.1/*MDM4*, 1q32.1/*LGR6*, 2p24 and 16q12.2/*FTO* regions in normal human mammary epithelial cells (HMEC) and triple negative breast cancer cells (MDAMB231).

First track shows FunciSNP result. The name of correlated SNP (rsnumber – r^2 value) is shown and colour coded to indicate the number of biofeatures. The bottom tracks are biofeature tracks and RefSeq genes/mRNA/Pseudogene tracks. rsnumber colour code for number of biofeatures (dark blue:0, green:5 brown:10). We collected 9,893 SNPs, which coincided with one or more biofeatures, in a 1Mb window of each of the four tagSNP from the 1000 genome projects in European ethnic group. Among them, 64 SNPs had R^2 value ≥ 0.5 with the tagSNP. Among the 64 SNPs, 17 SNPs were coinciding with 5 or more biofeatures

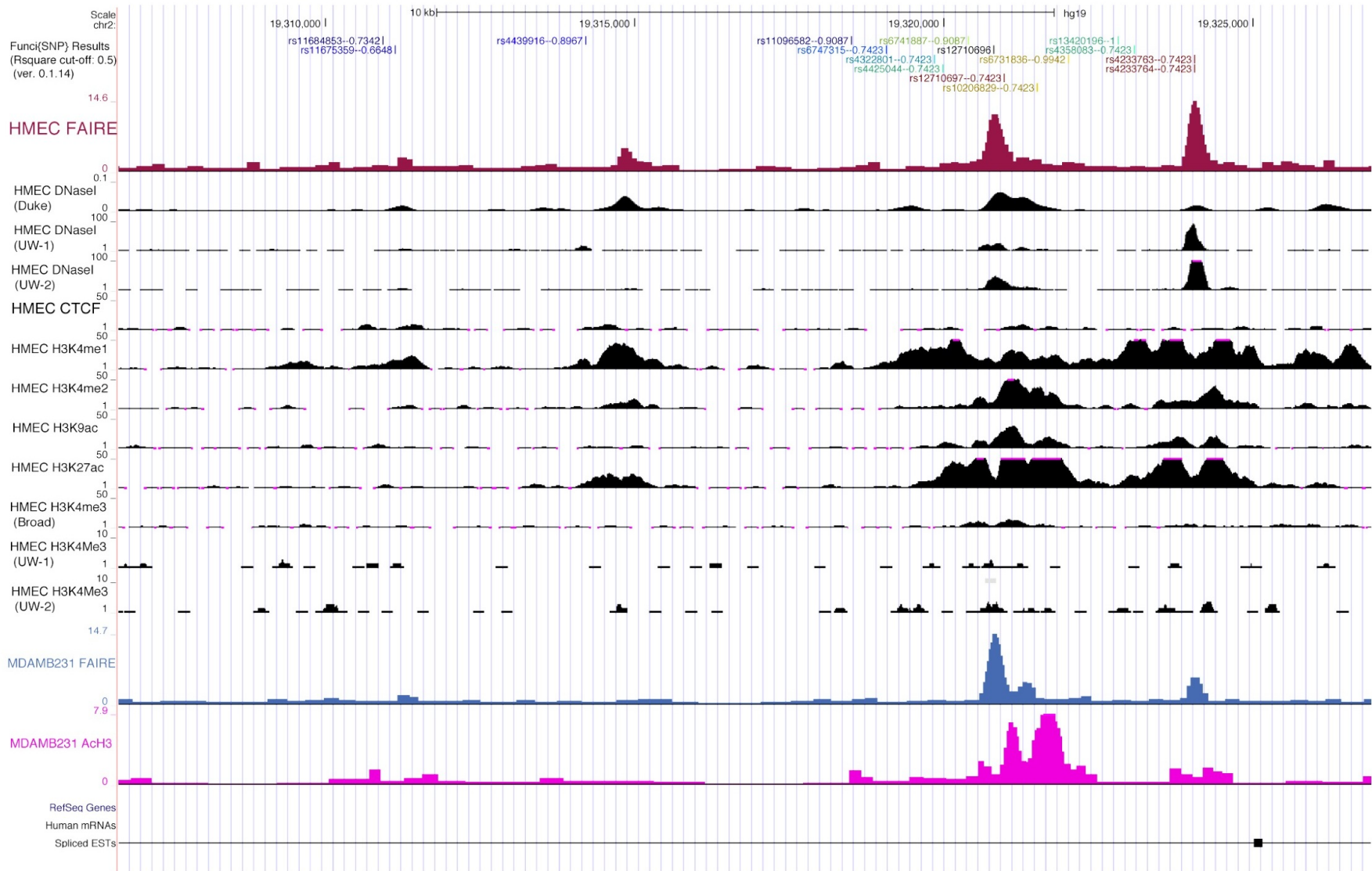
A. rs4245739 in 1a32.1/*MDM4*



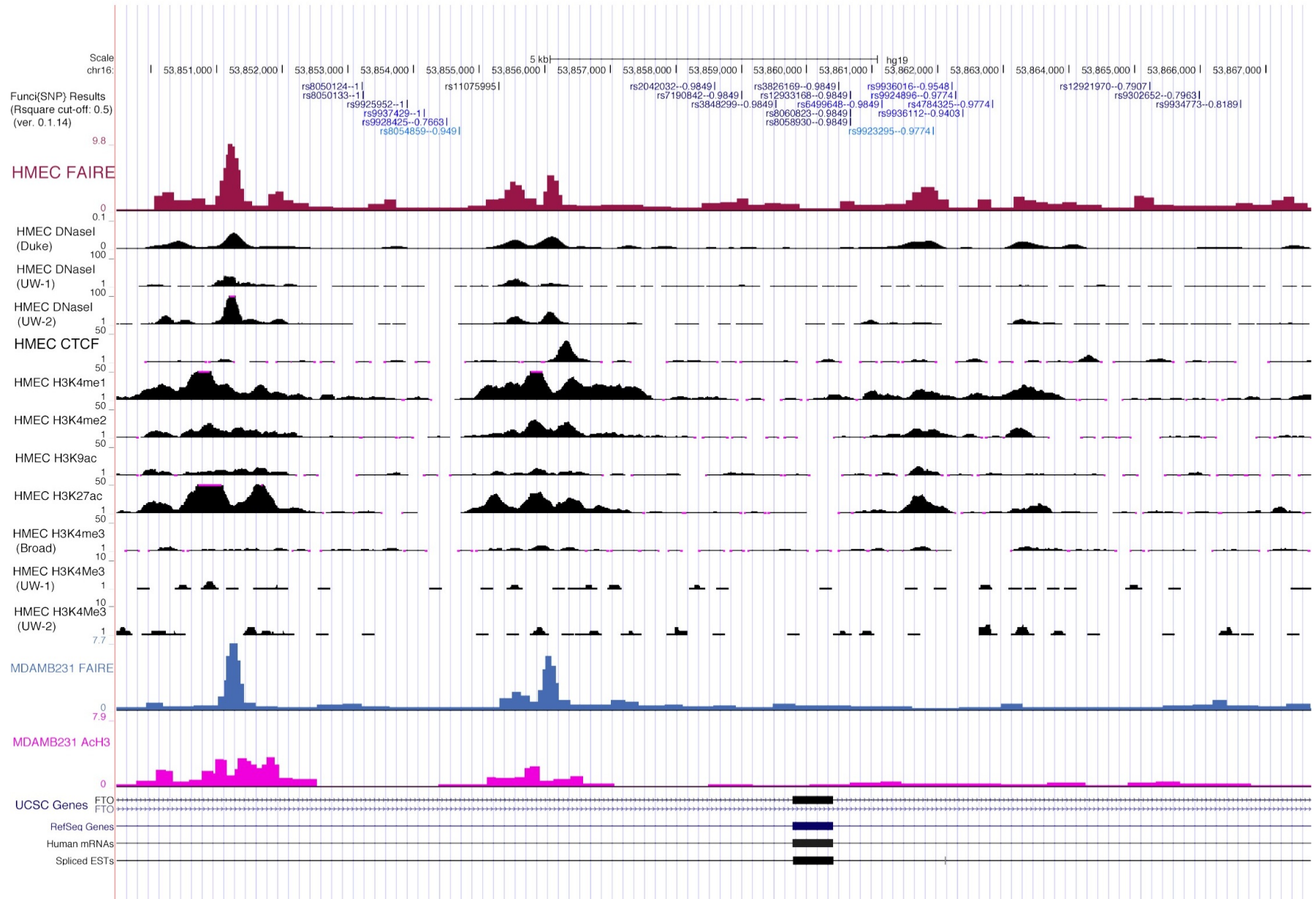
B. rs6678914 1q32.1/LGR6



C. rs12710696 2p24



D. rs11075995 6q12.2/*FTO*



Supplementary Table 1: Number of breast cancer cases and controls in each of the study populations. Numbers for BPC3, TNBCC, C-BCAC and BCAC replication in European populations exclude of subjects that overlapped between studies.

Consortium/Study	Study Abbreviation	Full Name	Country	Controls	ER + cases	ER - cases	TN cases
BPC3	CPS-II	Cancer Prevention Study II Nutrition Cohort	USA	295		293	66
Breast and Prostate Cancer Cohort Consortium	EPIC	European Prospective Investigation into Cancer and Nutrition	Europe	467		478	93
	NHS	The Nurses' Health Study	USA	184		234	86
	NHSII	The Nurses' Health Study II	USA	374		76	34
	PLCO	Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial	USA	340		255	98
	PBCS	Polish Breast Cancer Study	Poland	511		543	229
	WGHS	Women's Genome Health Study	USA	23,214		190	NA
		TOTAL		25,385		2,069	606
TNBCC	ABCTB	Australian Breast Cancer Tissue Bank	Australia				144
Triple Negative	BBCC	Bavarian Breast Cancer Cases and Controls	Germany				218
Breast Cancer Consortium	CGEMS	Cancer Genetic Markers of Susceptibility	USA	947			
	DFCI	Harvard Breast Cancer SPORE Blood Repository	USA				246
	FCCC	Fox Chase Cancer Center	USA				120
	GENICA	Gene Environment Interaction and Breast Cancer in Germany	Germany				59
	HEBCS	Helsinki Breast Cancer Study	Finland	219			83
	KORA	Cooperative Health Research in the Region of Augsburg	Germany	215			
	MARIE	Mammary Carcinoma Risk Factor Investigation	Germany				198
	MCBCS	Mayo Clinic Breast Cancer Study	USA				147
	MCCS	Melbourne Collaborative Cohort Study	Australia				39
	POSH	Prospective Study of Outcomes in Sporadic Versus Hereditary Breast Cancer	UK				266
	QIMR	Australian Twin Cohort study from the Queensland Institute of Medical Research	Australia	650			
	SBCS	Sheffield Breast Cancer Study	UK				42
	WTCCC	Wellcome Trust Case Control Consortium	UK	1,368			
		TOTAL		3,399			1,562
C-BCAC	ABCFS	Northern California Australian Breast Cancer Family Study	Australia	285		72	
Breast Cancer Association Consortium	MARIE	Mammary Carcinoma Risk Factor Investigation	Germany	470		76	
Combined GWAS	HEBCS	Helsinki Breast Cancer Study	Finland	1,012		145	
	SASBAC	Singapore and Sweden Breast Cancer Study	Sweden	756		109	
	UK2	UK Familial Breast Cancer Study	UK	3,887		160	
		TOTAL		6,410		562	
AABC	CARE	The Los Angeles component of The Women's Contraceptive and Reproductive Experiences Study	USA	215		130	
African-American Breast Cancer Consortium	CBCS	The Carolina Breast Cancer Study	USA	589		317	
	MEC-AA	Multiethnic Cohort	USA	990		176	
	NBHS	The Nashville Breast Health Study	USA	182		65	
	NC-BCFR	The Northern California Breast Cancer Family Registry	USA	50		121	
	PLCO	Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial	USA	116		6	
	SFBCS	The San Francisco Bay Area Breast Cancer Study	USA	220		50	
	WCHS	The Women's Circle of Health Study	USA	239		80	
	WFBC	Wake Forest University Breast Cancer Study	USA	144		43	
		TOTAL		2,745		988	
BCAC Replication	European						
	ABCFS	Australian Breast Cancer Family Study	Australia	551	382	204	
	ABCS	Amsterdam Breast Cancer Study	Netherlands	1,429	411	152	81
	BBCC	Bavarian Breast Cancer Study	Germany	457	454	47	24
	BBCS	British Breast Cancer Study	UK	1,397	493	108	29
	BIGGS	Breast Cancer In Galway Genetic Study	Ireland	719	476	147	35
	BSUCH	Breast Cancer Study of the University Clinic Heidelberg	Germany	954	479	147	75
	CECILE	CECILE Breast Cancer Study	France	999	743	130	67
	CGPS	Copenhagen General Population Study	Denmark	4,086	1,919	357	80
	CNIO-BCS	Spanish National Cancer Centre Breast Cancer Study	Spain	876	216	80	32

CTS*	California Teachers Study	USA	71		17	17
DEMOKRITOS*	Demokritos	Greece	95		413	413
ESTHER	ESTHER Breast Cancer Study	Germany	502	302	98	23
GC-HBOC ^a	German Consortium for Hereditary Breast & Ovarian Cancer, and Städtisches Klinikum Karlsruhe Deutsches Krebsforschungszentrum Study	Germany	139			
GENICA	Gene Environment Interaction and Breast Cancer in Germany	Germany	427	327	66	5
HEBCS	Helsinki Breast Cancer Study	Finland	1,233	1,231	213	82
HMBCS	Hannover-Minsk Breast Cancer Study	Belarus	130	35	8	
KARBAC	Karolinska Breast Cancer Study	Sweden	662	338	63	
KBCP	Kuopio Breast Cancer Project	Finland	251	288	89	60
LMBC	Leuven Multidisciplinary Breast Centre	Belgium	1,388	2,068	379	215
MARIE	Mammary Carcinoma Risk Factor Investigation	Germany	1,778	1,257	229	51
MBCSG	Milan Breast Cancer Study Group	Italy	400	128	40	9
MCBCS	Mayo Clinic Breast Cancer Study	USA	1,931	1,271	123	26
MCCS	Melbourne Collaborative Cohort Study	Australia	511	350	88	34
MEC	Multi-ethnic Cohort	USA	741	412	87	8
MTLGEBCS	Montreal Gene-Environment Breast Cancer Study	Canada	436	421	64	45
NBCS*	Norwegian Breast Cancer Study	Norway	70		22	21
NBHS*	The Nashville Breast Health Study	USA	118		125	125
OBCS	Oulu Breast Cancer Study	Finland	414	403	97	62
OFBCR	Ontario Familial Breast Cancer Registry	Canada	511	630	266	
ORIGO	Leiden University Medical Centre Breast Cancer Study	Netherlands	327	211	68	5
OSUCCG*	Ohio State University	USA	203		207	207
RBCS	Rotterdam Breast Cancer Study	Netherlands	699	366	125	11
RPCI*	Roswell Park Cancer Institute	USA	126		47	47
SASBAC	Singapore and Sweden Breast Cancer Study	Sweden	661	198	43	
SBCS	Sheffield Breast Cancer Study	UK	848	356	89	17
SEARCH	Study of Epidemiology and Risk factors in Cancer Heredity	UK	8,068	5,113	1,163	400
SKK(DKFZS) ^a	Städtisches Klinikum Karlsruhe and Deutsches Krebsforschungszentrum Breast Cancer Study	Germany	29		134	134
SZBCS	IHCC-Szczecin Breast Cancer Study	Poland	315	149	51	6
UKBGS	UK Breakthrough Generations Study	UK	470	88	18	3
kConFab/AOCS	kConFab/AOCS	Australia	896	126	47	18
pKARMA	Karolinska Mammography Project for Risk Prediction of Breast Cancer - prevalent cases	Sweden	5,537	3,586	663	
		TOTAL	41,455	25,227	6,514	2,467
Asian						
ACP	Asia Cancer Program	Thailand	636	91	52	
HERPACC	Hospital-based Epidemiologic Research Program at Aichi Cancer Center	Japan	1,376	342	124	29
LAABC	Los Angeles County Asian-American Breast Cancer Case-Control Study	USA	990	527	138	
MYBRCA	Malaysian Breast Cancer Genetic Study	Malaysia	610	422	291	84
SBCGS	Shanghai Breast Cancer Genetic Study	China	892	498	271	
SEBCS	Seoul Breast Cancer Study	Korea	1,129	622	363	68
SGBCC	Singapore Breast Cancer Cohort	Singapore	502	261	103	41
TBCS	IARC-Thai Breast Cancer Study	Thailand	253	26	26	
TWBCS	Taiwanese Breast Cancer Study	Taiwan	236	395	179	12
		TOTAL	6,624	3,184	1,547	234
African-American						
NBHS	The Nashville Breast Health Study	USA	252	176	91	14
TOTAL ALL STUDIES			86,270	28,587	11,771	4,883

ER+: Estrogen receptor (ER) positive

ER-: Estrogen receptor (ER) negative

TN: triple-negative

* These four TNBCC studies only provided controls for other studies and are thus not counted as separate studies.

** These follow up studies were genotyped as part of the TNBCC.

^a GC-HBOC contains controls only - to be used as controls for SKKDKFZS.

Supplementary Table 2: Conditional analyses of risk of ER-negative breast cancer for the two loci in 1q32.1 (*MDM4* and *LGR6*), and for the two 16q12.2/*FTO* loci (based on BCAC replication data only)

Locus	SNP	OR	95% CI		<i>P</i>		OR	95% CI		<i>P</i>
1q32.1	rs4245739	1.14	1.09	1.19	7.0×10^{-9}	rs6678914	1.08	1.04	1.12	2.2×10^{-4}
16q12.2	rs11075995	1.13	1.08	1.18	2.3×10^{-7}	rs17817449	1.13	1.09	1.18	2.1×10^{-9}

Supplementary Table 3: Genotype-specific odds ratios for the most significant SNPs in the 1q32.1/MDM4, 1q32.1/LGR6, 2p24 and 16q12.2/FTO loci and risk of ER-negative breast cancer (based on BCAC replication data only)

Rsnnumber/cytoband/gene/ position (NCBI build 36)	N Studies	Cases	Controls	OR	95% CI		P value
Genotypes							
rs4245739 / 1q32.1 / 202785465 / MDM4							
AA	40	3,318	22,825	1.00			Ref.
AC		2,637	15,798	1.13	1.06	1.20	4.7x10 ⁻⁵
CC		557	2,828	1.31	1.18	1.46	3.6x10 ⁻⁷
Total		6,512	41,451				
				P for departure from log-additivity			0.666
rs6678914 / 1q32.1 / 200453799 / LGR6							
AA	40	1,008	7,036	1.00			Ref.
AG		3,078	20,201	1.02	0.96	1.11	0.545
GG		2,428	14,215	1.15	1.06	1.25	1.3x10 ⁻³
Total		6,514	41,452				
				P for departure from log-additivity			0.138
rs12710696 / 2p24.1 / 19184284							
GG	40	2,427	17,123	1.00			Ref.
AG		3,102	19,092	1.10	1.03	1.17	0.002
AA		983	5,238	1.23	1.13	1.34	2.3x10 ⁻⁶
Total		6,512	41,453				
				P for departure from log-additivity			0.744
rs11075995 / 16q12.2 / 52412792 / FTO							
AA	40	3,624	23,826	1.00			Ref.
AT		2,443	15,290	1.06	1.00	1.12	0.061
TT		446	2,337	1.30	1.16	1.46	4.4x10 ⁻⁶
Total		6,513	41,453				
				P for departure from log-additivity			0.039

Supplementary Table 4: Distribution of ER, PR, HER2 and triple-negative status in BCAC replication samples of invasive breast cancer cases of European ancestry with ER data

Study	Total	ER status			PR status				HER2 status				TN status in ER- cases			
		Negative	Positive	% neg	Negative	Positive	Missing	% neg	Negative	Positive	Missing	% neg	TN	non-TN	Missing	% TN
ABCFS	586	204	382	35	167	419	0	28	0	0	586		0	0	204	
ABCS	563	152	411	27	235	325	3	42	332	203	28	62	81	66	5	55
BBCC	501	47	454	9	115	386	0	23	433	51	17	89	24	22	1	52
BBCS	601	108	493	18	126	256	219	33	201	50	350	80	29	17	62	63
BIGGS	623	147	476	24	126	390	107	24	328	87	208	79	35	55	57	39
BSUCH	626	147	479	23	192	432	2	31	495	98	33	83	75	65	7	54
CECILE	873	130	743	15	249	613	11	29	560	84	229	87	67	29	34	70
CGPS	2,276	357	1,919	16	635	1,163	478	35	677	110	1,489	86	80	39	238	67
CNIO-BCS	296	80	216	27	127	158	11	45	153	42	101	78	32	22	26	59
CTS*	17	17	0		17	0	0		17	0	0		17	0	0	
DEMOKRITOS*	413	413	0		413	0	0		413	0	0		413	0	0	
ESTHER	400	98	302	25	135	257	8	34	126	49	225	72	23	18	57	56
GENICA	393	66	327	17	90	303	0	23	192	84	117	70	5	36	25	12
HEBCS	1,444	213	1,231	15	455	983	6	32	756	73	615	91	82	32	99	72
HMBCS	43	8	35	19	0	0	43		0	0	43		0	0	8	
KARBAC	401	63	338	16	83	267	51	24	0	0	401		0	0	63	
KBCP	377	89	288	24	139	236	2	37	346	23	8	94	60	27	2	69
LMBC	2,447	379	2,068	15	568	1,866	13	23	1,937	295	215	87	215	122	42	64
MARIE	1,486	229	1,257	15	412	1,073	1	28	1,035	285	166	78	51	148	30	26
MBCSG	168	40	128	24	51	117	0	30	60	57	51	51	9	17	14	35
MCBCS	1,394	123	1,271	9	263	1,130	1	19	970	190	234	84	26	71	26	27
MCCS	438	88	350	20	141	297	0	32	336	59	43	85	34	38	16	47
MEC	499	87	412	17	132	334	33	28	74	20	33	79	8	11	68	42
MTLGBCS	485	64	421	13	127	357	1	26	422	49	14	90	45	17	2	73
NBCS*	22	22	0		22	0	0		21	0	1		21	0	1	
NBHS*	125	125	0		125	0	0		125	0	0		125	0	0	
OBCS	500	97	403	19	144	355	1	29	431	69	0	86	62	35	0	64
OFBCR	896	266	630	30	339	534	23	39	0	0	896		0	0	266	
ORIGO	279	68	211	24	85	144	50	37	9	0	270		5	0	63	
OSUCCG*	207	207	0		207	0	0		207	0	0		207	0	0	
RBCS	491	125	366	25	146	271	74	35	69	10	412	87	11	2	112	85
RPCI*	47	47	0		47	0	0		47	0	0		47	0	0	
SASBAC	241	43	198	18	67	168	6	29	0	0	241		0	0	43	
SBCS	445	89	356	20	65	109	271	37	188	4	253	98	17	14	58	55
SEARCH	6,276	1,163	5,113	19	898	2,138	3,240	30	2,730	107	3,439	96	400	169	594	70
SKK(DKFZS)*	134	134	0		134	0	0		134	0	0		134	0	0	
SZBCS	200	51	149	26	26	93	81	22	49	55	96	47	6	10	35	38
UKBGS	106	18	88	17	23	54	29	30	31	7	68	82	3	1	14	75
kConFab/AOCS	173	47	126	27	45	108	20	29	102	15	56	87	18	11	18	62
pKARMA	4,249	663	3,586	16	1,246	2,923	80	30	0	0	4,249		0	0	663	
Total	31,741	6,514	25,227		8,617	18,259	4,865		14,006	2,176	15,559		2,467	1,094	2,953	

Table includes only invasive breast cancer cases in iCOGS with data on ER status (i.e. 9,354 invasive breast cancer cases in iCOGS with missing ER data (21% of all cases) are excluded from this table. * Studies including only triple-negative cases (Part of TNBCC). GC-HBOC not shown because it has only controls to be used as controls for SKKDKFZS.

Supplementary Table 5: Association with risk of breast cancer for most significant SNPs in the 1q32.1/*MDM4*, 1q32.1/*LGR6*, 2p24 and 16q12.2/*FTO* loci, stratified by breast cancer tumour subtypes

rsnumber/cytoband/position /neighbourhood genes	Consortium	N Studies	Cases	Controls	OR	95% CI		P value
rs4245739/1q32.1/202785465/<i>MDM4</i>								
All cases vs controls	BCAC/iCOGS	40	41,090	41,451	1.02	1.00	1.04	0.080
ER+ cases vs controls	BCAC/iCOGS	33	25,225	40,600	0.99	0.97	1.02	0.563
ER- cases vs controls	BCAC/iCOGS	40	6,512	41,451	1.14	1.09	1.19	5.6x10 ⁻⁹
ER- vs ER+ cases	BCAC/iCOGS	33	5,547	25,225	0.88	0.84	0.92	2.8x10 ⁻⁸
TN cases vs controls	BCAC/iCOGS	34	2,465	33,400	1.17	1.09	1.26	3.1x10 ⁻⁵
non-TN ER- cases vs controls	BCAC/iCOGS	26	1,094	32,222	1.02	0.92	1.12	0.711
TN cases vs non-TN ER- cases	BCAC/iCOGS	26	1,496	1,094	1.11	0.98	1.27	0.103
	BPC3	5	606	429	1.31	1.07	1.60	0.009
	<i>Combined</i>							
	<i>BCAC+BPC3</i>	31	2,102	1,523	1.17	1.05	1.30	0.005
rs6678914 / 1q32.1 / 200453799 / <i>LGR6</i>								
All cases vs controls	BCAC/iCOGS	40	41,090	41,452	1.00	0.98	1.02	0.857
ER+ cases vs controls	BCAC/iCOGS	33	25,223	40,601	0.99	0.96	1.01	0.212
ER- cases vs controls	BCAC/iCOGS	40	6,514	41,452	1.08	1.04	1.12	1.6x10 ⁻⁴
ER- vs ER+ cases	BCAC/iCOGS	33	5,549	25,223	0.90	1.00	0.94	1.6x10 ⁻⁶
TN cases vs controls	BCAC/iCOGS	34	2,467	33,400	1.03	0.96	1.10	0.414
non-TN ER- cases vs controls	BCAC/iCOGS	26	1,094	32,222	1.11	1.01	1.21	0.027
TN cases vs non-TN ER- cases	BCAC/iCOGS	26	1,498	1,094	0.97	0.86	1.09	0.603
	BPC3	5	606	429	1.02	0.85	1.21	0.869
	<i>Combined</i>							
	<i>BCAC+BPC3</i>	31	2,104	1,523	0.98	0.89	1.09	0.734
rs12710696 /2p24.1/19184284								
All cases vs controls	BCAC/iCOGS	40	41,090	41,453	1.04	1.01	1.06	9.7x10 ⁻⁴
ER+ cases vs controls	BCAC/iCOGS	33	25,225	40,602	1.01	0.98	1.03	0.534
ER- cases vs controls	BCAC/iCOGS	40	6,512	41,453	1.11	1.06	1.15	1.0x10 ⁻⁶
ER- vs ER+ cases	BCAC/iCOGS	33	5,547	25,225	0.91	0.87	0.95	2.7x10 ⁻⁵
TN cases vs controls	BCAC/iCOGS	34	2,466	33,401	1.15	1.07	1.23	6.7x10 ⁻⁵
non-TN ER- cases vs controls	BCAC/iCOGS	26	1,094	32,223	1.16	1.06	1.26	0.001
TN cases vs non-TN ER- cases	BCAC/iCOGS	26	1,497	1,094	0.98	0.87	1.11	0.802
	BPC3	5	606	429	0.91	0.76	1.10	0.342
	<i>Combined</i>							
	<i>BCAC+BPC3</i>	31	2,103	1,523	0.96	0.87	1.07	0.468
rs11075995 /16q12.2 / 52412792 / <i>FTO</i>								
All cases vs controls	BCAC/iCOGS	40	41,085	41,453	1.04	1.02	1.06	7.5x10 ⁻⁴
ER+ cases vs controls	BCAC/iCOGS	33	25,220	40,602	1.02	1.00	1.05	0.083
ER- cases vs controls	BCAC/iCOGS	40	6,513	41,453	1.10	1.05	1.15	3.6x10 ⁻⁵
ER- vs ER+ cases	BCAC/iCOGS	33	5,548	25,220	0.93	0.89	0.98	0.003
TN cases vs controls	BCAC/iCOGS	34	2,466	33,401	1.11	1.03	1.20	0.007
non-TN ER- cases vs controls	BCAC/iCOGS	26	1,094	32,223	1.13	1.02	1.25	0.016
TN cases vs non-TN ER- cases	BCAC/iCOGS	26	1,497	1,094	1.04	0.91	1.19	0.547
	BPC3	5	606	429	1.14	0.93	1.41	0.210
	<i>Combined</i>							
	<i>BCAC+BPC3</i>	31	2,103	1,523	1.07	0.91	1.19	0.239

Supplementary Table 6: Association with risk of ER-negative breast cancer for most significant SNPs in the 1q32.1/MDM4, 1q32.1/LGR6, 2p24 and 16q12.2/FTO loci in populations of Asian and African ancestry

Rsnumber /cytoband / gene / position (NCBI build 36) – risk allele/reference allele	T/I	Ethnicity	N Studies	Cases	Controls	RAF	OR	95% CI	P	P test for difference in OR compared to Europeans
rs4245739/1q32.1/MDM4/ 202,785,465 –C/A										
AABC	T	African	9	1,004	2,773	0.24	1.07	0.95 1.21	0.291	
BCAC	T	African	1	91	252	0.23	1.22	0.83 1.79	0.304	
Meta-analysis in Africans		African	10	1095	3025		1.08	0.96 1.22	0.186	0.440
BCAC	T	Asian	9	1547	6622	0.06	0.97	0.81 1.16	0.723	0.086
rs6678914 / 1q32.1/LGR6 /200,453,799 – G/A										
AABC	T	African	9	1,004	2,773	0.67	1.00	0.89 1.12	0.988	
BCAC	T	African	1	91	252	0.67	0.90	0.62 1.31	0.573	
Meta-analysis in Africans		African	10	1095	3025		0.99	0.89 1.10	0.882	0.076
BCAC	T	Asian	9	1547	6623	0.76	1.04	0.95 1.15	0.385	0.330
rs12710696 /2p24.1/ 19,184,284 – T/C										
AABC	I	African	9	1,004	2,773	0.54	1.00	0.90 1.11	0.997	
BCAC	T	African	1	91	252	0.52	0.91	0.65 1.28	0.601	
Meta-analysis in Africans		African	10	1095	3025		0.99	0.90 1.10	0.875	0.065
BCAC/iCOGS	T	Asian	9	1547	6623	0.33	1.05	0.96 1.14	0.295	0.339
rs11075995 /16q12.2 / FTO, KIAA1752 / 52,412,792 –A/T										
AABC	I	African	9	1,004	2,773	0.19	1.13	0.98 1.29	0.087	
BCAC	T	African	1	21	252	0.15	1.32	0.81 2.14	0.262	
Meta-analysis in Africans		African	9	1025	3025		1.14	1.00 1.30	0.050	0.688
BCAC	T	Asian	9	1547	6623	0.30	1.03	0.94 1.13	0.489	0.135

I/T indicates imputed and typed SNPs. RAF: risk allele frequency. P-study het.: Q-test for study heterogeneity of estimated ORs.

Estimates for Europeans (meta-analysis) are shown in Table 1.

Supplementary Table 7: Association with risk of ER-negative breast cancer risk for most significant SNPs in the 1q32.1/MDM4, 1q32.1/LGR6, 2p24 and 16q12.2/FTO loci, stratified by 5-year age categories (based on BCAC replication data in studies of European ancestry).

RS number Age category, years	ER- vs controls						P-het
	ER-	Controls	OR	95%CI		P	
rs4245739							
<40	531	3,791	1.28	1.11	1.49	0.001	0.008
40-<45	526	3,433	1.15	0.99	1.34	0.076	0.138
45-<50	583	4,433	1.14	0.99	1.31	0.073	0.144
50-<55	775	6,354	1.17	1.04	1.32	0.010	0.055
55-<60	827	6,198	0.99	0.88	1.12	0.875	Ref.
60-<65	779	5,558	1.10	0.98	1.24	0.119	0.227
65-<70	567	4,529	1.19	1.04	1.37	0.014	0.049
>=70	582	3,732	1.00	0.87	1.16	0.977	0.902
Total	5,170	38,028				<i>P trend in ER- cases=0.314</i>	
rs6678914							
<40	532	3,791	1.00	0.87	1.15	0.382	0.063
40-<45	526	3,433	1.03	0.90	1.18	0.508	0.118
45-<50	583	4,434	1.11	0.98	1.27	0.900	0.469
50-<55	775	6,354	1.17	1.05	1.31	0.994	0.873
55-<60	827	6,197	1.19	1.06	1.32	0.998	Ref.
60-<65	779	5,558	1.05	0.94	1.17	0.670	0.125
65-<70	567	4,530	1.09	0.96	1.24	0.838	0.346
>=70	582	3,732	1.04	0.91	1.19	0.593	0.146
Total	5,171	38,029				<i>P trend in ER- cases=0.315</i>	
rs12710696							
<40	531	3,790	1.14	0.99	1.31	0.067	0.560
40-<45	526	3,433	1.09	0.95	1.25	0.225	0.916
45-<50	583	4,434	1.11	0.97	1.26	0.124	0.769
50-<55	774	6,354	1.15	1.03	1.29	0.014	0.427
55-<60	827	6,199	1.08	0.97	1.21	0.179	Ref.
60-<65	779	5,558	1.17	1.05	1.31	0.005	0.302
65-<70	567	4,529	1.06	0.93	1.21	0.417	0.807
>=70	582	3,732	1.06	0.93	1.21	0.392	0.832
Total	5,169	38,029				<i>P trend in ER- cases=0.694</i>	
rs11075995							
<40	532	3,791	1.07	0.91	1.25	0.423	0.852
40-<45	526	3,433	1.20	1.03	1.40	0.018	0.165
45-<50	582	4,433	0.95	0.82	1.10	0.502	0.327
50-<55	775	6,354	1.08	0.96	1.23	0.215	0.711
55-<60	827	6,199	1.05	0.93	1.18	0.468	Ref.
60-<65	779	5,558	1.11	0.98	1.26	0.115	0.537
65-<70	567	4,529	1.27	1.10	1.46	0.001	0.044
>=70	582	3,732	1.19	1.03	1.37	0.020	0.193
Total	5,170	38,029				<i>P trend in ER- cases=0.841</i>	

Supplementary Table 8: Association with risk of ER-negative breast cancer risk for most significant SNPs in the 1q32.1/MDM4, 1q32.1/LGR6, 2p24 and 16q12.2/FTO loci, stratified by family history (FH) of breast cancer in first degree relatives (based on iCOGS data from studies of European ancestry)

Family History	ER + vs controls							ER- vs controls					FH+ vs FH- in ER- cases				
	ER+	Controls	OR	95%CI	P	P-het		ER-	Controls	OR	95%CI	P		OR	95%CI	P	
rs4245739																	
No	8,783	15,317	0.99	0.95	1.03	0.575	Ref.	2,121	15,440	1.21	1.12	1.30	3.1x10 ⁻⁷				Ref.
Yes	2,403	1,891	0.95	0.86	1.05	0.305	0.473	490	1,919	1.01	0.86	1.19	0.885	0.91	0.80	1.04	0.172
Total	11,186	17,208						2,611	17,359								
rs6678914																	
No	8,783	15,318	1.00	0.96	1.03	0.809	Ref.	2,121	15,441	1.13	1.06	1.21	2.7x10 ⁻⁴				Ref.
Yes	2,403	1,891	0.98	0.89	1.07	0.632	0.731	491	1,919	0.97	0.84	1.12	0.684	0.89	0.79	1.00	0.049
Total	11,186	17,209						2,612	17,360								
rs12710696																	
No	8,782	15,318	1.01	0.97	1.05	0.758	Ref.	2,120	15,441	1.13	1.05	1.21	0.001				Ref.
Yes	2,403	1,891	1.04	0.95	1.14	0.408	0.523	491	1,919	1.12	0.97	1.30	0.134	0.98	0.87	1.10	0.719
Total	11,185	17,209						2,611	17,360								
rs12710696																	
No	8,783	15,316	1.05	1.00	1.10	0.043	Ref.	2,121	15,439	1.12	1.04	1.21	0.003				Ref.
Yes	2,403	1,891	1.04	0.94	1.15	0.478	0.886	491	1,919	1.10	0.93	1.30	0.283	0.98	0.86	1.12	0.773
Total	11,186	17,207						2,612	17,358								

Supplementary Table 9: Association with risk of ER-negative breast cancer for known breast cancer risk loci in populations of European ancestry (meta-analysis of BPC3, TNBCC, Combined ER-negative GWAS and BCAC replication data in studies of European ancestry). SNPs with P<0.05 are shown in bold.

Cytoband	Locus	RS number	Position	Minor Allele	Other Allele	MAF	OR	(95% C.I.)		P
Previously reported loci¹										
1p11.2		rs11249433	120982136	G	A	0.405	1.00	0.97	1.04	0.796
2q33.1	CASP8	rs1045485	201857834	C	G	0.115	0.94	0.89	0.98	0.008
2q35		rs13387042	217614077	G	A	0.489	0.95	0.92	0.98	0.002
3p24.1	SLC4A7	rs4973768	27391017	T	C	0.472	1.04	1.01	1.07	0.018
5p15.33	TERT	rs10069690	1332790	T	C	0.321	1.15	1.11	1.20	4.5x10⁻¹²
5p12		rs10941679	44742255	G	A	0.338	1.04	1.00	1.08	0.029
5q11.2	MAP3K1	rs889312	56067641	C	A	0.334	1.05	1.01	1.09	0.006
6q14.1		rs17530068	82249828	C	T	0.237	1.09	1.05	1.13	3.3x10⁻⁶
6q25.1	ESR1	rs3757318	151955806	A	G	0.071	1.22	1.15	1.30	2.5x10⁻¹¹
6q25.1	ESR1	rs2046210	151990059	A	G	0.423	1.15	1.11	1.19	4.9x10⁻¹⁶
8q24.21		rs13281615	128424800	G	A	0.411	1.03	0.99	1.06	0.113
9p21.3	CDKN2A/B	rs1011970	22052134	T	G	0.169	1.09	1.05	1.14	3.9x10⁻⁵
9q31.2		rs865686	109928299	G	T	0.377	0.98	0.95	1.02	0.325
10p15.1	ANKRD16	rs2380205	5926740	T	C	0.440	1.00	0.97	1.03	0.903
10q21.2	ZNF365	rs10995190	63948688	A	G	0.154	0.89	0.85	0.93	1.3x10⁻⁷
10q22.3	ZMIZ1	rs704010	80511154	T	C	0.383	1.05	1.01	1.08	0.006
10q26.13	FGFR2	rs2981579	123327325	A	G	0.410	1.02	0.99	1.05	0.273
11p15.5	LSP1	rs3817198	1865582	G	A	0.312	1.06	1.02	1.09	0.002
11q13.3		rs614367	69037945	T	C	0.150	1.03	0.98	1.07	0.224
12p11.22	PTHLH	rs10771399	28046347	C	T	0.105	0.83	0.79	0.87	2.4x10⁻¹²
12q24.21		rs1292011	114320905	G	A	0.420	0.99	0.96	1.02	0.443
14q24.1	RAD51L1	rs999737	68104435	A	G	0.234	0.94	0.91	0.98	0.001
16q12.1	TOX3	rs3803662	51143842	T	C	0.267	1.14	1.10	1.18	5.5x10⁻¹³
17q22	COX11	rs6504950	50411470	A	G	0.364	0.96	0.93	0.99	0.024
19p13.11	MERIT40	rs8170	17250704	A	G	0.191	1.15	1.11	1.20	9.3x10⁻¹³
21q21.1	NRIP1	rs2823093	15442703	A	G	0.268	0.99	0.96	1.03	0.595
Newly identified loci (Michailidou, K. et al. Nature Genetics, In Press)										
PTPN22:BCL2L15:										
1p13.2	AP4B1:DCLE1B:HIPK1	rs11552449	114249912	T	C	0.266	1.06	1.01	1.10	0.009
1p36.22	PEX14	rs616488	10488802	G	A	0.335	0.91	0.88	0.94	1.0x10⁻⁸
2q14.2		rs4849887	120961592	T	C	0.099	0.93	0.88	0.99	0.013
2q31.1	METAP1D:DLX1:DLX2	rs2016394	172681217	A	G	0.475	1.00	0.97	1.04	0.854
2q31.1	CDCA7	rs1550623	173921140	G	A	0.160	0.96	0.92	1.00	0.051
2q35	DIRC3	rs16857609	218004753	T	C	0.229	1.07	1.04	1.11	1.0x10⁻⁴
3p26.1	ITPR1:EGOT	rs6762644	4717276	G	A	0.395	1.01	0.98	1.04	0.572
3p24.1	TGFBR2	rs12493607	30657943	C	G	0.422	1.00	0.97	1.04	0.830
4q24	TET2	rs9790517	106304227	T	C	0.316	1.04	1.00	1.08	0.028
4q34.1	ADAM29	rs6828523	176083001	A	C	0.216	0.99	0.95	1.04	0.774
5q11.2	RAB3C	rs10472076	58219818	C	T	0.332	1.04	1.01	1.08	0.015
5q11.2	PDE4D,PDE4DN2	rs1353747	58373238	G	T	0.096	0.95	0.90	1.00	0.046
5q33.3	EBF1	rs1432679	158176661	C	T	0.435	1.08	1.04	1.11	6.7x10⁻⁶
6p25.3	FOXQ1	rs11242675	1263878	C	T	0.382	0.95	0.91	0.98	0.001
6p23	RABBP9	rs204247	13830502	G	A	0.439	1.02	0.99	1.06	0.134
7q35	ARHGEF5:NOBOX	rs1240475	143705862	A	G	0.255	1.01	0.97	1.05	0.587
8p12		rs9693444	29565535	A	C	0.324	1.06	1.02	1.09	0.001
8q21.11		rs6472903	76392856	G	T	0.277	0.95	0.91	0.99	0.016
8q21.11	HNF4G	rs2943559	76580492	G	A	0.194	1.12	1.05	1.18	2.5x10⁻⁴
8q24.21	MIR1208	rs11780156	129263823	T	C	0.167	1.05	1.00	1.09	0.037
9q31.2		rs10759243	109345936	A	C	0.262	1.04	1.00	1.07	0.057
10p12.31	MLLT10:DNAJC1	rs7072776	22072948	A	G	0.285	0.98	0.95	1.02	0.322
10p12.31	DNAJC1	rs11814448	22355849	C	A	0.132	1.20	1.08	1.35	0.001
10q25.2	TCF7L2	rs7904519	114763917	G	A	0.462	1.06	1.03	1.09	2.9x10⁻⁴
10q26.12		rs11199914	123083891	T	C	0.320	1.01	0.97	1.04	0.741
DKFZp761E198:OVOL1:SNX32:CF L1:MUS81										
11q13.1		rs3903072	65339642	T	G	0.414	0.97	0.94	1.00	0.027
11q24.3		rs11820646	128966381	T	C	0.479	0.94	0.91	0.97	2.3x10⁻⁴
12p13.1		rs12422552	14305198	C	G	0.344	1.05	1.02	1.09	0.005
12q22	NTN4	rs17356907	94551890	G	A	0.298	0.92	0.89	0.96	9.3x10⁻⁶
13q13.1	BRCA2,N4BP2L1	rs11571833	31870626	T	A	0.496	1.52	1.31	1.77	6.0x10⁻⁶
14q13.3	PAX9:SLC25A21	rs2236007	36202520	A	G	0.291	0.97	0.94	1.02	0.218
14q24.1	RAD51L1	rs2588809	67730181	T	C	0.248	1.00	0.96	1.05	0.940
14q32.11	CCDC88C	rs941764	90910822	G	A	0.415	1.03	0.99	1.06	0.117
16q12.2	MIR1972-2:FTO	rs17817449	52370868	G	T	0.474	0.92	0.89	0.95	6.2x10⁻⁷
16q23.2	CDYL2	rs13329835	79208306	G	A	0.223	1.02	0.98	1.06	0.269
18q11.2		rs527616	22591422	C	G	0.447	0.95	0.92	0.99	0.006
18q11.2	CHST9	rs1436904	22824665	G	T	0.399	1.00	0.97	1.03	0.995
19p13.11	SSBP4:ISYNA1:ELL	rs4808801	18432141	G	A	0.349	0.93	0.90	0.96	5.1x10 ⁻⁵
19q13.31	C19orf61:KCNN4:LYPD5:ZNF283	rs3760982	48978353	A	G	0.466	1.04	1.01	1.07	0.016
22q12.2	EMID1:RHBDD3:EWSR1	rs132390	27951477	C	T	0.035	1.08	0.98	1.19	0.117
22q13.1	MKL1	rs6001930	39206180	C	T	0.107	1.14	1.08	1.20	1.6x10⁻⁶

¹ rs2284378 at 20q11 previously reported by Siddiq, A. et al. (ref. 7) is not included because it was not well tagged in the iCOGS array used for BCAC replication.

Supplementary Note

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