

Fine-scale mapping of 8q24 locus identifies multiple independent risk variants for breast cancer

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What's new?

Previous genome-wide association studies identified rs13281615 and rs11780156 on 8q24 as breast cancer susceptibility loci. The authors performed a fine-mapping study including 55,540 breast cancer cases and 51,168 controls within the Breast Cancer Association Consortium and identified three additional, represented by rs35961416, rs7815245, and rs2033101, respectively.

In silico analysis indicated two putatively functional variants rs7815245 and rs1121948.

Abstract

Previous genome-wide association studies among women of European ancestry identified two independent breast cancer susceptibility loci represented by single nucleotide polymorphisms (SNPs) rs13281615 and rs11780156 at 8q24. We conducted a fine-mapping study across 2.06 Mb (chr8:127,561,724 -129,624,067, hg19) in 55,540 breast cancer cases and 51,168 controls within the Breast Cancer Association Consortium. We found three additional independent association signals in women of European ancestry, represented by rs35961416 (OR = 0.95, 95% CI = 0.93-0.97, conditional $P = 5.8 \times 10^{-6}$), rs7815245 (OR = 0.94, 95% CI = 0.91-0.96, conditional $P = 1.1 \times 10^{-6}$), and rs2033101 (OR = 1.05, 95% CI = 1.02-1.07, conditional $P = 1.1 \times 10^{-4}$). Integrative analysis using functional genomic data from the Roadmap Epigenomics, the Encyclopedia of DNA Elements project, the Cancer Genome Atlas, and other public resources implied that SNPs rs7815245 in Signal 3, and rs1121948 in Signal 5 (in linkage disequilibrium with rs11780156, $r^2 = 0.77$), were putatively functional variants for two of the five independent association signals. Our results highlight multiple 8q24 variants associated with breast cancer susceptibility in women of European ancestry.

Introduction

Breast cancer is one of the most common malignancies among women worldwide.¹ Genome-wide association studies (GWASs) have identified approximately 100 loci associated with breast cancer.² Multiple independent variants on 8q24 have been shown to confer susceptibility for multiple types of cancer, including breast,^{3,4} prostate, colorectal, bladder, ovarian, renal cell, glioma, chronic lymphocytic leukemia, and Hodgkin's lymphoma,⁵ (also see Supplementary Figure S1). Although most of these loci are located in a "gene desert" region, several hundred kilobases (kb) telomeric to several genes including *FAM84B*, *POU5F1B*, *MYC*, and the long non-coding gene *PVT1*. A growing number of studies have shown that the 8q24 locus may harbor long-range regulatory elements involved in regulating expression of the *MYC*⁶ or *PVT1* genes.⁷

In most GWAS, only the single nucleotide polymorphism (SNP) showing the strongest statistical association at each locus (hereinafter referred to as the index SNP) is reported. Those index SNPs themselves are usually not the causal variants but are in linkage disequilibrium (LD) with the functional variants. In addition to the common variants identified by GWAS, low-frequency variants in susceptible loci may also be associated with disease risk.⁸ Furthermore, in each locus, there may exist allelic heterogeneity and multiple independent variants that may be associated with complex diseases.⁸ Some of the missing heritability for disease may be derived from the incomplete coverage of genetic variants and poor representation of the full spectrum of causal variants on commercial genotyping arrays.^{9,10} Therefore, it is necessary to conduct fine-scale mapping studies to investigate comprehensively all genetic variants in the LD blocks where a GWAS index SNP is located.

We conducted a fine-mapping study of the 8q24 region using data from 106,708 individuals within the Breast Cancer Association Consortium (BCAC). We systematically evaluated the associations with breast cancer risk of the SNPs across 2.06 Mb in this chromosome region. We aimed to identify additional independent association signals and potentially functional variants that may be responsible for the observed associations of variants in this locus with breast cancer risk.

Materials and Methods

Ethics statement

All studies were approved by the relevant institutional review committee and informed consent was obtained from all participants.

Subjects

Epidemiological and genotype data were obtained from 50 breast cancer case-control studies participating in the BCAC.⁴ The sample set for the current project included 48,155 cases and 43,612 controls of European ancestry from 39 studies, 6,269 cases and 6,624 controls of Asian ancestry from 9 studies, and 1,116 cases and 932 controls of African ancestry from 2 studies.

The estrogen receptor (ER) status of the primary tumor was available for 35,824 cases of European ancestry; 28,038 (78%) cases were ER+ and 7,786 (22%) were ER-.

SNP selection and genotyping

Fine-mapping SNPs were selected for inclusion on the custom Illumina iSelect array (iCOGS),^{4,11–13} with the following criteria: 1) Defining the interval to include all SNPs with $r^2 > 0.1$ with the index SNPs rs13281615 and rs11780156 based on HapMap 2 CEU, which identified a region of 2.06 Mb (base positions 127,561,724 -129,624,067; NCBI build 37 assembly); 2) Identifying all SNPs in the interval using the 1000 Genomes Project CEU (April 2010), and HapMap 3; 3) Selecting high-quality SNPs: only variants with the minor allele called at least twice in the 1000 Genomes Project and an Illumina designability score > 0.8 were included; 4) Selecting all SNPs with $r^2 > 0.1$ with the index SNPs rs13281615 and rs11780156 from the CEU data set of the 1000 Genomes Project or HapMap 3; 5) Selecting tagging SNPs at $r^2 > 0.9$ to capture the remaining SNPs that are not in LD with the index SNPs ($r^2 < 0.1$). Genotyping of the iCOGS array and details of the genotyping calling and quality control has been described elsewhere.^{4,11,12} In order to improve SNP density and imputation quality, we conducted one-step imputation (without phasing) using the program IMPUTE2 (see URLs) with the March 2012 release of the 1000 Genomes Project as reference. Genotypes were successfully imputed for 10,593 variants in samples of European ancestry, 9,218 variants in samples of Asian ancestry, and 17,964 variants in samples of African ancestry, all with imputation- $r^2 > 0.3$. After excluding SNPs with minor allele frequency (MAF) < 0.02 , the final genotype data in this project included 6,631 SNPs in samples of European ancestry, 6,459 SNPs in samples of Asian ancestry, and 10,830 SNPs in samples of African ancestry.

Statistical analysis

The per-allele odds ratio (OR) and 95% confidence interval (CI) for each SNP was estimated for breast cancer risk using a log-additive logistic model with covariates of study site and principal components (PC; eight PCs with one additional principal component from the LMBC study in Europeans, two PCs in Asians and two in African Americans). Per-allele ORs and CIs were estimated separately for each population for overall disease, for ER+ and for ER- breast cancer. To identify potential independent susceptibility variant(s), stepwise forward logistic regression analyses were employed with or without the index SNPs rs13281615 and rs11780156 forced in the model. SNPs with a P value $< 10^{-4}$ from the single variant analysis were included in this analysis.¹¹ To identify potentially functional variant candidate(s), we computed a likelihood ratio for each SNP relative to the representative SNP in each signal and excluded SNPs with a likelihood ratio < 0.01 . Because no SNPs showed $P < 1 \times 10^{-4}$ in Asian or African ancestry data, such analyses were performed only on data from subjects of European ancestry. We used the haplo.stats package in R for haplotype analyses for the SNPs that are independently associated with breast cancer risk in women of European ancestry, with study sites and principal components as covariates. The familial relative risk (FRR) was estimated with the formula $\ln(\lambda)/\ln(\lambda_o)$, where λ is the FRR to offspring of an affected individual due to a single genetic locus or assumed multiplicatively interacting loci and λ_o is the overall FRR, which was assumed to be 1.8 for breast cancer.¹⁴ All analyses were conducted using R version 3.0.1.

Functional annotation

We annotated a total of 245 breast cancer risk associated variants ($P < 10^{-4}$ from univariate analysis) for potential functional significance using data from the Encyclopedia of DNA Elements (ENCODE), the Roadmap Epigenomics Mapping Consortium, and The Cancer

Genome Atlas (TCGA) (see URLs). For each variant, we investigated whether it is mapped to transcriptional elements primarily associated with enhancers (H3K4me1) or promoters (H3K4me3), in any of nine cell lines: normal human mammary epithelial cell line (HMEC), GM12878, H1-hESC, K562, HepG2, HSMM, HUVEC, NHEK, and NHLF. The epigenetic landscape of histone markers H3K4Me1, H3K4Me3, and H3K27Ac was also examined through layered histone tracks on seven ENCODE cell lines, including GM12878, H1-hESC, K562, HSMM, HUVEC, NHEK, and NHLF from the UCSC Genome Browser (see URLs). DNase I hypersensitive and transcription factor (TF) ChIP-Seq datasets were investigated in all available ENCODE cell lines, including HMEC and the breast cancer cell lines T-47D and MCF-7. Publicly available tools RegulomeDB¹⁵ and HaploReg v4.1¹⁶ were also used to evaluate potential functional variants.

For regions lacking ChIP-seq peaks data, we collected raw ChIP-seq data for the estrogen receptor-α (ESR1) and forkhead box protein A1 (FOXA1) in MCF-7, TAMR and ZR751 breast cancer cell lines (Supplementary Table S1) from the study by Hurtado *et al.*¹⁷ The raw ChIP-seq data in .FASTQ format from different lanes in the same experiment were first merged and mapped to the human reference genome (hg19) using the Bowtie2 program¹⁸ with the default setting. Aligned data were processed and converted into Binary Sequence Alignment/Map format (BAM) files using the SAMtools program.¹⁹ After removing duplicated reads, we used the MACS14 (version 1.4.2) algorithm²⁰ to identify peaks with 50 bp resolution using the matched DNA input data as the control. The peaks were ranked by the number of uniquely aligned reads and only the top 5% of peaks were selected for motif discovery. The summits of the top 5% peaks were extended by 100 bp on either side. Similar methodological strategy has been used elsewhere.^{21,22} Motifs between 5 and 30 bp in length were identified on both strands. We

employed the MEME 4.9.1 toolkit²³ to search DNA motifs and enrichment significance for ESR1 and FOXA1.

Expression quantitative trait (eQTL) analysis

eQTL analysis was performed followings the method described previously.²⁴ Briefly, RNA-Seq V2 data (level 3) of 1,006 breast cancer tumor tissues were downloaded from the TCGA data portal (see URLs). DNA methylation data measured by the Illumina HumanMethylation450 BeadChip and genotype data from the Affymetrix SNP 6.0 array were also retrieved from TCGA level 3 data. Genotype data of the flanking 2 Mb region of the index SNPs on 8q24 were extracted and then imputed to the 1000 Genomes Project data with Minimac (see URLs). Only common SNPs (MAF > 0.05) with high imputation quality ($r^2 > 0.3$) were included in the present study. For the interrogated 2 Mb region, copy number variation (CNV) data spanning the 8q24 genes *FAM84B*, *POU5F1B*, *MYC*, and *PVT1* from TCGA tumor tissue samples were collected from the CbioPortal (see URLs).

We used the TCGA breast cancer data described above to perform *cis*-eQTL analyses in tumor tissues. Several steps were taken to reduce the batch and other technical effects on gene expressions following the approach described by Pickrell et al.²⁵ First, the RNA-Seq by Expectation-Maximization value of each gene was log2 transformed and genes with a median expression level of 0 across tissues were removed. We then performed the principal component correction on gene expression to remove potential batch effects. A linear regression of expression values on the first five principal components was constructed and the residuals were used to replace the expression values of each gene among tissues. To make the data more closely conform to the linear model for the eQTL analysis, we further transformed the gene expression

levels to fit quantiles of $N(0,1)$ distribution based on the ranks of the expression values to their respective quantiles. Finally, to further adjust for the potential effects of methylation and CNV on the expression of each gene in tumor tissues, we constructed residual linear regression models to detect eQTLs according to the approach used by Li et al.²⁶

Results

Associations with breast cancer risk among women of European ancestry

We first conducted univariate analysis for 2,391 genotyped and 4,240 well-imputed SNPs in samples from women of European ancestry. A total of 359 SNPs were associated with breast cancer risk with a statistical significance of $P < 10^{-4}$ (Figure 1 and Supplementary Table S2). Confirming previous GWAS results, the index SNPs rs13281615 (Signal 2 in Table 1) and rs11780156 (Signal 5 in Table 1) showed significant associations with ORs of 1.11 (95% CI = 1.08-1.13, $P = 2.0 \times 10^{-24}$) and 1.07 (95% CI = 1.05-1.10, $P = 4.1 \times 10^{-8}$), respectively (Table 1, univariate analysis). We then conducted forward stepwise regression analysis for each of the 359 SNPs to identify potential independent association signals. When two index SNPs rs13281615 and rs11780156 were forced into the model, we found two additional independent association signals at statistical significance of $P < 1 \times 10^{-4}$ and a third one with suggestive evidence ($P = 1.1 \times 10^{-4}$) (Table 1 and Supplementary Figure S2). The first independent signal (Signal 1 in Table 1), represented by rs35961416 (chr8:128213561:I) with an insertion of base A, showed a P value of 5.8×10^{-6} after adjustment for other four signals (conditional OR = 0.95, 95% CI = 0.93-0.97). The second independent signal (Signal 3) represented by rs7815245 (conditional OR = 0.94, 95% CI = 0.91-0.96, $P = 1.1 \times 10^{-6}$, Table 1), was in moderate LD with the index SNP

rs13281615 in Signal 2 ($r^2 = 0.48$) but not with the second index SNP rs11780156 in Signal 5 ($r^2 < 0.01$). The third suggestive independent variant (Signal 4, rs2033101), not in LD with either of the two index SNPs, showed a conditional P value of 1.1×10^{-4} (OR = 1.05, 95% CI = 1.02-1.07, Table 1). We also performed forward stepwise regression analysis without the two index SNPs forced into the model. Five similar independent breast cancer risk associated SNPs were selected: Signal 1 (rs35961416) (conditional $P = 3.2 \times 10^{-6}$) and the suggestive Signal 4 (rs2033101) (conditional $P = 1.4 \times 10^{-4}$) remained the same; Signal 2 (rs13281615) was tagged by the highly correlated SNP rs10110330 ($r^2 = 0.97$, conditional OR = 1.06, 95% CI = 1.04-1.09, $P = 9.5 \times 10^{-6}$), Signal 3 (rs7815245) tagged by the most significant SNP rs17465052 ($r^2 = 0.93$, conditional OR = 0.94, 95% CI = 0.91-0.97, $P = 3.2 \times 10^{-6}$), and Signal 5 (rs11780156) tagged by c8_pos129263191 (rs67397162, $r^2 = 1$, conditional OR = 1.07, 95% CI = 1.05-1.10, $P = 1.1 \times 10^{-7}$). These results consistently showed four independent risk association signals and another suggestive one (Supplementary Figure S2). No significant evidence of between-study heterogeneity was observed for any of these independently risk-associated SNPs (data not shown).

Stratified by ER status, all five independent signals showed significant associations for ER+ breast cancer; however, with the exception of rs11780156 showing a P value of 0.012 (signal 5), no significant associations were observed for ER- breast cancer (Table 2).

Haplotype analyses were performed using data from the five independent risk signals (Table 3). In women of European ancestry, a total of 16 haplotypes with frequency of > 1% were observed. Compared to the reference haplotype, which carries the alleles associated with a reduced risk in all five SNPs, most haplotypes were associated with increased breast cancer risk. Haplotype 5, which carries the risk-associated alleles of the signals 1-3, showed the most

significant association ($P = 3.4 \times 10^{-11}$ for overall breast cancer) while Haplotype 1, which carries the risk-associated alleles of all signals except for Signal 4, was associated with the highest estimated OR (OR = 1.27, 95% CI = 1.15-1.39 for overall breast cancer) (Table 3). As shown in Table 3, similar haplotype associations were observed for ER+ but not for ER- breast cancer.

Association with breast cancer risk in women of Asian or African ancestry

Of the five independently risk-associated variants identified in women of European ancestry, only rs35961416 (Signal 1) showed a nominal association in African-American women at $P < 0.05$ ($P = 0.04$, Table 4). Based on univariate analyses of all SNPs on 8q24 that passed QC, SNP rs76382129 showed a P value of 8.3×10^{-4} in women of Asian ancestry and five SNPs showed P values of between 9.6×10^{-4} and 1.6×10^{-4} in women of African ancestry (Supplementary Table S3). Another 16 SNPs showed breast cancer risk association with P values between 0.01 and 0.001 in either population and in the same direction across the two populations (Table 4).

Functional annotation

For each of the five independent signals identified among women of European ancestry, we excluded SNPs with $r^2 \leq 0.2$ with the representative SNP in each signal region and then calculated the likelihood of all risk-associated variants to select potentially functional variant candidates. Setting a likelihood ratio threshold of > 0.01 relative to the representative/index SNP in each signal region, we did not identify any functional variant candidates for rs35961416

(Signal 1) and rs2033101 (Signal 4) whereas we identified 154 functional variant candidates for Signal 2, 170 variants for Signal 3 (143 variants overlap with those for Signal 2), and 62 variants for Signal 5, respectively (Supplementary Tables S4-S6). Thus, a total of 245 unique SNPs including the five representative SNPs in five signal regions were further evaluated for their potentially functional significance.

Our integrative functional annotation from ENCODE, Roadmap Epigenomics, the RegulomeDB¹⁵, the HaploReg databases¹⁶, and other public data identified the representative SNP rs7815245 in Signal 3 and SNP rs1121948 (in LD with rs11780156) in Signal 5 as most likely functional variant candidates underlying respective independent association signals (Figure 2). Based on the Roadmap Epigenomics data, SNP rs7815245 in Signal 3 is mapped to a conserved enhancer region with a genomic evolutionary rate profiling (GERP) score of 5.04 among eight tissues including breast variant human mammary epithelial cells (vHMEC) and breast myoepithelial primary cells. It is in a DNase I hypersensitive region in eight tissues including vHMEC. It is also predicted to change the transcription factor TCF12 binding motif. This SNP is also located in the binding regions of two critical nuclear hormone responsible receptors, estrogen receptor- α (ESR1), and forkhead box protein A1 (FOXA1) (Supplementary Figure S3). ChIP-seq data from different breast cancer cell lines and technical replicates showed consistent results (Supplementary Figure S3A). DNA binding motif analysis further confirmed that SNP rs7815245 is located in the ESR1 DNA binding motif ($P = 1.5 \times 10^{-3}$) and is very close to the FOXA1 DNA binding motif ($P = 5.2 \times 10^{-3}$) (Supplementary Figure S3B). In addition, the breast cancer risk-associated T allele was correlated with decreased expression of the *POU5F1B* gene ($P = 0.04$, Supplementary Table S7).

SNP rs1121948, which is in strong LD with the index SNP rs11780156 ($r^2=0.77$) in Signal 5, resides in the binding motifs of the TFs GATA-binding protein 3 (GATA3) and MYC-associated factor X (MAX) in the breast cancer cell line MCF-7. HaploReg data shows that this SNP resides in promoter regions of lung and muscle tissues, in strong enhancer regions of 14 tissues including HSMM and NHLF cells, and in DNase I hypersensitive sites of four tissues. Two active epigenetic markers (H3K4Me1 and H3K27Ac) were enriched in the interval containing rs1121948 in seven ENCODE cell lines (Figure 2C). We examined the effect of the associations of the 62 SNPs from the likelihood analysis for Signal 5 and expression of genes within 1 Mb of the index SNP rs11780156. We found that the risk-associated G allele of rs1121948 was weakly associated with decreased expression of the *PVT1* gene ($P=0.037$, Supplementary Table S7).

Discussion

In this study, we conducted a fine-mapping investigation at the breast cancer susceptibility locus on 8q24. Among women of European ancestry, we identified four independent association signals represented by rs35961416, rs13281615, rs7815245 and rs11780156, respectively, and another suggestive one tagged by rs2033101. This discovery increases the proportion of familial risk of breast cancer explained by variation on 8q24 from 0.25% (due to the GWAS index SNPs rs13281615 in Signal 2 and rs11780156 in Signal 5) to 0.55%.

SNP rs7815245 (Signal 3) showed a more significant association than the previously GWAS-identified index SNPs rs13281615 (Signal 2) and rs11780156 (Signal 5). This SNP is located in an enhancer region among eight tissues including breast variant HMEC and

myoepithelial cells. TF occupancy data showed that SNP rs7815245 falls within the DNA binding motifs for ESR1 and FOXA1, two critical DNA binding proteins for the development of several hormone-dependent cancers including breast cancer. Breast cancer susceptibility variants rs4784227 on 16q12.1 and rs2981578 on 10q26 have also been reported to modulate the affinity for these two transcription factors.^{11,27} In addition, FOXA1 has shown a critical role in estrogen-ESR1 activity and endocrine response in breast cancer cells.^{17,28,29} These results imply that the association between SNP rs7815245 at Signal 3 and breast cancer risk might be mediated by their functional effects through these two transcription factors. The risk allele T of rs7815245 down-regulated expression of its downstream gene *POU5F1B*, which encodes a weak transcriptional activator highly similar to the POU class 5 homeobox 1 transcription factor and is overexpressed in prostate cancer.³⁰ However, further functional studies are needed to clarify the biological mechanism of this SNP in breast cancer susceptibility.

The most attractive candidate gene for cancer risk variants in the gene-desert 8q24 region is the proto-oncogene *MYC*, because it plays a vital role in tumorigenesis and metastasis of several types of cancer including breast cancer.^{31–33} As a key transcription factor, MYC forms heterodimers with MAX, and then regulates transcription of genes involved in cell growth, and proliferation.³¹ Aberrant MYC signaling can promote cell transformation and tumor progression.^{32,33} Although most of the GWAS-identified SNPs on 8q24 for multiple types of cancers^{5,34} are not mapped to the *MYC* genic region, they may cis-regulate nearby genes including *MYC* and its 53-kb downstream non-coding gene *PVT1*.⁵ For example, cancer risk-associated variants may regulate *MYC* expression by forming a large chromatin loop with the *MYC* locus.^{6,26,35} This hypothesis has been partially supported by the fact that trait-associated loci are frequently found to be *cis*-eQTL.^{26,36,37} Our e-QTL analysis of the TCGA breast cancer tumor

tissues showed a trend that rs1121948 in Signal 5 might affect *MYC* or *PVT1* expression levels (Supplementary Table 7), consistent with a co-expression pattern.³⁸ However, the risk-increased alleles are associated with down-regulated gene expression of *MYC* or *PVT1*. This is inconsistent with overexpression of these two genes commonly observed in breast cancer tumors,^{39–42} leaving challenges to link the risk alleles and the possible candidate gene(s) in malignancy.

Of the five independent association signals observed among women of European ancestry, only rs35961416 showed a significant association in women of African ancestry. This could be due to small effect size, different allele frequency, or allelic heterogeneity by race. Differences in GWAS findings across populations have commonly been observed for breast cancer and many other complex traits.^{43–45} Taking the GWAS index SNP rs13281615 as an example, the risk allele frequency in women of European ancestry was 0.40.⁴⁶ Under an additive inheritance mode to detect the same per-allele effect ($OR = 1.08$) at $P = 0.05$, our Asian sample with 6,269 breast cancer cases and 6,624 controls (risk allele frequency of 0.53) and African American sample with 1,116 breast cancer cases and 932 controls (risk allele frequency of 0.44) has a power of 0.09% and 0.1%, respectively.

In addition to a smaller sample size for women of Asian or African ancestry, there are several other limitations in this study. First, no functional laboratory experiments were conducted for any of the putative functional SNPs implicated in our study, preventing us from drawing a more definitive conclusion regarding the functionality of these variants. For example, our *in silico* analyses suggest that rs1121948 is located in binding sites of GATA3 and MAX, which may regulate *MYC* expression, but such potential interaction needs to be demonstrated experimentally.^{47–50} Second, we limited our investigation to variants with a MAF > 0.02, and

thus it is possible that some rare variants in these loci may also contribute to the risk of breast cancer.

In conclusion, our fine mapping study identified two additional and another suggestive independent association signals on 8q24 among women of European ancestry, which together with two previous reported GWAS index signals explain approximately 0.55% of excess familial risk of breast cancer. In addition, our functional analyses revealed two putatively functional variants that can be further investigated experimentally. Our study provides additional evidence of the importance of common independent variants on 8q24 in breast cancer susceptibility.

URLs. 1000 Genomes, <http://browser.1000genomes.org>; BCAC, <http://apps.ccge.medschl.cam.ac.uk/consortia/bcac/>; CbioPortal, <http://www.cbioportal.org/public-portal/>; ENCODE, <http://genome.ucsc.edu/ENCODE/>; HaploReg v4.1, <http://www.broadinstitute.org/mammals/haploreg/haploreg.php>; HapMap project, <http://hapmap.ncbi.nlm.nih.gov/>; iCOGs, <http://ccge.medschl.cam.ac.uk/research/consortia/icogs/>; IMPUTE v.2.2, https://mathgen.stats.ox.ac.uk/impute/impute_v2.html; LocusZoom, <http://csg.sph.umich.edu/locuszoom/>; Minimac, <http://genome.sph.umich.edu/wiki/Minimac>; R version 3.0.1, <http://www.r-project.org/>; RegulomeDB, <http://regulome.stanford.edu/>; UCSC Genome Browser, <http://genome.ucsc.edu>; TCGA, <http://cancergenome.nih.gov/>.

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References

1. Mavaddat N, Antoniou AC, Easton DF, et al. Genetic susceptibility to breast cancer. *Mol Oncol* 2010;4:174–91.
2. Welter D, MacArthur J, Morales J, et al. The NHGRI GWAS Catalog, a curated resource of SNP-trait associations. *Nucleic Acids Res* 2014;42:D1001–1006.
3. Easton DF, Pooley KA, Dunning AM, et al. Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature* 2007;447:1087–93.
4. Michailidou K, Hall P, Gonzalez-Neira A, et al. Large-scale genotyping identifies 41 new loci associated with breast cancer risk. *Nat Genet* 2013;45:353–361, 361e1–2.
5. Huppi K, Pitt JJ, Wahlberg BM, et al. The 8q24 gene desert: an oasis of non-coding transcriptional activity. *Front Genet* 2012;3:69.
6. Ahmadiyeh N, Pomerantz MM, Grisanzio C, et al. 8q24 prostate, breast, and colon cancer risk loci show tissue-specific long-range interaction with MYC. *Proc Natl Acad Sci U S A* 2010;107:9742–6.
7. Meyer KB, Maia A-T, O'Reilly M, et al. A Functional Variant at a Prostate Cancer Predisposition Locus at 8q24 Is Associated with PVT1 Expression. *PLoS Genet* 2011;7:e1002165.
8. Manolio TA, Collins FS, Cox NJ, et al. Finding the missing heritability of complex diseases. *Nature* 2009;461:747–53.
9. McCarthy MI, Abecasis GR, Cardon LR, et al. Genome-wide association studies for complex traits: consensus, uncertainty and challenges. *Nat Rev Genet* 2008;9:356–69.
10. Sanna S, Li B, Mulas A, et al. Fine mapping of five loci associated with low-density lipoprotein cholesterol detects variants that double the explained heritability. *PLoS Genet* 2011;7:e1002198.
11. Meyer KB, O'Reilly M, Michailidou K, et al. Fine-scale mapping of the FGFR2 breast cancer risk locus: putative functional variants differentially bind FOXA1 and E2F1. *Am J Hum Genet* 2013;93:1046–60.
12. Agarwal D, Pineda S, Michailidou K, et al. FGF receptor genes and breast cancer susceptibility: results from the Breast Cancer Association Consortium. *Br J Cancer* 2014;110:1088–100.
13. Glubb DM, Maranian MJ, Michailidou K, et al. Fine-scale mapping of the 5q11.2 breast cancer locus reveals at least three independent risk variants regulating MAP3K1. *Am J Hum Genet* 2015;96:5–20.

14. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet* 2001;358:1389–99.
15. Boyle AP, Hong EL, Hariharan M, et al. Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res* 2012;22:1790–7.
16. Ward LD, Kellis M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Res* 2012;40:D930–934.
17. Hurtado A, Holmes KA, Ross-Innes CS, et al. FOXA1 is a key determinant of estrogen receptor function and endocrine response. *Nat Genet* 2011;43:27–33.
18. Langmead B, Salzberg SL. Fast gapped-read alignment with Bowtie 2. *Nat Methods* 2012;9:357–9.
19. Li H, Handsaker B, Wysoker A, et al. The Sequence Alignment/Map format and SAMtools. *Bioinforma Oxf Engl* 2009;25:2078–9.
20. Zhang Y, Liu T, Meyer CA, et al. Model-based analysis of ChIP-Seq (MACS). *Genome Biol* 2008;9:R137.
21. Jothi R, Cuddapah S, Barski A, et al. Genome-wide identification of in vivo protein-DNA binding sites from ChIP-Seq data. *Nucleic Acids Res* 2008;36:5221–31.
22. Ramagopalan SV, Heger A, Berlanga AJ, et al. A ChIP-seq defined genome-wide map of vitamin D receptor binding: associations with disease and evolution. *Genome Res* 2010;20:1352–60.
23. Bailey TL, Boden M, Buske FA, et al. MEME SUITE: tools for motif discovery and searching. *Nucleic Acids Res* 2009;37:W202–208.
24. Cai Q, Zhang B, Sung H, et al. Genome-wide association analysis in East Asians identifies breast cancer susceptibility loci at 1q32.1, 5q14.3 and 15q26.1. *Nat Genet* 2014;46:886–90.
25. Pickrell JK, Marioni JC, Pai AA, et al. Understanding mechanisms underlying human gene expression variation with RNA sequencing. *Nature* 2010;464:768–72.
26. Li Q, Seo J-H, Stranger B, et al. Integrative eQTL-based analyses reveal the biology of breast cancer risk loci. *Cell* 2013;152:633–41.
27. Cowper-Sal lari R, Zhang X, Wright JB, et al. Breast cancer risk-associated SNPs modulate the affinity of chromatin for FOXA1 and alter gene expression. *Nat Genet* 2012;44:1191–8.

28. Carroll JS, Liu XS, Brodsky AS, et al. Chromosome-wide mapping of estrogen receptor binding reveals long-range regulation requiring the forkhead protein FoxA1. *Cell* 2005;122:33–43.
29. Bernardo GM, Lozada KL, Miedler JD, et al. FOXA1 is an essential determinant of ERalpha expression and mammary ductal morphogenesis. *Dev Camb Engl* 2010;137:2045–54.
30. Kastler S, Honold L, Luedke M, et al. POU5F1P1, a putative cancer susceptibility gene, is overexpressed in prostatic carcinoma. *The Prostate* 2010;70:666–74.
31. Chen Y, Olopade OI. MYC in breast tumor progression. *Expert Rev Anticancer Ther* 2008;8:1689–98.
32. Hynes NE, Stoelzle T. Key signalling nodes in mammary gland development and cancer: Myc. *Breast Cancer Res* 2009;11:210.
33. Wolfer A, Ramaswamy S. MYC and metastasis. *Cancer Res* 2011;71:2034–7.
34. Grisanzio C, Freedman ML. Chromosome 8q24-Associated Cancers and MYC. *Genes Cancer* 2010;1:555–9.
35. Wright JB, Brown SJ, Cole MD. Upregulation of c-MYC in cis through a Large Chromatin Loop Linked to a Cancer Risk-Associated Single-Nucleotide Polymorphism in Colorectal Cancer Cells. *Mol Cell Biol* 2010;30:1411–20.
36. Nicolae DL, Gamazon E, Zhang W, et al. Trait-associated SNPs are more likely to be eQTLs: annotation to enhance discovery from GWAS. *PLoS Genet* 2010;6:e1000888.
37. Li Q, Stram A, Chen C, et al. Expression QTL-based analyses reveal candidate causal genes and loci across five tumor types. *Hum Mol Genet* 2014;23:5294–302.
38. Colombo T, Farina L, Macino G, et al. PVT1: a rising star among oncogenic long noncoding RNAs. *BioMed Res Int* 2015;2015:304208.
39. Guan Y, Kuo W-L, Stilwell JL, et al. Amplification of PVT1 contributes to the pathophysiology of ovarian and breast cancer. *Clin Cancer Res Off J Am Assoc Cancer Res* 2007;13:5745–55.
40. Sørlie T, Perou CM, Tibshirani R, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proc Natl Acad Sci U S A* 2001;98:10869–74.
41. Sotiriou C, Neo S-Y, McShane LM, et al. Breast cancer classification and prognosis based on gene expression profiles from a population-based study. *Proc Natl Acad Sci U S A* 2003;100:10393–8.
42. Xu J, Chen Y, Olopade OI. MYC and Breast Cancer. *Genes Cancer* 2010;1:629–40.

43. Zheng W, Zhang B, Cai Q, et al. Common genetic determinants of breast-cancer risk in East Asian women: a collaborative study of 23 637 breast cancer cases and 25 579 controls. *Hum Mol Genet* 2013;22:2539–50.
44. Bojesen SE, Pooley KA, Johnatty SE, et al. Multiple independent variants at the TERT locus are associated with telomere length and risks of breast and ovarian cancer. *Nat Genet* 2013;45:371–384, 384e1–2.
45. Wu Y, Waite LL, Jackson AU, et al. Trans-ethnic fine-mapping of lipid loci identifies population-specific signals and allelic heterogeneity that increases the trait variance explained. *PLoS Genet* 2013;9:e1003379.
46. Easton DF, Pooley KA, Dunning AM, et al. Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature* 2007;447:1087–93.
47. Tomlinson I, Webb E, Carvajal-Carmona L, et al. A genome-wide association scan of tag SNPs identifies a susceptibility variant for colorectal cancer at 8q24.21. *Nat Genet* 2007;39:984–8.
48. Junttila MR, Westermarck J. Mechanisms of MYC stabilization in human malignancies. *Cell Cycle Georget Tex* 2008;7:592–6.
49. Ghoussaini M, Song H, Koessler T, et al. Multiple Loci With Different Cancer Specificities Within the 8q24 Gene Desert. *JNCI J Natl Cancer Inst* 2008;100:962–6.
50. Lin CY, Lovén J, Rahl PB, et al. Transcriptional amplification in tumor cells with elevated c-Myc. *Cell* 2012;151:56–67.

FIGURE LEGENDS

Figure 1. Manhattan plot of overall breast cancer risk association in Europeans at the 8q24 locus. SNPs are plotted based on their chromosomal positions (hg19) and $-\log_{10} P$ -values for univariate association. The regions spanning five independent association signals (representative SNP for each signal are shown in Table 1) and their highly correlated SNPs are indicated by dashed rectangles.

Figure 2. Functional annotation of the independent signal regions. (A) Chromatin states across the 45.6 kb region harboring two associated signals rs13281615 and rs7815245. The top 3 tracks show enrichment of transcription regulatory histone markers H3K4me1, H3K4me3 and H3K27ac from seven cell lines in ENCODE. The next 9 tracks are the chromatin state annotation by ChromHMM derived from 9 cell types. ChromHMM color coding is as follows: orange, strong enhancer; yellow, weak enhancer; light green, weak transcribed; light gray, low signal. The next 5 tracks show the designated histone modifications in the HMEC cell line. The last two tracks show the open chromatin enrichment from DNase clusters and evolutionary conservation measurement by PhastCons from 100 vertebrates. (B) LD structure of the region harboring the index SNP rs13281615 and the independent signal rs7815245 in European samples. (C) Chromatin states across the 58.9 kb region harboring the second index SNP rs11780156 and the potential underlying functional SNP rs1121948. The contents of the tracks are the same as described in (A). (D) LD structure of the 58.9 kb region wherein SNPs rs11780156 and rs1121948 lie, marked with red arrows.

Table 1. Identification of five independent association signals for overall breast cancer risk among women of European ancestry: a collaborative study of 48,155 breast cases and 43,612 controls.

Signal	SNP	Base position		MAF	r^2	LD ^b (r^2)	Univariate Analysis		Conditional Analysis	
		(hg 19)	Alleles ^a				per-allele OR (95% CI) ^c	P ^c	Adjusted per-allele OR (95% CI) ^d	Adjusted P ^d
Signal 1	rs35961416	128213561	A/-	0.44	0.75	-	0.95(0.93-0.97)	1.3x10 ⁻⁵	0.95(0.93-0.97)	5.8x10 ⁻⁶
Signal 2	rs13281615 ^e	128355618	G/A	0.40	0.97	-	1.11(1.08-1.13)	2.0x10 ⁻²⁴	1.06(1.03-1.09)	6.6x10 ⁻⁶
Signal 3	rs7815245	128383597	T/C	0.42	1	0.48	0.90(0.88-0.92)	1.3x10 ⁻²⁷	0.94(0.91-0.96)	1.1x10 ⁻⁶
Signal 4	rs2033101	128964222	T/C	0.19	0.95	-	1.05(1.03-1.08)	5.2x10 ⁻⁵	1.05(1.02-1.07)	1.1x10 ⁻⁴
Signal 5	rs11780156 ^e	129194641	T/C	0.16	1	-	1.07(1.05-1.10)	4.1x10 ⁻⁸	1.07(1.04-1.10)	1.7x10 ⁻⁷
	rs1121948	129165056	G/A	0.20	1	0.77	1.07(1.04-1.09)	2.0x10 ⁻⁷	-	-

Abbreviations: LD, linkage disequilibrium; OR, odds ratio; CI, confidence interval; MAF, minor (effect) allele frequency.

^a Minor/major alleles; effect alleles are shown in bold.

^b r^2 for linkage disequilibrium with index SNP rs13281615 (0.48) and rs11780156 (0.77), respectively; "-" indicates $r^2 < 0.01$ with any index SNPs.

^c Adjusted for age, study site and principal components.

^d Adjusted for the other four signals, age, study site and principle components.

^e Independent index SNPs rs13281615 and rs11780156 from previously reported genome-wide association studies.

Table 2. Association of the five independent signals with breast cancer risk by ER status among women of European ancestry.

SNP	ER+ cases (n=28,038)		ER- cases (n=7,786)		<i>P</i> for heterogeneity test ^b
	Adjusted per-allele OR (95% CI) ^a	Adjusted <i>P</i> ^a	Adjusted per-allele OR (95% CI) ^a	Adjusted <i>P</i> ^a	
rs35961416	0.93(0.91-0.96)	4.8x10 ⁻⁷	0.97(0.93-1.01)	0.138	0.217
rs13281615	1.08(1.04-1.11)	3.1x10 ⁻⁶	1.00(0.95-1.05)	0.971	0.032
rs7815245	0.94(0.91-0.97)	1.6x10 ⁻⁴	0.96(0.91-1.01)	0.104	0.276
rs2033101	1.06(1.03-1.09)	1.3x10 ⁻⁴	1.04(0.99-1.08)	0.140	0.307
rs11780156	1.08(1.05-1.11)	6.6x10 ⁻⁷	1.06(1.01-1.12)	0.012	0.118

Abbreviations: ER, estrogen receptor; OR, odds ratio; CI, confidence interval.

^a Adjusted for other four independent signal, age, study site and principle components.

^b Heterogeneity test between ER-positive and ER-negative disease.

Table 3. Haplotype analyses of the two independent signals in relation to breast cancer risk among women of European ancestry.

Haplotypes						All cases (n=48,155)			ER+ cases (n=28,038)			ER- cases (n=7,786)							
	SNP 1 ^a		SNP 2 ^a		SNP 3 ^a		SNP 4 ^a		SNP 5 ^a		Frequency ^b (95% CI) ^c	per-allele OR	<i>P</i> ^c	Frequency ^b (95% CI) ^c	per-allele OR	<i>P</i> ^c	Frequency ^b (95% CI) ^c	per-allele OR	<i>P</i> ^c
	A/-	G/A	T/C	T/C	T/C	T/C	T/C	T/C	T/C	T/C									
Baseline	A	A	T	C	C	0.125	Reference (1.00)	-	0.127	Reference (1.00)	-	0.130	Reference (1.00)	-					
Haplo.1	-	G	C	C	T	0.029	1.27(1.15-1.39)	1.1×10^{-6}	0.028	1.30(1.17-1.46)	2.9×10^{-6}	0.028	1.22(1.03-1.46)	0.024					
Haplo.2	-	A	C	C	T	0.017	1.24(1.11-1.40)	2.1×10^{-4}	0.016	1.29(1.12-1.48)	2.9×10^{-4}	0.016	1.19(0.96-1.48)	0.115					
Haplo.3	-	G	C	T	C	0.033	1.23(1.13-1.35)	3.2×10^{-6}	0.033	1.28(1.15-1.42)	3.0×10^{-6}	0.032	1.10(0.93-1.30)	0.276					
Haplo.4	A	G	C	T	C	0.031	1.22(1.12-1.33)	1.2×10^{-5}	0.031	1.21(1.09-1.35)	3.6×10^{-4}	0.030	1.08(0.91-1.28)	0.370					
Haplo.5	-	G	C	C	C	0.140	1.17(1.12-1.22)	3.4×10^{-11}	0.139	1.20(1.13-1.26)	1.1×10^{-10}	0.136	1.06(0.97-1.15)	0.220					
Haplo.6	A	G	C	C	C	0.131	1.13(1.07-1.19)	2.2×10^{-5}	0.131	1.13(1.06-1.21)	2.1×10^{-4}	0.130	1.04(0.94-1.16)	0.470					
Haplo.7	-	A	T	C	T	0.029	1.13(1.03-1.23)	0.117	0.028	1.12(1.01-1.25)	0.038	0.029	1.04(0.87-1.24)	0.654					
Haplo.8	A	G	C	C	T	0.024	1.11(1.01-1.23)	0.036	0.024	1.06(0.94-1.20)	0.339	0.024	1.03(0.85-1.25)	0.758					
Haplo.9	-	A	C	C	C	0.089	1.11(1.05-1.17)	2.3×10^{-4}	0.090	1.12(1.05-1.19)	5.7×10^{-4}	0.089	1.02(0.92-1.13)	0.688					
Haplo.10	-	A	T	T	C	0.037	1.11(1.02-1.20)	0.011	0.037	1.13(1.03-1.24)	9.5×10^{-3}	0.037	1.05(0.90-1.22)	0.529					
Haplo.11	-	A	C	T	C	0.020	1.09(0.98-1.21)	0.121	0.020	1.04(0.92-1.18)	0.510	0.021	1.27(1.05-1.53)	0.013					
Haplo.12	A	A	C	C	C	0.034	1.05(0.97-1.15)	0.229	0.033	1.01(0.91-1.12)	0.877	0.035	1.09(0.93-1.28)	0.300					
Haplo.13	A	A	T	C	T	0.023	1.04(0.92-1.16)	0.548	0.023	1.05(0.91-1.20)	0.494	0.023	1.11(0.90-1.37)	0.318					
Haplo.14	-	A	T	C	C	0.148	1.02(0.97-1.08)	0.445	0.149	1.03(0.96-1.09)	0.447	0.153	1.03(0.92-1.14)	0.618					
Haplo.15	A	A	T	T	C	0.029	0.97(0.88-1.08)	0.596	0.030	0.97(0.86-1.10)	0.654	0.030	0.96(0.80-1.16)	0.697					
Haplo.rare	*	*	*	*	*	0.060	1.20(1.13-1.28)	7.0×10^{-9}	0.060	1.26(1.17-1.35)	6.1×10^{-10}	0.058	1.09(0.96-1.22)	0.183					

Abbreviations: ER, estrogen receptor; OR, odds ratio; CI, confidence interval.

^a SNPs1-5 represent signals rs35961416, rs13281615, rs7815245, rs2033101, and rs11780156, respectively; effect alleles are shown in bold.

^b Haplotype frequency.

^c Adjusted for age, study site, and principal components.

Table 4. Association of top SNPs identified in women of European and non-European ancestry with breast cancer risk among women of Asian (6,269 cases and 6,624 controls) and African ancestry (1,116 cases and 932 controls).

Top SNPs	Alleles ^a	Univariate Analysis (Asian)			Univariate Analysis (African)		
		EAF	OR(95% CI) ^b	P ^b	EAF	OR(95% CI) ^b	P ^b
Identified in women of European ancestry							
rs35961416	A/-	0.10	1.01(0.91-1.13)	0.804	0.39	0.85(0.73-0.99)	0.040
rs13281615	G/A	0.53	1.02(0.97-1.08)	0.357	0.44	1.02(0.90-1.16)	0.721
rs7815245 ^c	T/C	0.17	0.96(0.89-1.02)	0.202	0.36	0.99(0.87-1.13)	0.908
rs2033101	T/C	0.33	1.00(0.95-1.05)	0.957	0.09	0.85(0.67-1.07)	0.174
rs11780156	T/C	0.20	0.99(0.93-1.06)	0.842	0.04	0.97(0.70-1.34)	0.838
Identified in women of non-European ancestry							
rs16901629	G/A	0.14	1.12(1.03-1.22)	6.6×10 ⁻³	0.38	1.07(0.92-1.24)	0.407
rs974451	A/G	0.23	0.91(0.85-0.96)	1.4×10 ⁻³	0.56	0.99(0.88-1.13)	0.915
rs7014860	C/A	0.24	1.14(1.03-1.25)	9.8×10 ⁻³	0.25	1.01(0.83-1.24)	0.896
rs979200	C/T	0.45	1.07(1.02-1.13)	8.2×10 ⁻³	0.67	1.09(0.95-1.24)	0.230
rs16901857	G/A	0.24	1.08(1.02-1.15)	6.6×10 ⁻³	0.08	1.02(0.82-1.28)	0.841
rs75127456	A/C	0.10	0.89(0.81-0.97)	8.9×10 ⁻³	0.07	0.92(0.71-1.19)	0.524
rs56005245	C/T	0.26	1.09(1.03-1.16)	2.5×10 ⁻³	0.37	1.02(0.89-1.16)	0.780
chr8:128272219:I	A/AG	0.04	1.32(1.10-1.59)	2.9×10 ⁻³	0.12	1.04(0.83-1.32)	0.715
rs28392817	T/G	0.17	1.10(1.03-1.18)	7.1×10 ⁻³	0.78	1.1(0.94-1.28)	0.237
rs4733807	A/G	0.12	0.89(0.82-0.96)	3.6×10 ⁻³	0.16	0.99(0.83-1.18)	0.907
rs55971392	G/A	0.10	0.88(0.8-0.96)	4.5×10 ⁻³	0.04	0.88(0.61-1.27)	0.501
rs35686742	C/T	0.09	0.87(0.79-0.96)	4.4×10 ⁻³	0.03	0.91(0.62-1.32)	0.619
rs6988558	G/C	0.44	0.98(0.93-1.04)	0.476	0.49	0.83(0.73-0.96)	9.6×10 ⁻³
rs73356177	A/G	0.05	1.05(0.93-1.19)	0.426	0.10	1.36(1.11-1.67)	2.8×10 ⁻³
rs1516964	C/T	0.04	0.88(0.76-1.01)	0.072	0.09	0.67(0.51-0.89)	6.1×10 ⁻³
rs56142222	G/A	0.03	1.08(0.92-1.25)	0.351	0.22	1.22(1.05-1.42)	9.8×10 ⁻³

Abbreviations: EAF, effect allele frequency; OR, odds ratio; CI, confidence interval.

^a Effect/reference allele; effect alleles are shown in bold.

^b Adjusted for study site and two principal components for each population.

^c Except for r^2 of 0.23 and 0.43 for linkage disequilibrium between rs7815245 and the index SNP rs13281615 in Asians and African American, all other SNPs are not in LD with either of the index SNPs rs13281615 or rs11780156 in non-European populations ($r^2 < 0.02$).

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure S1. Previously reported GWAS loci for various types of cancer on 8q24 spanning 128Mb-131Mb (hg19). For each locus, originally identified variant is plotted based on its chromosome position and $-\log_{10} P$ -value from cancer risk association analysis. These susceptibility loci for respective cancers include rs6983267 and rs1447295,¹ rs16901979,² rs16902094 and rs445114,³ rs1016343,⁴ and rs1456315⁵ for prostate cancer; rs13281615⁶ and rs11780156⁷ for breast cancer; rs6983267 for colorectal cancer;⁸ rs9642880 for Bladder cancer;⁹ rs10088218 for ovarian cancer;¹⁰ rs35252396 for renal cell carcinoma;¹¹ rs4295627 for glioma;¹² rs2456449 for chronic lymphocytic leukemia;¹³ and rs2019960 for Hodgkin's lymphoma.¹⁴ Note that rs6983267 confers risk for both prostate¹ and colorectal cancer.⁸ The middle panel shows the LD (r^2) between each of cancer risk-associated SNPs based on European ancestry subjects included in the 1000 Genomes Project (released in Mar 2012). All of these SNPs are not related except for two prostate cancer associated SNPs rs1016343 and rs1456315 ($r^2 = 0.29$) and the prostate cancer associated SNP rs445114 and the breast cancer associated SNP rs13281615 ($r^2 = 0.37$). The lower panel shows genes from the NCBI RNA reference sequences and the highlighted region where two breast cancer susceptibility loci locate.

Supplementary Figure S2. Regional association plots for 8q24 fine-mapping SNPs in Europeans. (a) Overall breast cancer risk association from univariate Logistic regression analysis with adjustment for age, study site and principal components. (b) Regional regression association plots for Signals 1-5 when other four representative SNPs are also included in the model. The index SNP is set as rs13281615 in Signal 2 (the purple diamond). The LD (r^2) between the index SNP and other tested SNPs is computed based on European ancestry subjects included in the 1000 Genomes Project (released in Mar 2012). The plots are generated for SNPs showing P values <0.05 using LocusZoom.¹⁵

Supplementary Figure S3. Transcription factor binding annotation of the independent Signal 3. (A) The plot represents the ESR1 and FOXA1 ChIP-seq peaks covering the independent signal rs7815245 in MCF-7, TAMR and ZR751 breast cancer cell lines. The y-axis denotes the read per million (RPM) normalized for ChIP-seq peaks. The synopses shown to the left of each row represent the ChIP experiments in the specific condition and cell types. See the

study by Hurtado et al¹⁶ for details. (B) The DNA sequence around the SNP rs7815245 harbors two DNA binding motifs, for ESR1 and FOXA1.

References

1. Yeager M, Orr N, Hayes RB, et al. Genome-wide association study of prostate cancer identifies a second risk locus at 8q24. *Nat Genet* 2007;39:645–9.
2. Gudmundsson J, Sulem P, Manolescu A, et al. Genome-wide association study identifies a second prostate cancer susceptibility variant at 8q24. *Nat Genet* 2007;39:631–7.
3. Gudmundsson J, Sulem P, Gudbjartsson DF, et al. Genome-wide association and replication studies identify four variants associated with prostate cancer susceptibility. *Nat Genet* 2009;41:1122–6.
4. Eeles RA, Kote-Jarai Z, Giles GG, et al. Multiple newly identified loci associated with prostate cancer susceptibility. *Nat Genet* 2008;40:316–21.
5. Takata R, Akamatsu S, Kubo M, et al. Genome-wide association study identifies five new susceptibility loci for prostate cancer in the Japanese population. *Nat Genet* 2010;42:751–4.
6. Easton DF, Pooley KA, Dunning AM, et al. Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature* 2007;447:1087–93.
7. Michailidou K, Hall P, Gonzalez-Neira A, et al. Large-scale genotyping identifies 41 new loci associated with breast cancer risk. *Nat Genet* 2013;45:353–361, 361e1–2.
8. Tomlinson I, Webb E, Carvajal-Carmona L, et al. A genome-wide association scan of tag SNPs identifies a susceptibility variant for colorectal cancer at 8q24.21. *Nat Genet* 2007;39:984–8.
9. Kiemeney LA, Thorlacius S, Sulem P, et al. Sequence variant on 8q24 confers susceptibility to urinary bladder cancer. *Nat Genet* 2008;40:1307–12.
10. Goode EL, Chenevix-Trench G, Song H, et al. A genome-wide association study identifies susceptibility loci for ovarian cancer at 2q31 and 8q24. *Nat Genet* 2010;42:874–9.
11. Gudmundsson J, Sulem P, Gudbjartsson DF, et al. A common variant at 8q24.21 is associated with renal cell cancer. *Nat Commun* 2013;4:2776.
12. Shete S, Hosking FJ, Robertson LB, et al. Genome-wide association study identifies five susceptibility loci for glioma. *Nat Genet* 2009;41:899–904.

13. Crowther-Swanepoel D, Broderick P, Di Bernardo MC, et al. Common variants at 2q37.3, 8q24.21, 15q21.3 and 16q24.1 influence chronic lymphocytic leukemia risk. *Nat Genet* 2010;42:132–6.
14. Enciso-Mora V, Broderick P, Ma Y, et al. A genome-wide association study of Hodgkin's lymphoma identifies new susceptibility loci at 2p16.1 (REL), 8q24.21 and 10p14 (GATA3). *Nat Genet* 2010;42:1126–30.
15. Pruim RJ, Welch RP, Sanna S, et al. LocusZoom: regional visualization of genome-wide association scan results. *Bioinformatics* 2010;26:2336–7.
16. Hurtado A, Holmes KA, Ross-Innes CS, et al. FOXA1 is a key determinant of estrogen receptor function and endocrine response. *Nat Genet* 2011;43:27–33.

Supplementary Table 1. Summary of publically accessible ChIP-seq data for ESR1 and FOXA1 in breast cancer cells.

Sample ID	Description	Cell line	Experimental treatment	Synopsis
GSM631452	[E-MTAB-223] E2_ER_ChIP_exp1_lane1	MCF-7	100 nM estrogen (E2) for 1h	MCF7 E2 ER exp1
GSM631453	[E-MTAB-223] E2_ER_ChIP_exp1_lane2	MCF-7	100 nM estrogen (E2) for 1h	MCF7 E2 ER exp1
GSM631454	[E-MTAB-223] E2_ER_ChIP_exp2_lane1	MCF-7	100 nM estrogen (E2) for 1h	MCF7 E2 ER exp2
GSM631455	[E-MTAB-223] E2_ER_ChIP_exp2_lane2	MCF-7	100 nM estrogen (E2) for 1h	MCF7 E2 ER exp2
GSM631456	[E-MTAB-223] E2_ER_ChIP_exp3	MCF-7	100 nM estrogen (E2) for 1h	MCF7 E2 ER exp3
GSM631457	[E-MTAB-223] E2_ER_ChIP_siNT_exp1_lane1	MCF-7	siControl transfection and 100 nM estrogen for 1 h	MCF7 E2 ER siNT
GSM631458	[E-MTAB-223] E2_ER_ChIP_siNT_exp1_lane2	MCF-7	siControl transfection and 100 nM estrogen for 1 h	MCF7 E2 ER siNT MCF7 FoxA1 full
GSM631459	FoxA1_ChIP_MCF7_full_media	MCF-7	Full media	Media
GSM631460	[E-MTAB-223] FoxA1_ChIP_ZR751_full_media	ZR751	Full media	ZR751 FoxA1 full
GSM631461	[E-MTAB-223] FoxA1_ChIP_TAMR_full_media	TAMR	Full media	Media
GSM631462	[E-MTAB-223] full_ER_ChIP_MCF7_exp1_lane1	MCF-7	Full media	TAMR FoxA1 full
GSM631463	[E-MTAB-223] full_ER_ChIP_MCF7_exp1_lane2	MCF-7	Full media	Media
GSM631464	[E-MTAB-223] full_ER_ChIP_MCF7_exp1_lane3	MCF-7	Full media	TAMR Media
GSM631465	[E-MTAB-223] full_ER_ChIP_MCF7_exp2_lane1	MCF-7	Full media	MCF7 full ER exp1
GSM631466	[E-MTAB-223] full_ER_ChIP_MCF7_exp2_lane2	MCF-7	Full media	MCF7 full ER exp1
GSM631467	[E-MTAB-223] full_ER_ChIP_MCF7_exp2_lane3	MCF-7	Full media	MCF7 full ER exp1
GSM631468	[E-MTAB-223] full_ER_ChIP_MCF7_input_lane1	MCF-7	no	MCF7 input
GSM631469	[E-MTAB-223] full_ER_ChIP_MCF7_input_lane2	MCF-7	no	MCF7 input
GSM631470	[E-MTAB-223] full_ER_ChIP_ZR751_input_lane1	ZR751	no	ZR751 input
GSM631471	[E-MTAB-223] full_ER_ChIP_ZR751_input_lane2	ZR751	no	ZR751 input
GSM631472	[E-MTAB-223] full_ER_ChIP_TAMR_input	TAMR	no	TAMR input

Supplementary Table 2. Association of top SNPs with breast cancer risk (combined *P* value $<1\times10^{-4}$) in women of European ancestry.

SNP ^a	Base position ^b	Alleles ^c	LD ^d (r^2)	EAF ^e	Imputation (r^2)	OR(95%CI) ^f	$P_{\text{overall}}^{\text{f}}$	OR(95%CI) _{ER+} ^g	$P_{\text{ER+}}^{\text{g}}$	OR(95%CI) _{ER-} ^h	$P_{\text{ER-}}^{\text{h}}$	$P_{\text{het}}^{\text{i}}$
rs13252265	128203859	A/T	<0.01/<0.01	0.104	1.000	1.06(1.03-1.1) 0.95(0.93- 0.97)	7.73E- 05 1.32E- 05	1.1(1.06-1.14) 0.94(0.91-0.96)	4.57E- 07 1.67E- 06	1(0.94-1.06) 0.97(0.93-1.01)	8.74E- 01 1.14E- 01	1.52E- 02 2.79E- 01
chr8:128213561:i	128213561	CA/C	<0.01/<0.01	0.431	0.752	0.95(0.93- 0.97)	8.86E- 05	0.94(0.92-0.97)	2.38E- 04	0.98(0.93-1.03)	3.79E- 01 3.03E- 01	2.07E- 01 2.51E- 01
rs4871776	128273489	A/G	0.05/<0.01	0.287	0.635	0.95(0.92- 0.97)	3.56E- 05	0.94(0.92-0.97)	1.82E- 04	0.97(0.93-1.02)	5.73E- 01 0.96(0.93-1)	2.58E- 01 1.01E- 01
chr8:128274050:D	128274050	G/GC	0.06/<0.01	0.297	0.645	0.95(0.93- 0.97)	4.55E- 05	0.94(0.92-0.97)	2.71E- 04	0.97(0.93-1.02)	5.73E- 01 0.96(0.93-1)	2.58E- 01 1.01E- 01
rs11777807	128280808	T/C	0.08/<0.01	0.428	1.000	0.96(0.94- 0.98)	7.67E- 07	0.95(0.93-0.97)	3.00E- 06	0.96(0.93-1)	1.01E- 02 0.96(0.93-1)	4.28E- 01 1.01E- 01
rs2198149	128283434	G/T	0.05/<0.01	0.487	1.000	0.96(0.94- 0.98)	5.61E- 05	0.96(0.94-0.98)	3.22E- 04	0.97(0.94-1.01)	6.92E- 01 0.97(0.94-1.01)	5.33E- 01 1.01E- 01
rs17450088	128285583	A/T	0.06/<0.01	0.478	1.000	0.96(0.94- 0.98)	5.15E- 05	0.96(0.94-0.98)	6.99E- 04	0.97(0.93-1)	2.19E- 02 0.98(0.94-1.01)	1.11E- 01 2.19E- 01
rs55753707	128285968	G/T	0.08/<0.01	0.451	0.994	0.96(0.94- 0.97)	2.21E- 06	0.95(0.93-0.97)	1.05E- 06	0.98(0.94-1.01)	4.64E- 02 0.98(0.94-1.01)	6.69E- 01 2.19E- 01
rs17450137	128287355	A/G	0.03/<0.01	0.117	0.858	0.93(0.9-0.96) 0.95(0.94- 0.97)	1.23E- 05	0.94(0.91-0.98)	4.12E- 03	0.94(0.88-1)	8.28E- 02 0.94(0.88-1)	2.29E- 01 8.28E- 01
rs62529474	128287615	A/G	0.07/<0.01	0.423	0.990	0.94(0.91- 0.97)	1.76E- 06	0.95(0.93-0.97)	8.00E- 06	0.97(0.93-1)	7.58E- 02 0.97(0.93-1)	1.05E- 01 7.58E- 01
chr8:128287943:i	128287943	GTA/G	0.05/<0.01	0.412	0.699	0.94(0.92- 0.96)	1.08E- 08	0.93(0.9-0.95)	3.02E- 08	0.96(0.92-1)	2.23E- 02 0.96(0.92-1)	4.94E- 01 2.23E- 01
rs62529475	128287945	A/G	0.08/<0.01	0.412	0.775	0.95(0.93- 0.96)	3.22E- 08	0.92(0.9-0.95)	7.50E- 09	0.97(0.93-1.02)	5.79E- 01 0.97(0.93-1.02)	2.37E- 03 5.79E- 01
rs17378189	128288920	T/C	0.08/<0.01	0.433	0.987	0.95(0.94- 0.97)	1.24E- 07	0.94(0.92-0.97)	4.60E- 07	0.96(0.93-1)	7.30E- 02 0.96(0.93-1)	2.43E- 01 7.30E- 01
rs4871780	128291578	T/C	0.07/<0.01	0.424	1.000	0.96(0.94- 0.97)	2.71E- 06	0.95(0.93-0.97)	2.17E- 06	0.97(0.93-1)	8.03E- 02 0.97(0.93-1)	4.51E- 01 8.03E- 01
rs11993023	128293345	C/A	0.06/<0.01	0.482	0.998	0.95(0.93- 0.98)	5.36E- 05	0.96(0.94-0.98)	2.14E- 04	0.97(0.93-1)	7.07E- 02 0.97(0.93-1)	2.11E- 01 7.07E- 01
rs62529476	128293916	C/G	0.08/<0.01	0.426	0.994	0.96(0.94- 0.97)	2.66E- 07	0.95(0.93-0.97)	2.92E- 06	0.97(0.93-1)	2.31E- 02 0.97(0.93-1)	8.09E- 01 2.31E- 01
rs17378569	128302639	T/C	0.04/<0.01	0.460	1.000	0.96(0.94- 0.98)	2.49E- 05	0.96(0.94-0.98)	1.80E- 04	0.96(0.92-0.99)	2.58E- 02 0.96(0.92-0.99)	7.29E- 01 2.58E- 01
chr8:128303091:i	128303091	TCA/T	0.04/<0.01	0.468	0.994	0.96(0.94- 0.98)	4.55E- 05	0.96(0.94-0.98)	3.54E- 04	0.96(0.92-1)	2.55E- 02 0.96(0.92-1)	7.92E- 01 2.55E- 01
rs12216777	128303372	T/C	0.04/<0.01	0.464	1.000	1.06(1.03- 1.09)	3.80E- 05	0.96(0.94-0.98)	1.20E- 04	0.96(0.92-0.99)	1.77E- 02 0.96(0.92-0.99)	9.12E- 01 1.77E- 01
rs283717	128305596	C/G	0.09/<0.01	0.153	0.908			1.07(1.03-1.1)	4.04	1.07(1.01-1.12)	4.04	9.12E- 01 1.07(1.01-1.12)

rs283718	128307082	T/C	0.04<0.01	0.577	1.000	0.96(0.94-0.98)	1.55E-05	0.96(0.94-0.98)	5.49E-04	0.98(0.95-1.02)	3.22E-01	1.51E-01
rs17450934	128308837	A/G	0.04<0.01	0.127	0.998	0.94(0.91-0.97)	1.72E-05	0.95(0.92-0.98)	2.21E-03	0.95(0.9-1)	7.15E-02	5.71E-01
rs12549518	128309591	A/G	0.12<0.01	0.433	0.998	0.94(0.92-0.96)	7.57E-10	0.94(0.92-0.96)	2.73E-08	0.96(0.93-1)	5.32E-02	1.02E-01
rs6996866	128310155	T/C	0.12<0.01	0.432	1.000	0.94(0.92-0.96)	6.31E-10	0.94(0.92-0.96)	3.07E-08	0.96(0.93-1)	4.21E-02	1.19E-01
rs283721	128310493	G/A	0.07<0.01	0.132	0.998	1.06(1.03-1.09)	5.22E-05	1.07(1.04-1.11)	1.77E-05	1.05(0.99-1.1)	1.08E-01	8.12E-01
chr8:128310713:I	128310713	GA/G	0.07<0.01	0.131	0.992	1.06(1.03-1.09)	3.75E-05	1.08(1.04-1.11)	1.41E-05	1.05(0.99-1.1)	1.04E-01	7.97E-01
rs283724	128310849	G/C	0.07<0.01	0.131	0.990	1.06(1.03-1.09)	3.88E-05	1.08(1.04-1.11)	1.53E-05	1.05(0.99-1.1)	1.05E-01	8.05E-01
rs283725	128311352	C/T	0.07<0.01	0.131	0.987	1.06(1.03-1.09)	3.94E-05	1.08(1.04-1.11)	1.67E-05	1.05(0.99-1.1)	1.05E-01	8.12E-01
rs10111296	128312065	A/T	0.02<0.01	0.877	1.000	0.94(0.92-0.97)	6.98E-05	0.94(0.91-0.97)	5.91E-04	0.93(0.88-0.98)	6.12E-03	3.01E-01
rs283727	128313360	A/G	0.24<0.01	0.542	1.000	1.07(1.05-1.09)	1.44E-12	1.08(1.05-1.1)	5.90E-11	1.03(1-1.07)	7.74E-02	1.03E-02
rs283728	128313500	A/T	0.26<0.01	0.549	0.999	1.07(1.05-1.09)	1.89E-13	1.08(1.06-1.1)	3.01E-11	1.03(1-1.07)	8.72E-02	7.92E-03
rs4871015	128314516	G/A	0.24<0.01	0.413	1.000	0.93(0.91-0.94)	3.49E-15	0.93(0.9-0.95)	2.33E-11	0.96(0.93-1)	3.81E-02	2.11E-02
rs34882299	128314913	G/A	0.23<0.01	0.498	1.000	1.07(1.05-1.09)	4.45E-11	1.07(1.04-1.09)	1.70E-08	1.03(0.99-1.07)	5.26E-02	1.28E-02
chr8:128315379:I	128315379	AGCC/A	0.18<0.01	0.544	0.971	1.07(1.05-1.09)	1.38E-11	1.07(1.04-1.09)	1.55E-08	1.04(1-1.08)	5.32E-02	2.74E-01
rs283704	128315582	G/A	0.25<0.01	0.580	1.000	1.08(1.05-1.1)	2.08E-13	1.08(1.05-1.1)	1.63E-10	1.04(1-1.08)	1.03E-02	5.89E-02
rs56983490	128316676	G/A	0.18<0.01	0.438	0.989	0.93(0.91-0.94)	1.19E-15	0.93(0.9-0.95)	7.83E-11	0.95(0.92-0.99)	1.70E-02	6.84E-02
rs283705	128317450	T/C	0.22<0.01	0.524	1.000	1.08(1.06-1.1)	8.58E-14	1.08(1.05-1.1)	1.54E-11	1.05(1.01-1.08)	1.06E-02	8.88E-02
rs7006593	128317585	T/A	0.18<0.01	0.444	1.000	0.93(0.91-0.95)	1.96E-15	0.93(0.91-0.95)	3.82E-10	0.95(0.92-0.99)	6.92E-02	9.11E-02
c8_pos128387070	128317888	A/G	0.05<0.01	0.045	1.000	1.11(1.06-1.16)	3.09E-05	1.12(1.06-1.18)	1.11E-05	1.08(0.99-1.18)	2.26E-02	5.86E-01
rs10107982	128318755	C/T	0.25<0.01	0.282	1.000	1.06(1.03-1.08)	2.37E-07	1.06(1.04-1.09)	3.54E-06	1.03(0.98-1.07)	7.22E-01	8.42E-02
rs7017081	128319347	A/C	0.05<0.01	0.046	0.995	1.1(1.05-1.15)	1.57E-05	1.12(1.06-1.18)	1.21E-05	1.08(0.99-1.18)	5.66E-02	8.33E-01
c8_pos128388895	128319713	A/G	0.04<0.01	0.048	1.000	1.1(1.05-1.15)	1.63E-05	1.12(1.07-1.18)	1.32E-05	1.09(1-1.18)	5.76E-02	8.09E-01
rs6984136	128320138	T/C	0.04<0.01	0.048	1.000	1.1(1.05-1.15)	1.63E-05	1.12(1.07-1.18)	1.32E-05	1.09(1-1.18)	5.76E-02	8.09E-01

							05		05		02	01
rs7838810	128321202	C/T	0.4/<0.01	0.350	1.000	1.07(1.05-1.09)	5.08E-11	1.07(1.05-1.1)	3.33E-09	1.03(0.99-1.07)	9.58E-02	8.24E-02
rs453875	128321411	A/G	0.42/<0.01	0.432	0.992	1.08(1.06-1.1)	1.05E-13	1.08(1.06-1.11)	4.59E-12	1.03(1-1.07)	7.37E-02	2.25E-02
chr8:128322698:D	128322698	T/TA	0.22/<0.01	0.377	0.988	0.92(0.9-0.94) 1.06(1.04-1.08)	2.45E-16 8.56E-10	0.92(0.9-0.94)	7.85E-13	0.96(0.92-0.99)	1.79E-02	2.61E-02
rs445114	128323181	C/T	0.37/<0.01	0.371	1.000	1.06(1.04-1.08)	1.25E-08	1.07(1.04-1.09)	1.70E-08	1.02(0.98-1.06)	3.59E-01	9.43E-03
rs378854	128323819	T/C	0.36/<0.01	0.359	1.000	1.06(1.04-1.08)	2.62E-09	1.06(1.04-1.08)	2.82E-07	1.02(0.98-1.06)	3.98E-01	1.96E-02
rs421094	128323874	A/G	0.37/<0.01	0.367	0.997	1.06(1.04-1.08)	2.10E-08	1.07(1.04-1.09)	4.30E-08	1.02(0.98-1.06)	2.97E-01	2.08E-02
rs382434	128324147	T/C	0.3/<0.01	0.337	0.993	1.06(1.04-1.08)	4.06E-08	1.06(1.04-1.08)	5.60E-07	1.03(0.99-1.07)	1.48E-01	5.76E-02
rs7832541	128325183	C/T	0.33/<0.01	0.346	0.938	1.06(1.04-1.08)	4.59E-08	1.06(1.04-1.09)	4.32E-07	1.02(0.98-1.06)	4.19E-01	2.44E-02
rs184916014	128327509	A/T	0.05/<0.01	0.049	0.957	1.1(1.05-1.15)	2.03E-05	1.11(1.05-1.17)	1.26E-04	1.08(0.99-1.18)	8.26E-02	9.87E-01
rs618477	128327641	G/C	0.36/<0.01	0.358	0.966	1.06(1.04-1.08)	1.12E-09	1.07(1.04-1.09)	5.10E-08	1.03(0.99-1.07)	2.00E-01	3.39E-02
rs112175013	128327800	A/G	0.26/<0.01	0.405	0.987	0.92(0.9-0.94) 1.07(1.05-1.09)	3.46E-17	0.92(0.9-0.94)	5.55E-14	0.96(0.92-0.99)	2.57E-02	1.52E-02
rs617894	128327828	G/A	0.2/<0.01	0.507	0.956	1.06(1.04-1.09)	3.97E-11	1.07(1.05-1.1)	4.44E-09	1.03(0.99-1.07)	1.27E-01	2.40E-02
rs79297161	128328709	T/C	0.28/<0.01	0.373	0.884	1.06(1.04-1.08)	7.74E-08	1.07(1.04-1.09)	2.90E-07	1.02(0.98-1.06)	3.22E-01	3.16E-02
rs11781932	128330178	T/C	0.26/<0.01	0.403	0.986	0.92(0.9-0.94)	7.14E-18	0.92(0.89-0.94)	4.75E-14	0.96(0.92-1)	2.93E-02	1.21E-02
rs11785664	128330424	C/T	0.26/<0.01	0.403	0.987	0.92(0.9-0.94)	2.90E-18	0.92(0.89-0.94)	4.54E-14	0.96(0.92-0.99)	2.46E-02	1.48E-02
rs56154314	128330748	A/C	0.26/<0.01	0.396	0.966	0.92(0.9-0.93) 0.91(0.89-0.93)	2.79E-18	0.91(0.89-0.93)	8.35E-14	0.95(0.92-0.99)	1.48E-02	2.30E-02
rs187403989	128331797	A/G	0.24/<0.01	0.373	0.916	0.91(0.89-0.93)	1.41E-18	0.91(0.89-0.93)	7.31E-14	0.95(0.91-0.98)	3.63E-03	2.48E-02
rs4397364	128331799	A/G	0.27/<0.01	0.466	0.912	1.07(1.05-1.1) 1.06(1.04-1.08)	4.48E-12	1.08(1.06-1.11)	2.46E-11	1.02(0.98-1.06)	3.39E-01	1.21E-03
rs13271897	128332878	T/C	0.19/<0.01	0.499	0.957	1.07(1.05-1.08)	1.26E-10	1.07(1.04-1.09)	1.82E-08	1.02(0.98-1.06)	1.24E-01	1.67E-02
rs13272693	128332975	A/G	0.24/<0.01	0.504	0.967	1.07(1.05-1.09)	2.18E-12	1.08(1.05-1.1)	9.87E-10	1.03(0.99-1.07)	7.81E-01	2.90E-02
rs13272305	128333116	G/A	0.21/<0.01	0.465	0.886	1.07(1.05-1.1) 1.07(1.05-1.09)	6.12E-12	1.08(1.05-1.1)	1.11E-09	1.04(1-1.08)	3.03E-02	9.88E-03
rs622856	128333180	T/C	0.36/<0.01	0.354	0.948	1.07(1.05-1.09)	1.1E-11	1.08(1.05-1.1)	1.02(0.98-1.06)	1.02(0.98-1.06)	1.02(0.98-1.06)	1.02(0.98-1.06)

rs622853	128333181	A/G	0.37<0.01	0.352	0.944	1.07(1.05-1.09)	6.39E-11	1.08(1.05-1.1)	9.13E-10	1.02(0.98-1.06)	3.14E-01	8.84E-03
rs622556	128333197	C/T	0.22<0.01	0.516	0.990	1.07(1.05-1.09)	4.42E-12	1.07(1.05-1.1)	7.85E-10	1.03(0.99-1.06)	1.63E-01	1.35E-02
rs452529	128333259	C/G	0.22<0.01	0.518	1.000	1.07(1.05-1.09)	1.03E-11	1.07(1.05-1.1)	1.76E-09	1.03(0.99-1.06)	1.68E-01	1.58E-02
rs444318	128333513	G/A	0.22<0.01	0.518	1.000	1.07(1.05-1.09)	1.26E-11	1.07(1.05-1.1)	1.97E-09	1.03(0.99-1.06)	1.78E-01	1.52E-02
chr8:128334141:D	128334141	C/CCT	0.17<0.01	0.482	0.915	1.07(1.05-1.09)	3.25E-11	1.07(1.05-1.1)	4.33E-09	1.03(0.99-1.07)	1.18E-01	3.36E-02
chr8:128334150:D	128334150	C/CTT	0.21<0.01	0.510	0.977	1.07(1.05-1.09)	2.25E-11	1.07(1.05-1.1)	2.51E-09	1.02(0.99-1.06)	2.07E-01	1.39E-02
rs606677	128334485	C/T	0.21<0.01	0.524	0.996	1.07(1.05-1.09)	3.46E-11	1.07(1.04-1.09)	6.95E-09	1.02(0.99-1.06)	1.90E-01	1.82E-02
rs606345	128334499	A/T	0.22<0.01	0.518	0.999	1.07(1.05-1.09)	1.04E-11	1.07(1.05-1.1)	1.79E-09	1.03(0.99-1.06)	1.68E-01	1.56E-02
rs2691039	128334662	G/A	0.22<0.01	0.518	0.999	1.07(1.05-1.09)	1.05E-11	1.07(1.05-1.1)	1.80E-09	1.03(0.99-1.06)	1.67E-01	1.57E-02
rs13256367	128334900	C/A	0.41<0.01	0.349	0.994	1.07(1.05-1.09)	5.93E-11	1.07(1.05-1.1)	3.25E-09	1.03(0.99-1.06)	1.94E-01	3.30E-02
rs594154	128334911	A/G	0.22<0.01	0.518	0.998	1.07(1.05-1.09)	1.06E-11	1.07(1.05-1.1)	1.83E-09	1.03(0.99-1.07)	1.68E-01	1.55E-02
rs594076	128334966	C/G	0.22<0.01	0.518	0.999	1.07(1.05-1.09)	1.06E-11	1.07(1.05-1.1)	1.86E-09	1.03(0.99-1.06)	1.67E-01	1.58E-02
rs373701	128334992	A/C	0.22<0.01	0.518	0.999	1.07(1.05-1.09)	1.06E-11	1.07(1.05-1.1)	1.87E-09	1.03(0.99-1.06)	1.67E-01	1.58E-02
rs437980	128335246	C/A	0.22<0.01	0.518	0.999	1.06(1.03-1.09)	5.68E-11	1.07(1.05-1.1)	3.23E-09	1.03(0.99-1.06)	1.71E-01	1.06E-02
rs62516012	128335526	G/C	0.27<0.01	0.288	0.990	1.06(1.04-1.08)	4.67E-07	1.06(1.03-1.09)	8.44E-06	1.03(0.99-1.07)	3.28E-01	1.14E-01
rs620861	128335673	A/G	0.38<0.01	0.371	1.000	1.06(1.04-1.09)	4.67E-10	1.07(1.05-1.1)	8.44E-09	1.02(0.98-1.06)	2.16E-01	7.25E-02
rs620808	128335714	T/C	0.22<0.01	0.489	0.933	1.07(1.05-1.09)	3.39E-12	1.08(1.05-1.1)	1.71E-10	1.02(0.99-1.06)	2.75E-01	6.79E-03
rs590574	128335715	G/A	0.21<0.01	0.481	0.921	1.07(1.05-1.09)	4.01E-11	1.08(1.05-1.1)	7.33E-10	1.02(0.98-1.06)	3.23E-01	1.13E-03
rs443053	128335796	T/G	0.38<0.01	0.371	1.000	1.07(1.05-1.09)	4.01E-10	1.07(1.05-1.1)	4.68E-09	1.02(0.98-1.06)	1.69E-01	1.42E-02
chr8:128335999:I	128335999	TAA/T	0.21<0.01	0.506	0.966	1.07(1.05-1.09)	2.82E-12	1.07(1.05-1.1)	4.68E-10	1.03(0.99-1.06)	1.54E-01	1.94E-02
rs11775799	128336236	G/A	0.28<0.01	0.418	0.983	0.92(0.9-0.93)	5.23E-19	0.91(0.89-0.93)	3.35E-15	0.96(0.92-0.99)	9.62E-02	3.04E-02
rs400818	128336546	C/T	0.23<0.01	0.508	0.999	1.07(1.05-1.09)	1.57E-12	1.07(1.05-1.1)	3.04E-10	1.03(0.99-1.07)	2.07E-02	2.02E-02
rs78015822	128336740	G/A	0.24<0.01	0.475	0.927	1.08(1.05-1.1)	3.12E-11	1.08(1.06-1.11)	1.96E-11	1.03(0.99-1.07)	1.05E-01	1.89E-01

															01	02
rs74588857	128336741	T/C	0.24<0.01	0.475	0.927	1.08(1.05-1.1)	3.12E-	13	1.08(1.06-1.11)	1.96E-	11	1.03(0.99-1.07)	1.05E-	1.89E-		
rs34628978	128336744	A/G	0.23<0.01	0.507	0.995	1.07(1.05-1.09)	1.38E-	12	1.07(1.05-1.1)	3.25E-	10	1.03(0.99-1.07)	9.33E-	3.14E-		
rs386883	128336871	A/G	0.23<0.01	0.508	1.000	1.07(1.05-1.09)	1.42E-	12	1.07(1.05-1.1)	3.17E-	10	1.03(0.99-1.07)	9.52E-	3.04E-		
chr8:128337049:i	128337049	CAG/C	0.24<0.01	0.508	0.998	1.07(1.05-1.09)	1.34E-	12	1.07(1.05-1.1)	3.19E-	10	1.03(0.99-1.07)	9.33E-	3.12E-		
rs377649	128337241	T/G	0.24<0.01	0.506	0.976	1.07(1.05-1.09)	9.42E-	13	1.07(1.05-1.1)	2.38E-	10	1.03(0.99-1.07)	9.15E-	2.94E-		
rs432523	128337927	T/A	0.23<0.01	0.508	0.999	1.07(1.05-1.09)	1.41E-	12	1.07(1.05-1.1)	3.30E-	10	1.03(0.99-1.07)	9.68E-	3.03E-		
rs430693	128338594	T/G	0.23<0.01	0.507	0.998	1.07(1.05-1.09)	1.45E-	12	1.07(1.05-1.1)	3.33E-	10	1.03(0.99-1.07)	9.68E-	3.04E-		
rs684254	128338693	A/G	0.23<0.01	0.508	0.999	1.07(1.05-1.09)	1.36E-	12	1.07(1.05-1.1)	3.13E-	10	1.03(0.99-1.07)	9.68E-	3.00E-		
rs1395287	128338702	G/C	0.41<0.01	0.350	0.993	1.07(1.05-1.09)	4.14E-	11	1.07(1.05-1.1)	2.84E-	09	1.03(0.99-1.07)	1.81E-	3.43E-		
rs631845	128338760	A/G	0.23<0.01	0.507	0.995	1.07(1.05-1.09)	1.04E-	12	1.07(1.05-1.1)	2.91E-	10	1.03(1-1.07)	8.42E-	3.53E-		
rs653605	128338847	T/G	0.23<0.01	0.508	0.999	1.07(1.05-1.09)	1.41E-	12	1.07(1.05-1.1)	3.10E-	10	1.03(0.99-1.07)	9.92E-	2.89E-		
rs432470	128339044	T/C	0.33<0.01	0.551	1.000	1.09(1.07-1.11)	1.02E-	17	1.09(1.07-1.12)	1.35E-	14	1.05(1.01-1.08)	1.71E-	3.52E-		
rs424281	128339426	A/G	0.33<0.01	0.551	0.999	1.09(1.07-1.11)	8.46E-	18	1.09(1.07-1.12)	1.22E-	14	1.05(1.01-1.08)	1.72E-	3.50E-		
rs1668875	128341103	C/G	0.51<0.01	0.405	1.000	1.08(1.06-1.1)	1.18E-	15	1.09(1.07-1.12)	9.54E-	14	1.04(1-1.08)	4.30E-	2.94E-		
rs7002712	128341612	T/A	0.28<0.01	0.411	0.986	0.92(0.9-0.93)	7.84E-	19	0.91(0.89-0.93)	6.93E-	15	0.96(0.92-0.99)	1.53E-	2.44E-		
rs587948	128341680	G/T	0.51<0.01	0.403	0.999	1.08(1.06-1.1)	4.45E-	15	1.09(1.06-1.11)	3.76E-	13	1.04(1-1.08)	4.80E-	3.81E-		
rs623401	128341727	G/C	0.51<0.01	0.403	1.000	1.08(1.06-1.1)	1.07(1.05-1.09)	15	1.09(1.06-1.11)	1.23E-	13	1.04(1-1.08)	1.80E-	2.80E-		
rs35049703	128342114	A/C	0.4<0.01	0.347	0.938	1.06(1.04-1.08)	3.03E-	11	1.08(1.05-1.1)	1.09	1.03(0.99-1.07)	1.10E-	1.29E-			
rs10956359	128342154	C/T	0.28<0.01	0.294	1.000	1.06(1.04-1.08)	1.35E-	07	1.06(1.04-1.09)	4.92E-	07	1.03(0.99-1.07)	7.71E-	8.98E-		
rs17464492	128342866	G/A	0.29<0.01	0.290	1.000	1.05(1.03-1.08)	9.44E-	09	1.07(1.04-1.1)	5.31E-	08	1.04(1-1.08)	8.86E-	1.62E-		
rs35603878	128343341	C/G	0.27<0.01	0.222	0.939	1.08(1.04-1.08)	2.23E-	05	1.06(1.03-1.08)	1.03E-	04	1(0.95-1.04)	9.00E-	1.30E-		
chr8:128343601:i	128343601	GT/G	0.14<0.01	0.096	0.948	1.08(1.04-1.12)	5.00E-	06	1.08(1.03-1.12)	2.49E-	04	1(0.94-1.07)	9.00E-	1.30E-		

rs420101	128343879	A/G	0.93<0.01	0.398	1.000	1.1(1.08-1.12)	1.27E-22	1.11(1.09-1.14)	2.94E-19	1.02(0.98-1.05)	4.05E-01	3.45E-05
rs7838714	128343948	C/T	0.48<0.01	0.410	0.998	0.9(0.88-0.92)	1.18E-27	0.89(0.87-0.91)	9.16E-22	0.96(0.93-1)	4.15E-02	3.85E-04
rs389143	128344380	T/C	0.94<0.01	0.400	0.992	1.1(1.08-1.12)	1.21E-22	1.11(1.09-1.14)	3.64E-19	1.02(0.98-1.06)	3.96E-01	3.56E-05
rs688201	128344402	T/G	0.93<0.01	0.401	0.998	1.1(1.08-1.12)	1.20E-22	1.11(1.09-1.14)	1.39E-19	1.02(0.98-1.06)	3.89E-01	2.82E-05
rs595821	128344410	A/G	0.94<0.01	0.399	0.999	1.1(1.08-1.12)	7.80E-23	1.11(1.09-1.14)	3.60E-19	1.02(0.98-1.06)	3.53E-01	4.62E-05
rs687324	128344591	C/T	0.94<0.01	0.400	0.998	1.1(1.08-1.12) 1.11(1.08-1.13)	8.55E-23	1.11(1.09-1.14)	3.64E-19	1.02(0.98-1.06)	3.64E-01	4.13E-05
rs594869	128344601	C/T	0.91<0.01	0.383	0.955	1.1(1.08-1.12)	3.18E-23	1.11(1.09-1.14)	1.65E-19	1.02(0.98-1.06)	4.28E-01	2.57E-05
rs594868	128344602	A/G	0.92<0.01	0.390	0.975	1.1(1.08-1.13)	5.40E-23	1.11(1.09-1.14)	3.95E-19	1.02(0.98-1.06)	4.41E-01	3.45E-05
rs687279	128344624	T/C	0.62<0.01	0.304	1.000	1.08(1.06-1.1)	7.19E-14	1.09(1.06-1.12)	2.58E-12	1.02(0.98-1.06)	3.14E-01	2.06E-03
rs436238	128345028	T/C	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	8.66E-23	1.11(1.09-1.14)	3.79E-19	1.02(0.98-1.06)	3.66E-01	4.00E-05
rs581761	128345231	T/G	0.94<0.01	0.397	0.992	1.1(1.08-1.12)	2.20E-23	1.11(1.09-1.14)	9.06E-19	1.02(0.98-1.06)	3.34E-01	3.61E-05
rs673745	128345269	T/C	0.94<0.01	0.399	0.990	1.1(1.08-1.13)	5.00E-23	1.11(1.09-1.14)	1.95E-20	1.02(0.98-1.06)	3.61E-01	3.09E-05
rs688937	128345381	A/T	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	4.69E-23	1.11(1.09-1.14)	1.91E-19	1.02(0.98-1.06)	3.52E-01	3.30E-05
rs672888	128345463	G/A	0.94<0.01	0.400	0.998	1.1(1.08-1.12)	1.34E-23	1.11(1.09-1.14)	4.86E-19	1.02(0.98-1.06)	5.53E-01	2.32E-05
rs7826557	128345731	A/C	0.47<0.01	0.405	0.999	0.9(0.88-0.92)	4.97E-26	0.9(0.88-0.92)	1.84E-21	0.96(0.93-1)	3.58E-02	3.15E-04
chr8:128345939:I	128345939	CCTT/C	0.94<0.01	0.400	0.998	1.1(1.08-1.12) 1.11(1.09-1.13)	1.92E-23	1.11(1.09-1.14)	5.71E-19	1.02(0.98-1.06)	1.07E-01	4.04E-05
chr8:128345943:I	128345943	CTT/C	0.75<0.01	0.336	0.837	1.1(1.08-1.12)	5.03E-20	1.11(1.08-1.14)	1.76E-16	1.04(0.99-1.08)	3.66E-01	2.91E-03
rs419018	128346259	G/A	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	4.90E-23	1.11(1.09-1.14)	1.57E-19	1.02(0.98-1.06)	3.68E-01	2.92E-05
rs418269	128346358	A/G	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	4.05E-23	1.11(1.09-1.14)	1.37E-19	1.02(0.98-1.06)	3.63E-01	2.83E-05
chr8:128346646:D	128346646	A/AT	0.94<0.01	0.399	0.995	1.1(1.08-1.13)	5.55E-23	1.11(1.09-1.14)	2.02E-19	1.02(0.98-1.06)	3.57E-01	3.38E-05
rs385278	128347017	C/T	0.94<0.01	0.400	1.000	1.1(1.08-1.12) 1.05(1.03-1.08)	1.41E-23	1.11(1.09-1.14)	7.43E-19	1.02(0.98-1.06)	8.07E-01	1.14E-05
rs391640	128347124	G/A	0.36<0.01	0.200	1.000	1.08	5.79E-05	1.06(1.03-1.09)	2.06E-05	0.99(0.95-1.04)	1.01E-01	1.02E-02
rs670725	128347157	C/A	0.94<0.01	0.400	0.995	1.1(1.08-1.12)		1.11(1.09-1.14)		1.02(0.98-1.06)	3.58E-01	3.28E-05

							23		19		01	05
rs77209413	128347562	T/A	0.13<0.01	0.085	0.982	1.08(1.05-1.12)	6.02E-06	1.08(1.04-1.13)	9.45E-05	0.99(0.92-1.05)	6.90E-01	2.64E-02
rs382824	128347724	G/T	0.94<0.01	0.400	0.998	1.1(1.08-1.12)	5.58E-23	1.11(1.09-1.14)	2.13E-19	1.02(0.98-1.06)	3.52E-01	3.53E-05
rs383205	128347977	A/G	0.94<0.01	0.400	0.999	1.1(1.08-1.12)	6.74E-23	1.11(1.09-1.14)	2.52E-19	1.02(0.98-1.06)	3.56E-01	3.55E-05
rs373616	128348062	C/T	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	7.94E-23	1.11(1.09-1.14)	2.59E-19	1.02(0.98-1.06)	3.72E-01	3.34E-05
rs400772	128348298	T/G	0.94<0.01	0.399	1.000	1.1(1.08-1.12)	1.13E-22	1.11(1.08-1.14)	4.00E-19	1.02(0.98-1.06)	3.85E-01	3.29E-05
rs13275275	128349727	G/A	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	5.92E-23	1.11(1.09-1.14)	2.01E-19	1.02(0.98-1.06)	3.49E-01	3.56E-05
rs13248140	128349888	A/G	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	6.49E-23	1.11(1.09-1.14)	2.35E-19	1.02(0.98-1.06)	3.47E-01	3.77E-05
rs10956360	128349970	A/G	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	5.32E-23	1.11(1.09-1.14)	2.08E-19	1.02(0.98-1.06)	3.42E-01	3.78E-05
rs10956361	128350106	A/G	0.94<0.01	0.399	0.997	1.1(1.08-1.12)	1.08E-22	1.11(1.09-1.14)	3.94E-19	1.02(0.98-1.06)	3.61E-01	4.26E-05
rs10956362	128350386	G/A	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	7.00E-23	1.11(1.09-1.14)	2.54E-19	1.02(0.98-1.06)	3.52E-01	3.65E-05
rs13249993	128350515	A/G	0.54<0.01	0.553	1.000	1.1(1.08-1.12) 1.11(1.09-1.13)	3.48E-26	1.11(1.09-1.14)	5.06E-21	1.03(1-1.07)	7.70E-02	2.64E-04
rs11777532	128350608	C/G	0.41<0.01	0.375	1.000	0.91(0.89-0.93)	2.55E-23	1.11(1.09-1.14)	2.83E-18	0.97(0.93-1)	3.72E-02	3.97E-04
chr8:128350707:D	128350707	C/CA	0.94<0.01	0.398	0.993	1.1(1.08-1.12)	1.16E-22	1.11(1.09-1.14)	3.60E-19	1.02(0.98-1.06)	3.48E-01	3.69E-05
c8_pos128420230	128351048	T/A	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	6.43E-23	1.11(1.09-1.14)	2.32E-19	1.02(0.98-1.06)	3.39E-01	3.88E-05
c8_pos128420624	128351442	C/A	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	5.59E-23	1.11(1.09-1.14)	1.74E-19	1.02(0.98-1.06)	3.88E-01	2.98E-05
chr8:128351524:I	128351524	AG/A	0.94<0.01	0.399	0.994	1.1(1.08-1.12)	8.25E-23	1.11(1.09-1.14)	1.74E-19	1.02(0.98-1.06)	3.36E-01	5.04E-05
rs10956363	128351773	A/G	0.94<0.01	0.398	0.994	1.1(1.08-1.12)	1.51E-22	1.11(1.08-1.14)	5.05E-19	1.02(0.98-1.06)	2.45E-01	5.31E-05
c8_pos128421136	128351954	T/C	0.64<0.01	0.311	0.999	1.08(1.06-1.1) 1.07(1.05-1.09)	9.13E-13	1.09(1.06-1.12)	6.38E-12	1.02(0.98-1.06)	5.16E-01	7.67E-03
rs36024485	128352205	C/T	0.52<0.01	0.268	0.999	1.07(1.05-1.09)	1.22E-10	1.07(1.05-1.1)	4.59E-08	1.01(0.97-1.06)	3.23E-01	6.71E-03
rs4871782	128352234	A/G	0.94<0.01	0.400	1.000	1.1(1.08-1.12)	1.01E-22	1.11(1.08-1.14)	6.61E-19	1.02(0.98-1.06)	2.21E-01	6.34E-05
rs28759353	128352363	T/G	0.64<0.01	0.311	1.000	1.08(1.06-1.1) 0.91(0.89-0.93)	2.18E-13	1.09(1.06-1.12)	3.11E-12	1.02(0.99-1.07)	2.66E-01	1.01E-03
rs10087810	128352730	T/C	0.82<0.01	0.567	0.999	0.93)	2.2E-22	0.9(0.88-0.93)	1.8E-18	0.98(0.94-1.02)	1.01E-01	4.04

chr8:128352967:D	128352967	C/CA	0.82<0.01	0.567	0.993	0.91(0.89-0.93)	2.72E-22	0.9(0.88-0.93)	3.82E-18	0.98(0.94-1.02)	2.55E-01	1.05E-04
rs12541832	128353171	A/C	0.64<0.01	0.311	1.000	1.08(1.06-1.1)	9.73E-14	1.09(1.06-1.12)	6.55E-12	1.03(0.99-1.07)	2.11E-01	6.75E-03
rs13262406	128353739	G/A	0.65<0.01	0.311	0.999	1.08(1.06-1.1)	4.17E-14	1.09(1.06-1.12)	2.94E-12	1.03(0.99-1.07)	1.88E-01	6.43E-03
rs17465052	128354080	A/G	0.48<0.01	0.411	0.995	0.9(0.88-0.91)	5.72E-28	0.89(0.87-0.91)	3.06E-22	0.96(0.92-1)	2.75E-02	6.08E-04
rs13270266	128354086	G/A	0.65<0.01	0.311	0.999	1.08(1.06-1.1)	5.03E-14	1.09(1.06-1.12)	3.25E-12	1.03(0.99-1.07)	1.88E-01	6.60E-03
rs13271658	128354313	A/G	0.14<0.01	0.827	0.999	0.93(0.91-0.95)	2.01E-08	0.93(0.9-0.96)	5.74E-07	0.98(0.94-1.03)	4.84E-01	4.98E-02
rs10095860	128354785	A/C	<0.01<0.01	0.678	0.992	0.95(0.93-0.97)	1.40E-07	0.95(0.92-0.97)	5.08E-06	0.97(0.93-1.01)	1.28E-01	3.16E-01
rs10098985	128355019	T/G	0.47<0.01	0.406	0.998	0.9(0.88-0.92)	6.23E-27	0.9(0.87-0.92)	2.16E-21	0.96(0.93-1)	3.68E-02	5.07E-04
rs13281615	128355618	G/A	-<0.01	0.421	0.969	1.11(1.08-1.13)	2.04E-24	1.11(1.09-1.14)	6.58E-21	1.03(0.99-1.06)	1.83E-01	1.43E-04
rs17465283	128355824	A/G	0.47<0.01	0.406	0.999	0.9(0.88-0.92)	7.44E-27	0.9(0.88-0.92)	2.67E-21	0.96(0.93-1)	3.25E-02	5.97E-04
c8_pos128425122	128355940	A/G	0.76<0.01	0.524	0.999	0.92(0.9-0.93)	2.19E-19	0.91(0.89-0.93)	1.52E-16	0.97(0.94-1.01)	1.66E-01	6.30E-04
rs13256275	128356226	A/G	0.4<0.01	0.516	0.996	1.11(1.09-1.11)	8.37E-20	1.1(1.07-1.12)	7.76E-16	1.03(0.99-1.06)	5.67E-01	4.97E-03
rs17465317	128356670	T/C	0.52<0.01	0.555	0.998	1.11(1.09-1.13)	1.27E-26	1.11(1.09-1.14)	9.10E-21	1.04(1-1.07)	3.24E-02	1.20E-04
c8_pos128426042	128356860	C/T	0.54<0.01	0.563	0.979	1.11(1.09-1.13)	3.91E-26	1.12(1.09-1.14)	4.87E-22	1.04(1-1.08)	3.69E-02	3.89E-03
rs13267780	128357817	A/G	0.48<0.01	0.252	0.993	1.08(1.05-1.1)	8.07E-11	1.09(1.06-1.11)	7.55E-10	1.02(0.98-1.06)	5.60E-01	4.90E-03
rs10447995	128357924	A/G	0.52<0.01	0.555	0.996	1.11(1.09-1.13)	3.98E-26	1.11(1.09-1.14)	1.80E-21	1.04(1-1.08)	2.87E-02	6.80E-04
rs6999578	128358795	T/C	0.47<0.01	0.408	0.994	0.9(0.88-0.92)	5.85E-27	0.89(0.87-0.92)	1.22E-21	0.96(0.92-1)	7.09E-02	7.52E-04
c8_pos128430362	128361180	C/T	0.18<0.01	0.111	1.000	1.06(1.03-1.1)	5.10E-05	1.06(1.02-1.1)	1.06E-03	0.99(0.93-1.05)	6.77E-01	6.92E-02
rs56142043	128361212	C/A	0.18<0.01	0.110	0.994	1.06(1.03-1.1)	3.58E-05	1.06(1.02-1.1)	1.61E-03	0.99(0.93-1.05)	2.89E-01	6.17E-02
rs7014657	128361241	G/A	0.47<0.01	0.408	0.993	0.9(0.88-0.92)	3.44E-27	0.89(0.87-0.92)	1.39E-21	0.96(0.92-1)	3.02E-02	5.68E-04
rs56110209	128361928	G/T	0.47<0.01	0.408	0.995	0.9(0.88-0.92)	4.05E-27	0.89(0.87-0.92)	2.29E-21	0.96(0.93-1)	3.28E-02	1.02E-04
chr8:128362790:I	128362790	TTTC/T	0.35<0.01	0.716	0.980	0.95(0.92-0.95)	4.06E-10	0.93(0.91-0.95)	2.28E-08	0.98(0.94-1.02)	3.27E-01	1.02E-02
chr8:128362796:I	128362796	CTTT/C	0.35<0.01	0.716	0.980	0.93(0.92-0.95)	4.06E-09	0.93(0.91-0.95)	2.28E-08	0.98(0.94-1.02)	3.27E-01	1.02E-02

						0.95)	10		08		01	02
rs13272866	128363367	G/A	0.45<0.01	0.414	0.994	0.9(0.89-0.92)	2.75E-25	0.9(0.88-0.92)	6.72E-20	0.96(0.93-1)	5.79E-02	4.70E-04
rs10097200	128363652	C/T	0.44<0.01	0.416	1.000	0.9(0.88-0.92)	1.15E-25	0.9(0.88-0.92)	6.92E-20	0.96(0.93-1)	4.32E-02	5.37E-04
rs7002826	128364271	C/G	0.45<0.01	0.412	0.997	0.9(0.88-0.92)	6.11E-27	0.9(0.88-0.92)	3.97E-21	0.96(0.92-1)	2.84E-02	6.53E-04
rs7007568	128364906	C/G	0.45<0.01	0.412	1.000	0.9(0.88-0.92)	8.49E-27	0.9(0.88-0.92)	4.67E-21	0.96(0.93-1)	2.99E-02	6.57E-04
rs12156034	128364973	A/G	0.15<0.01	0.093	1.000	1.08(1.05-1.12)	3.98E-06	1.08(1.04-1.13)	2.99E-05	0.99(0.93-1.06)	7.89E-01	2.55E-02
rs139215928	128365212	C/T	0.03<0.01	0.022	0.892	1.17(1.09-1.25)	6.46E-06	1.15(1.07-1.25)	4.14E-04	1.15(1.02-1.31)	2.79E-02	9.38E-01
rs7842494	128366570	A/C	0.39<0.01	0.381	1.000	0.91(0.89-0.92)	3.78E-23	0.9(0.88-0.92)	8.24E-19	0.96(0.92-1)	2.79E-02	1.48E-03
rs5022926	128366829	C/A	0.45<0.01	0.412	1.000	0.9(0.88-0.92)	8.01E-27	0.9(0.88-0.92)	3.25E-21	0.96(0.92-1)	2.87E-02	6.38E-04
rs10112674	128367454	G/T	0.38<0.01	0.511	0.990	1.09(1.07-1.11)	5.08E-19	1.1(1.07-1.12)	2.33E-15	1.02(0.99-1.06)	2.34E-01	5.75E-04
rs113661590	128367510	A/G	0.07<0.01	0.099	0.852	0.92(0.89-0.95)	2.35E-06	0.92(0.88-0.96)	6.07E-05	0.95(0.89-1.01)	1.12E-01	1.56E-01
rs9693995	128368513	T/C	0.82<0.01	0.549	0.990	0.9(0.89-0.92)	2.93E-25	0.9(0.88-0.92)	1.29E-20	0.97(0.94-1.01)	1.49E-01	8.57E-05
rs117930653	128369231	A/C	0.04<0.01	0.023	0.893	1.17(1.1-1.25)	5.15E-06	1.16(1.07-1.26)	1.71E-04	1.16(1.02-1.31)	2.06E-02	9.40E-01
rs35440286	128369973	A/G	0.82<0.01	0.368	1.000	1.11(1.09-1.12)	1.43E-19	1.1(1.08-1.13)	3.48E-16	1.01(0.97-1.05)	5.23E-01	1.04E-04
rs35904426	128370183	T/G	0.97<0.01	0.407	1.000	1.13(1.09-1.13)	5.22E-24	1.11(1.09-1.14)	1.25E-20	1.03(0.99-1.07)	1.58E-01	1.60E-04
rs35112951	128370271	A/G	0.81<0.01	0.363	1.000	1.09(1.07-1.11)	5.22E-18	1.1(1.07-1.12)	4.10E-15	1.01(0.97-1.05)	6.44E-01	7.89E-05
rs10110330	128370755	A/G	0.97<0.01	0.408	0.996	1.11(1.09-1.13)	6.00E-25	1.12(1.09-1.14)	6.08E-21	1.03(0.99-1.07)	1.47E-01	1.33E-04
rs12550713	128370949	G/C	0.97<0.01	0.409	0.996	1.11(1.09-1.13)	1.63E-25	1.12(1.09-1.14)	1.83E-21	1.03(0.99-1.07)	1.42E-01	1.47E-04
c8_pos128441085	128371903	T/C	0.07<0.01	0.049	1.000	1.11(1.07-1.16)	9.86E-06	1.13(1.08-1.19)	1.32E-06	1.09(1-1.19)	3.78E-02	3.45E-01
rs10096351	128372172	G/A	0.52<0.01	0.557	0.995	0.91(0.89-1.13)	3.30E-27	1.12(1.09-1.14)	6.32E-21	1.04(1-1.08)	2.37E-02	7.68E-04
rs2121629	128373027	T/C	0.8<0.01	0.558	0.999	0.91(0.89-0.93)	2.46E-23	0.9(0.88-0.92)	1.35E-19	0.98(0.94-1.01)	3.11E-01	8.35E-05
rs12541305	128373756	C/T	0.45<0.01	0.411	0.996	0.9(0.88-0.92)	5.56E-26	0.9(0.88-0.92)	1.44E-20	0.96(0.93-1)	5.80E-02	1.67E-04
rs978683	128374117	G/A	0.68<0.01	0.604	1.000	0.92(0.9-0.94)	1.7	0.92(0.9-0.94)	1.3	0.99(0.95-1.03)	0.01	0.04

rs9297753	128375270	T/C	0.45<0.01	0.411	1.000	0.9(0.88-0.92) 0.91(0.89-0.92)	1.17E-26	0.9(0.88-0.92)	5.03E-21	0.96(0.93-1)	3.22E-02	5.96E-04
rs9283954	128375370	T/C	0.4<0.01	0.381	1.000	0.9(0.88-0.92) 0.91(0.89-0.92)	1.05E-22	0.9(0.88-0.92)	1.90E-18	0.96(0.92-1)	3.09E-02	1.58E-03
rs7831303	128376732	A/C	0.45<0.01	0.411	1.000	0.9(0.88-0.92) 0.91(0.89-0.92)	1.06E-26	0.9(0.88-0.92)	5.19E-21	0.96(0.93-1)	3.12E-02	6.42E-04
rs7815100	128376801	C/T	0.45<0.01	0.412	1.000	0.9(0.88-0.92) 0.94(0.92-0.96)	1.22E-26	0.9(0.88-0.92)	4.89E-21	0.96(0.93-1)	3.21E-02	5.93E-04
rs7835046	128376926	T/C	0.39<0.01	0.690	1.000	0.9(0.88-0.92) 0.91(0.89-0.96)	6.95E-10	0.93(0.91-0.96)	4.05E-08	0.99(0.95-1.03)	4.69E-01	6.44E-03
rs4143118	128377468	G/A	0.8<0.01	0.558	1.000	0.9(0.88-0.92) 0.91(0.89-0.93)	4.24E-23	0.9(0.88-0.92)	5.81E-19	0.98(0.94-1.02)	2.62E-01	5.94E-05
rs62516030	128377633	C/T	0.18<0.01	0.110	0.982	1.07(1.03-1.1) 0.91(0.89-0.92)	3.60E-05	1.06(1.03-1.1)	7.38E-04	0.99(0.93-1.05)	7.05E-01	6.83E-02
rs6988647	128377656	C/T	0.45<0.01	0.411	1.000	0.9(0.88-0.92) 0.91(0.89-0.92)	1.58E-26	0.9(0.88-0.92)	6.68E-21	0.96(0.93-1)	3.05E-02	6.61E-04
rs7006882	128377667	T/G	0.8<0.01	0.559	0.999	0.9(0.88-0.92) 0.91(0.89-0.92)	1.83E-23	0.9(0.88-0.92)	3.98E-19	0.98(0.94-1.02)	2.46E-01	8.18E-05
rs9692890	128377774	A/G	0.4<0.01	0.381	1.000	0.9(0.88-0.92) 0.91(0.89-0.92)	6.30E-23	0.9(0.88-0.92)	1.51E-18	0.96(0.92-1)	2.87E-02	1.62E-03
rs9693143	128378025	T/C	0.45<0.01	0.412	1.000	0.9(0.88-0.92) 0.91(0.89-0.93)	1.48E-26	0.9(0.88-0.92)	5.38E-21	0.96(0.93-1)	3.23E-02	6.38E-04
rs28524866	128378191	C/T	0.82<0.01	0.565	1.000	0.9(0.88-0.92) 0.95(0.93-0.93)	3.99E-22	0.91(0.89-0.93)	9.11E-18	0.98(0.94-1.02)	2.43E-01	1.44E-04
rs2060775	128378626	C/T	0.25<0.01	0.767	1.000	0.9(0.88-0.92) 0.95(0.93-0.97)	2.09E-05	0.95(0.93-0.98)	2.00E-04	1(0.96-1.04)	9.91E-01	1.91E-02
rs10956364	128378883	T/C	0.82<0.01	0.553	1.000	0.9(0.89-0.92) 0.91(0.89-0.92)	6.96E-25	0.9(0.88-0.92)	1.16E-20	0.97(0.94-1.01)	1.53E-01	8.86E-05
rs11776330	128378963	T/G	0.8<0.01	0.558	1.000	0.9(0.88-0.92) 0.91(0.89-0.92)	2.09E-23	0.9(0.88-0.92)	4.08E-19	0.98(0.94-1.01)	2.31E-01	8.02E-05
rs7845452	128379409	C/G	0.44<0.01	0.415	0.995	0.9(0.88-0.92) 0.91(0.89-0.93)	6.97E-25	0.9(0.88-0.92)	2.92E-19	0.96(0.93-1)	4.21E-02	6.83E-04
rs16902126	128382357	G/A	0.43<0.01	0.415	1.000	0.9(0.89-0.92) 0.93(0.93-0.97)	6.90E-25	0.9(0.88-0.92)	2.08E-19	0.97(0.93-1)	2.24E-02	7.05E-04
rs117952826	128383415	T/C	0.04<0.01	0.026	0.906	1.17(1.1-1.25) 0.93(0.91-0.95)	1.33E-07	1.17(1.09-1.26)	1.28E-05	1.15(1.02-1.29)	2.44E-02	5.12E-01
rs7815245	128383597	T/C	0.45<0.01	0.410	1.000	0.9(0.88-0.92) 0.95(0.93-0.95)	2.02E-27	0.89(0.87-0.92)	3.56E-21	0.96(0.92-0.99)	4.54E-02	2.67E-04
rs2121631	128386556	G/A	0.36<0.01	0.713	1.000	0.9(0.89-0.92) 0.95(0.93-0.97)	1.19E-10	0.93(0.91-0.95)	3.34E-09	0.98(0.95-1.03)	5.89E-01	2.15E-03
rs9643220	128386926	G/A	0.23<0.01	0.773	1.000	0.9(0.89-0.92) 0.95(0.93-0.97)	1.60E-05	0.95(0.92-0.97)	1.60E-05	1.01(0.97-1.06)	5.44E-01	1.32E-03
chr8:128387062:D	128387062	T/TTA	0.37<0.01	0.351	0.924	0.9(0.89-0.92) 0.9(0.88-0.92)	5.48E-21	0.9(0.88-0.92)	1.38E-17	0.96(0.92-1)	2.02E-02	1.32E-03
chr8:128387063:D	128387063	T/TATA	0.39<0.01	0.373	0.971	0.9(0.88-0.92) 0.9(0.88-0.92)	1.17E-05	0.9(0.88-0.92)	1.38E-13	0.96(0.92-0.99)	1.77E-01	1.98E-02

								24		19		02	03
chr8:128387067:D	128387067	A/ATAC	0.38<0.01	0.367	0.964	0.9(0.88-0.92)	3.14E-	24	0.9(0.87-0.92)	7.21E-	0.96(0.92-0.99)	1.99E-	1.36E-
rs1562430	128387852	C/T	0.45<0.01	0.412	1.000	0.9(0.88-0.92)	4.50E-	27	0.9(0.88-0.92)	3.10E-	0.96(0.93-1)	2.94E-	6.36E-
rs2392780	128388025	G/A	0.43<0.01	0.416	1.000	0.9(0.88-0.92)	1.42E-	25	0.9(0.88-0.92)	1.31E-	0.96(0.93-1)	4.53E-	6.18E-
rs7015780	128389507	T/C	0.44<0.01	0.407	0.953	0.9(0.88-0.92)	1.55E-	26	0.9(0.87-0.92)	1.60E-	0.96(0.92-1)	2.87E-	1.17E-
rs4871017	128389765	T/A	0.23<0.01	0.772	1.000	0.95(0.93-0.97)	1.53E-	05	0.95(0.92-0.97)	3.72E-	1.01(0.97-1.06)	6.00E-	2.26E-
c8_pos128460594	128391412	C/T	0.36<0.01	0.310	1.000	1.06(1.03-1.08)	2.13E-	07	1.07(1.05-1.1)	1.01E-	0.97(0.94-1.01)	1.83E-	1.19E-
rs2392781	128394289	G/A	0.24<0.01	0.304	0.838	1.06(1.04-1.09)	1.65E-	07	1.08(1.05-1.1)	8.76E-	1(0.96-1.04)	9.17E-	4.35E-
rs1949810	128394313	T/C	0.25<0.01	0.285	0.812	1.05(1.03-1.08)	2.87E-	05	1.06(1.04-1.09)	8.32E-	0.98(0.94-1.03)	4.20E-	1.14E-
rs2166690	128394475	G/T	0.2<0.01	0.336	0.989	0.92(0.9-0.93)	2.02E-	17	0.92(0.89-0.94)	5.18E-	0.95(0.91-0.98)	5.73E-	4.40E-
rs1949809	128394488	T/A	0.2<0.01	0.406	0.992	1.05(1.03-1.07)	1.45E-	06	1.06(1.04-1.08)	5.73E-	0.99(0.96-1.03)	7.90E-	4.68E-
c8_pos128464690	128395508	G/T	0.37<0.01	0.316	0.999	1.06(1.04-1.08)	1.22E-	08	1.08(1.05-1.11)	3.89E-	0.98(0.94-1.02)	2.73E-	7.13E-
c8_pos128465395	128396213	A/G	0.21<0.01	0.424	1.000	1.05(1.03-1.07)	5.02E-	07	1.06(1.03-1.08)	9.30E-	1(0.97-1.04)	9.21E-	8.91E-
rs6986543	128396316	A/C	0.18<0.01	0.343	1.000	0.92(0.9-0.94)	2.06E-	16	0.92(0.9-0.94)	4.53E-	0.95(0.92-0.99)	1.42E-	2.56E-
rs7820981	128400176	C/T	0.28<0.01	0.577	1.000	0.96(0.94-0.97)	3.54E-	06	0.95(0.92-0.97)	1.40E-	1(0.97-1.04)	8.19E-	5.52E-
rs2033101	128964222	T/C	<0.01<0.01	0.199	0.955	1.05(1.03-1.08)	5.24E-	05	1.06(1.03-1.09)	7.09E-	1.04(0.99-1.09)	1.23E-	2.83E-
rs4733596	129141856	T/C	<0.01/0.07	0.270	0.987	1.04(1.02-1.07)	8.52E-	05	1.05(1.02-1.08)	2.21E-	1.03(0.99-1.07)	1.72E-	2.55E-
chr8:129143192:D	129143192	A/AT	<0.01/0.34	0.208	0.974	1.06(1.03-1.08)	4.30E-	06	1.06(1.03-1.09)	6.37E-	1.04(1-1.09)	7.45E-	2.47E-
rs1499369	129143680	A/G	<0.01/0.68	0.126	0.985	1.07(1.04-1.1)	4.33E-	06	1.07(1.04-1.11)	6.81E-	1.05(1-1.11)	6.60E-	1.43E-
rs72722742	129144290	G/A	<0.01/0.68	0.127	0.985	1.07(1.04-1.1)	3.51E-	06	1.07(1.04-1.11)	5.16E-	1.05(1-1.11)	6.44E-	1.34E-
rs12542995	129145022	T/C	<0.01/0.68	0.126	0.987	1.07(1.04-1.1)	4.36E-	06	1.07(1.04-1.11)	7.19E-	1.05(1-1.11)	6.41E-	1.48E-
rs12676630	129145876	T/C	<0.01/0.68	0.127	0.998	1.07(1.04-1.1)	4.50E-	06	1.07(1.04-1.11)	7.21E-	1.05(1-1.11)	5.81E-	1.59E-
rs2648829	129147911	C/T	<0.01/0.35	0.202	1.000	1.07(1.04-1.09)	1.42E-	07	1.06(1.03-1.09)	1.31E-	1.05(1-1.11)	5.92E-	1.23E-

rs12680075	129148524	C/T	<0.01/0.67	0.125	0.991	1.07(1.04-1.1)	2.71E-06	1.07(1.04-1.11)	5.51E-05	1.06(1-1.12)	4.18E-02	2.10E-01	
rs10505509	129148754	A/G	<0.01/0.67	0.125	1.000	1.07(1.04-1.1)	1.95E-06	1.07(1.04-1.11)	3.78E-05	1.06(1-1.12)	4.33E-02	1.88E-01	
chr8:129149636:l	129149636	TTC/T	<0.01/0.46	0.165	0.950	1.06(1.04-1.09)	3.40E-06	1.06(1.03-1.1)	1.28E-04	1.04(0.99-1.09)	1.34E-01	1.22E-01	
chr8:129149637:l	129149637	TC/T	<0.01/0.49	0.160	0.960	1.07(1.04-1.09)	2.60E-06	1.07(1.03-1.1)	3.85E-05	1.03(0.98-1.09)	1.94E-01	5.24E-02	
rs2542418	129149638	C/T	<0.01/0.49	0.160	1.000	1.06(1.04-1.09)	2.13E-06	1.07(1.03-1.1)	3.70E-05	1.04(0.98-1.09)	1.74E-01	6.12E-02	
rs2648832	129150668	C/A	<0.01/0.26	0.244	0.998	1.06(1.03-1.08)	6.60E-07	1.06(1.03-1.09)	1.14E-05	1.03(0.99-1.08)	1.48E-01	1.17E-01	
rs2720681	129150989	A/C	<0.01/0.15	0.544	1.000	1.04(1.02-1.06)	9.05E-06	1.05(1.03-1.08)	1.09E-05	1.01(0.97-1.05)	6.61E-01	3.78E-03	
rs2720690	129157361	T/G	<0.01/0.15	0.553	1.000	1.04(1.02-1.06)	2.88E-05	1.05(1.03-1.07)	1.83E-05	1.01(0.97-1.04)	7.56E-01	3.02E-03	
rs2254778	129157468	C/T	<0.01/0.16	0.555	0.990	1.04(1.02-1.06)	3.12E-05	1.05(1.03-1.07)	1.73E-05	1.01(0.97-1.04)	7.56E-01	2.88E-03	
rs759650	129159249	C/T	<0.01/0.15	0.554	0.990	1.04(1.02-1.06)	3.53E-05	1.05(1.03-1.07)	1.78E-05	1.01(0.97-1.04)	7.48E-01	3.09E-03	
rs2058885	129160655	A/T	<0.01/0.15	0.553	1.000	1.04(1.02-1.06)	2.60E-05	1.05(1.03-1.07)	4.61E-05	1.01(0.97-1.04)	2.19E-01	3.51E-03	
rs7814495	129161453	C/G	<0.01/0.71	0.128	0.972	1.07(1.04-1.1)	7.58E-06	1.07(1.04-1.11)	1.10E-05	1.07(1.01-1.13)	4.31E-02	1.24E-01	
rs10956412	129162497	C/A	<0.01/0.75	0.153	1.000	1.07(1.04-1.1)	1.06(1.04-1.07)	1.68E-07	1.08(1.05-1.11)	9.42E-06	1.05(1-1.11)	8.94E-02	3.27E-01
rs12676304	129163295	C/A	<0.01/0.63	0.228	0.990	1.04(1.02-1.09)	3.41E-07	1.07(1.04-1.1)	1.34E-07	1.06(1.01-1.11)	8.75E-03	2.16E-01	
rs2648840	129163424	T/C	<0.01/0.16	0.554	0.984	1.06(1.04-1.06)	1.76E-05	1.05(1.03-1.08)	9.71E-05	1(0.97-1.04)	9.48E-01	3.25E-03	
rs759651	129164288	C/T	<0.01/0.63	0.229	1.000	1.07(1.04-1.09)	2.01E-07	1.07(1.04-1.1)	1.22E-07	1.06(1.01-1.11)	7.80E-03	2.40E-01	
rs1121948	129165056	G/A	<0.01/0.77	0.196	1.000	1.07(1.04-1.09)	2.71E-07	1.07(1.04-1.1)	5.95E-06	1.06(1.02-1.11)	1.99E-03	1.94E-01	
rs1121946	129165198	G/T	<0.01/0.81	0.142	0.981	1.07(1.05-1.1)	1.04(1.02-1.07)	4.44E-07	1.09(1.05-1.12)	1.53E-07	1.06(1.01-1.12)	9.48E-02	1.66E-01
rs759646	129165269	A/G	<0.01/0.16	0.551	1.000	1.06(1.04-1.06)	1.69E-05	1.05(1.03-1.07)	9.75E-05	1(0.97-1.04)	9.22E-01	3.18E-03	
rs12675643	129165692	A/T	<0.01/0.63	0.227	0.986	1.04(1.02-1.09)	4.46E-07	1.07(1.04-1.1)	1.66E-07	1.06(1.01-1.11)	9.06E-03	2.12E-01	
rs2392922	129166840	G/A	<0.01/0.16	0.553	0.983	1.04(1.02-1.06)	4.32E-05	1.05(1.03-1.07)	1.54E-05	1(0.97-1.04)	8.97E-01	2.16E-03	
rs2250909	129166880	C/T	<0.01/0.16	0.554	0.984	1.04(1.02-1.06)	1.05(1.03-1.07)	4.29E-05	1.05(1.03-1.07)	2.04E-05	1(0.97-1.04)	5.67E-01	8.15E-03
rs10956413	129167185	A/C	<0.01/0.56	0.248	0.985	1.05(1.03-1.05)							

							1.08)	06		06		02	02
rs759647	129168588	C/T	<0.01/0.56	0.248	0.988		1.05(1.03- 1.08)	4.43E- 06	1.06(1.04-1.09)	2.39E- 06	1.04(1-1.09)	5.42E- 02	8.61E- 02
rs7001706	129169758	C/G	<0.01/0.56	0.249	1.000		1.05(1.03- 1.08)	6.08E- 06	1.06(1.04-1.09)	3.26E- 06	1.04(1-1.09)	4.59E- 02	1.04E- 01
rs16893186	129170026	C/T	<0.01/0.56	0.250	0.985		1.05(1.03- 1.08)	3.43E- 06	1.07(1.04-1.09)	1.73E- 06	1.04(1-1.09)	5.37E- 02	8.16E- 02
rs2608029	129170126	G/C	<0.01/0.37	0.334	0.999		1.05(1.03- 1.07)	4.04E- 07	1.06(1.04-1.09)	4.36E- 07	1.03(0.99-1.07)	1.22E- 01	2.67E- 02
rs2648834	129171496	A/G	<0.01/0.16	0.555	0.986		1.04(1.02- 1.06)	4.38E- 05	1.05(1.03-1.08)	1.14E- 05	1(0.97-1.04)	9.51E- 01	1.49E- 03
rs2608027	129172462	G/T	<0.01/0.16	0.551	1.000		1.04(1.02- 1.06)	4.54E- 05	1.05(1.03-1.08)	1.44E- 05	1(0.97-1.04)	9.07E- 01	1.87E- 03
rs2608026	129172480	T/A	<0.01/0.16	0.551	1.000		1.04(1.02- 1.06)	3.97E- 05	1.05(1.03-1.08)	1.23E- 05	1(0.97-1.04)	9.23E- 01	1.66E- 03
rs10956414	129172633	A/G	<0.01/0.82	0.143	1.000		1.07(1.04-1.1) 1.05(1.03- 1.08)	3.12E- 07	1.08(1.05-1.12)	7.42E- 07	1.06(1.01-1.12)	2.27E- 02	1.99E- 01
rs1875028	129173675	C/G	<0.01/0.56	0.248	1.000		1.05(1.03- 1.08)	3.98E- 06	1.06(1.04-1.09)	2.47E- 06	1.04(1-1.09)	5.33E- 02	8.94E- 02
rs7002044	129177370	A/C	<0.01/0.56	0.248	1.000		1.04(1.02- 1.08)	3.96E- 06	1.06(1.04-1.09)	2.88E- 06	1.04(1-1.09)	4.81E- 02	1.04E- 01
rs2542401	129179357	G/C	<0.01/0.16	0.552	0.991		1.04(1.02- 1.06)	3.84E- 05	1.05(1.03-1.08)	1.36E- 05	1(0.97-1.04)	9.06E- 01	1.88E- 03
rs10956415	129179621	A/C	<0.01/0.56	0.249	0.990		1.05(1.03- 1.08)	3.34E- 06	1.06(1.04-1.09)	2.53E- 06	1.04(1-1.09)	4.69E- 02	9.81E- 02
rs2542402	129179799	G/A	<0.01/0.16	0.551	0.997		1.04(1.02- 1.06)	5.04E- 05	1.05(1.03-1.07)	1.77E- 05	1(0.97-1.04)	9.33E- 01	1.81E- 03
rs1499364	129179926	G/A	<0.01/0.59	0.240	1.000		1.06(1.03- 1.08)	8.74E- 07	1.07(1.04-1.1)	6.69E- 07	1.05(1.01-1.1)	2.50E- 02	1.27E- 01
rs12546580	129180513	A/G	<0.01/0.59	0.240	0.990		1.06(1.03- 1.08)	8.16E- 07	1.07(1.04-1.1)	6.34E- 07	1.05(1.01-1.1)	2.36E- 02	1.27E- 01
chr8:129180955:l	129180955	AC/A	<0.01/0.16	0.552	0.984		1.04(1.02- 1.06)	5.12E- 05	1.05(1.03-1.07)	1.83E- 05	1.05(1.01-1.1)	9.51E- 01	1.67E- 03
rs7006455	129181367	T/C	<0.01/0.6	0.242	0.983		1.06(1.04- 1.08)	5.73E- 07	1.07(1.04-1.1)	4.45E- 07	1(0.97-1.04)	2.71E- 02	1.06E- 01
rs11778142	129183417	C/T	<0.01/0.9	0.153	0.985		1.07(1.04-1.1)	1.99E- 07	1.08(1.05-1.12)	7.54E- 07	1.05(1.01-1.09)	1.91E- 02	1.88E- 01
rs12542202	129184555	A/G	<0.01/0.9	0.154	1.000		1.07(1.04-1.1) 1.06(1.04- 1.08)	2.24E- 07	1.08(1.05-1.12)	6.73E- 07	1.06(1.01-1.12)	2.38E- 02	1.63E- 01
rs1902789	129185104	G/A	<0.01/0.62	0.242	0.985		1.04(1.02- 1.08)	7.21E- 07	1.07(1.04-1.1)	2.24E- 07	1.05(1.01-1.09)	2.53E- 02	1.02E- 01
rs2936594	129185472	A/C	<0.01/0.16	0.554	0.988		1.04(1.02- 1.06)	8.91E- 05	1.05(1.03-1.07)	3.65E- 05	1(0.96-1.04)	9.60E- 01	1.95E- 03
rs2909235	129185918	G/T	<0.01/0.16	0.552	0.985		1.04(1.02- 1.06)	8.91E- 05	1.05(1.03-1.07)	3.65E- 05	1(0.96-1.04)	9.78E- 01	2.03E- 03

rs72722756	129186110	C/T	<0.01/0.99	0.165	0.981	1.07(1.05-1.1) 1.06(1.04- 1.08)	4.14E- 3.73E- 7.21E-	08 07 05	1.08(1.05-1.12) 1.07(1.04-1.1)	2.44E- 2.27E- 2.84E-	07 07 05	1.07(1.02-1.12) 1.05(1.01-1.09)	6.44E- 2.54E- 9.40E-	03 02 01	2.51E- 1.02E- 2.07E-
rs7825555	129186266	T/A	<0.01/0.62	0.242	0.986	1.04(1.02- 1.06)	1.04E- 6.31E-	07 05	1.07(1.04-1.1) 1.05(1.03-1.07)	2.44E- 2.44E-	07 05	1.05(1.01-1.09) 1(0.97-1.04)	2.54E- 9.40E- 9.29E-	02 01 03	1.02E- 2.07E- 1.97E-
rs2909236	129186365	G/T	<0.01/0.16	0.551	0.988	1.04(1.02- 1.06)	1.04E- 1.46E-	05 06	1.05(1.03-1.07) 1.05(1.03-1.07)	2.44E- 5.19E-	05 07	1(0.97-1.04) 1(0.97-1.04)	9.40E- 3.68E-	01 03	2.07E- 9.27E- 9.27E-
rs2925874	129188725	C/A	<0.01/0.16	0.551	1.000	1.06(1.03- 1.06)	1.06E- 1.46E-	05 06	1.05(1.03-1.07) 1.07(1.04-1.1)	2.44E- 1.26E-	05 07	1(0.97-1.04) 1.05(1-1.09)	9.29E- 2.98E-	01 02	1.97E- 8.05E- 8.05E-
rs28597394	129190148	G/A	<0.01/0.61	0.245	0.994	1.06(1.04- 1.08)	1.06E- 3.06E-	07 06	1.07(1.04-1.1) 1.07(1.05-1.1)	2.93E- 1.26E-	07 07	1.05(1-1.09) 1.05(1-1.09)	2.98E- 9.99E-	02 02	8.05E- 1.67E- 1.67E-
rs10956416	129190290	C/T	<0.01/0.62	0.245	0.982	1.04(1.02- 1.08)	1.04E- 7.87E-	05 07	1.07(1.05-1.1) 1.07(1.05-1.1)	2.93E- 1.26E-	05 07	1.05(1-1.09) 1.05(1-1.09)	9.99E- 2.98E-	01 02	1.67E- 8.42E- 8.42E-
rs2925872	129191121	G/C	<0.01/0.16	0.554	0.987	1.04(1.02- 1.06)	1.04E- 7.78E-	05 05	1.05(1.03-1.07) 1.05(1.03-1.07)	3.12E- 1.72E-	05 05	1(0.96-1.04) 1(0.96-1.04)	9.81E- 3.23E-	01 03	1.83E- 8.23E- 8.23E-
rs1030106	129191861	G/T	<0.01/0.16	0.551	0.999	1.06(1.04- 1.06)	1.06E- 3.73E-	05 05	1.05(1.03-1.07) 1.05(1.03-1.07)	3.12E- 1.72E-	05 05	1(0.96-1.04) 1(0.96-1.04)	9.81E- 3.23E-	01 03	1.83E- 8.42E- 8.42E-
rs6999335	129192584	G/A	<0.01/0.62	0.243	0.999	1.06(1.04- 1.08)	1.06E- 3.67E-	07 07	1.07(1.04-1.1) 1.07(1.04-1.1)	1.59E- 1.59E-	07 07	1.05(1-1.09) 1.05(1-1.09)	3.23E- 3.23E-	02 02	8.42E- 8.23E- 8.23E-
rs6999897	129192710	A/G	<0.01/0.62	0.243	0.990	1.06(1.04- 1.08)	1.06E- 2.76E-	07 07	1.07(1.04-1.1) 1.07(1.04-1.1)	1.12E- 1.12E-	07 07	1.05(1-1.09) 1.05(1-1.09)	3.13E- 3.13E-	02 02	7.68E- 8.23E- 8.23E-
rs10808567	129192961	T/G	<0.01/0.62	0.245	0.986	1.06(1.04- 1.08)	1.06E- 3.83E-	07 07	1.07(1.05-1.1) 1.07(1.05-1.1)	1.55E- 1.55E-	07 07	1.05(1-1.09) 1.05(1-1.09)	9.80E- 9.80E-	02 02	1.88E- 8.30E- 8.30E-
c8_pos129263191	129194009	T/C	<0.01/1	0.167	1.000	1.07(1.05-1.1) 1.06(1.04- 1.08)	1.07(1.05-1.1) 1.06(1.04- 1.08)	08 07	1.08(1.05-1.12) 1.08(1.05-1.12)	1.63E- 1.63E-	07 07	1.07(1.02-1.12) 1.07(1.02-1.12)	3.32E- 3.32E-	03 03	1.01E- 8.30E- 8.30E-
rs11783807	129194536	C/T	<0.01/0.62	0.244	0.984	1.07(1.05-1.1) 1.06(1.04- 1.08)	1.07(1.05-1.1) 1.06(1.04- 1.08)	08 07	1.07(1.04-1.1) 1.07(1.04-1.1)	1.69E- 1.69E-	07 07	1.05(1-1.09) 1.05(1-1.09)	9.81E- 9.81E-	02 02	1.90E- 8.16E- 8.16E-
rs11780156	129194641	T/C	<0.01/-	0.167	1.000	1.07(1.05-1.1) 1.06(1.04- 1.08)	1.07(1.05-1.1) 1.06(1.04- 1.08)	08 07	1.08(1.05-1.12) 1.08(1.05-1.12)	1.30E- 1.30E-	07 07	1.07(1.02-1.12) 1.07(1.02-1.12)	3.01E- 3.01E-	03 03	1.01E- 8.16E- 8.16E-
rs1902778	129194850	G/C	<0.01/0.62	0.245	0.985	1.06(1.04- 1.08)	1.06(1.04- 0.96(0.94- 1.08)	07 07	1.07(1.04-1.1) 1.07(1.04-1.1)	1.24E- 1.24E-	07 07	1.05(1-1.09) 1.05(1-1.09)	9.77E- 9.77E-	02 02	1.26E- 8.16E- 8.16E-
rs2160765	129195261	A/T	<0.01/0.16	0.443	0.976	1.06(1.04- 0.98)	1.06(1.04- 0.98)	05 05	0.95(0.93-0.97) 0.95(0.93-0.97)	1.48E- 1.48E-	05 05	1(0.96-1.04) 1(0.96-1.04)	9.92E- 9.92E-	01 03	1.27E- 8.16E- 8.16E-
rs10087518	129195543	A/G	<0.01/0.16	0.443	0.975	1.06(1.04- 0.98)	1.06(1.04- 0.98)	05 05	0.95(0.93-0.97) 0.95(0.93-0.97)	1.46E- 1.46E-	05 05	1(0.96-1.04) 1(0.96-1.04)	9.89E- 9.89E-	01 03	1.32E- 8.16E- 8.16E-
rs10087529	129195573	A/G	<0.01/0.16	0.443	0.976	1.06(1.04- 0.98)	1.06(1.04- 0.98)	05 05	0.95(0.93-0.97) 0.95(0.93-0.97)	1.61E- 1.61E-	05 05	1(0.96-1.04) 1(0.96-1.04)	3.34E- 3.34E-	01 03	8.29E- 8.29E- 8.29E-
rs56152647	129195921	A/G	<0.01/0.62	0.244	0.984	1.06(1.04- 1.08)	1.06(1.04- 1.08)	07 07	1.07(1.04-1.1) 1.07(1.04-1.1)	1.27E- 1.27E-	07 07	1.05(1-1.09) 1.05(1-1.09)	3.01E- 3.01E-	02 02	8.18E- 8.18E- 8.18E-
rs6470608	129196570	G/C	<0.01/0.62	0.245	0.986	1.06(1.04- 1.08)	1.06(1.04- 1.08)	07 07	1.07(1.04-1.1) 1.07(1.04-1.1)	1.74E- 1.74E-	07 07	1.05(1-1.09) 1.05(1-1.09)	3.17E- 3.17E-	02 02	8.47E- 8.47E- 8.47E-
rs6992491	129197903	G/C	<0.01/0.62	0.243	0.986	1.06(1.04- 1.08)	1.06(1.04- 1.08)	07 07	1.07(1.04-1.1) 1.07(1.04-1.1)	1.75E- 1.75E-	07 07	1.05(1-1.09) 1.05(1-1.09)	3.05E- 3.05E-	02 02	8.79E- 8.79E- 8.79E-
rs55929956	129199261	A/G	<0.01/0.62	0.243	0.987	1.06(1.04- 1.08)	1.06(1.04- 1.08)	07 07	1.07(1.04-1.1) 1.07(1.04-1.1)	2.32E- 2.32E-	07 07	1.05(1-1.09) 1.05(1-1.09)	8.83E- 8.83E-	02 02	1.93E- 8.79E- 8.79E-
rs56354710	129199352	A/T	<0.01/0.55	0.222	0.878	1.07(1.04- 1.08)	1.07(1.04- 1.08)	2.98E-	1.08(1.05-1.11)	2.32E-	1.06(1.02-1.11)	8.83E-	1.93E-		

							1.09)	07		07		03	01
rs1016578	129199566	A/G	<0.01/1	0.165	0.986		1.07(1.05-1.1)	4.37E-08	1.08(1.05-1.12)	1.87E-07	1.07(1.02-1.12)	9.65E-03	1.97E-01
chr8:129199913:D	129199913	T/TGC	<0.01/0.65	0.218	0.908		1.07(1.04-1.09)	2.34E-07	1.08(1.05-1.11)	2.25E-07	1.06(1.01-1.11)	1.77E-02	1.47E-01
rs3802173	129199914	T/G	<0.01/0.62	0.244	0.987		1.06(1.04-1.08)	2.98E-07	1.07(1.04-1.1)	1.32E-07	1.05(1-1.09)	3.02E-02	8.29E-02
rs3802172	129199915	T/C	<0.01/0.62	0.245	0.987		1.06(1.04-1.08)	2.99E-07	1.07(1.04-1.1)	1.36E-07	1.05(1-1.09)	2.91E-02	8.60E-02
rs3802171	129200759	G/A	<0.01/0.62	0.243	0.988		1.06(1.04-1.08)	3.83E-07	1.07(1.04-1.1)	2.00E-07	1.05(1-1.09)	3.03E-02	9.10E-02
rs10094063	129202426	T/C	<0.01/0.16	0.443	0.974		0.96(0.94-0.98)	5.67E-05	0.95(0.93-0.97)	1.81E-05	1(0.96-1.04)	9.94E-01	1.39E-03
chr8:129202905:I	129202905	TG/T	<0.01/0.63	0.239	0.967		1.06(1.04-1.08)	3.59E-07	1.07(1.04-1.1)	3.53E-07	1.05(1.01-1.1)	2.24E-02	1.20E-01
rs59183453	129202906	G/T	<0.01/0.62	0.239	0.967		1.06(1.04-1.08)	3.35E-07	1.07(1.04-1.1)	3.46E-07	1.05(1.01-1.1)	2.16E-02	1.22E-01
chr8:129202907:D	129202907	T/TTG	<0.01/0.43	0.170	0.796		1.06(1.03-1.09)	1.69E-05	1.08(1.05-1.12)	1.57E-06	1.06(1-1.11)	4.69E-02	2.20E-01
chr8:129202908:D	129202908	T/TG	<0.01/0.62	0.238	0.964		1.06(1.04-1.08)	3.90E-07	1.07(1.04-1.1)	3.79E-07	1.05(1.01-1.1)	2.30E-02	1.20E-01
rs72722764	129202909	T/G	<0.01/0.61	0.242	0.980		1.06(1.04-1.08)	4.64E-07	1.07(1.04-1.1)	3.55E-07	1.05(1.01-1.09)	3.11E-02	9.89E-02
rs10492292	129203191	A/C	<0.01/0.61	0.244	1.000		1.06(1.04-1.08)	3.67E-07	1.07(1.04-1.1)	2.14E-07	1.05(1-1.09)	2.76E-02	9.97E-02
rs992241	129203312	C/A	<0.01/0.61	0.244	0.990		1.06(1.04-1.08)	4.48E-07	1.07(1.04-1.1)	2.92E-07	1.05(1.01-1.09)	2.99E-02	1.01E-01
rs16902714	129203826	T/C	<0.01/0.61	0.244	1.000		1.06(1.04-1.08)	4.18E-07	1.07(1.04-1.1)	2.23E-07	1.05(1-1.09)	3.04E-02	9.41E-02
rs16902715	129203857	T/C	<0.01/0.61	0.244	0.991		1.06(1.04-1.08)	4.12E-07	1.07(1.04-1.1)	2.21E-07	1.05(1.01-1.09)	3.01E-02	9.33E-01
rs16902716	129203946	C/T	<0.01/0.61	0.245	0.991		1.06(1.03-1.08)	3.78E-07	1.07(1.04-1.1)	2.05E-07	1.05(1-1.09)	4.16E-02	5.06E-02
rs7017073	129204262	C/T	<0.01/0.74	0.211	1.000		1.06(1.04-1.08)	1.32E-06	1.07(1.04-1.1)	1.61E-07	1.05(1-1.09)	2.51E-02	1.11E-02
chr8:129204572:D	129204572	T/TA	<0.01/0.48	0.293	0.972		1.06(1.04-1.08)	1.52E-07	1.07(1.04-1.1)	1.61E-07	1.04(1-1.09)	3.27E-02	9.21E-02
rs72722767	129205103	A/G	<0.01/0.47	0.294	0.977		1.06(1.04-1.08)	1.81E-07	1.07(1.04-1.09)	1.84E-07	1.04(1-1.08)	4.38E-02	7.63E-02
rs10106296	129205610	A/G	<0.01/0.54	0.263	1.000		1.05(1.03-1.08)	2.86E-06	1.06(1.04-1.09)	1.49E-06	1.04(0.99-1.08)	1.06E-02	4.53E-02
rs7825915	129207365	A/T	<0.01/0.54	0.263	0.984		1.05(1.03-1.08)	2.14E-06	1.07(1.04-1.09)	9.32E-07	1.03(0.99-1.08)	4.71E-01	1.33E-02
rs4645528	129207959	C/T	<0.01/0.25	0.551	0.803		0.95(0.93-0.97)	1.01E-05	0.94(0.92-0.97)	2.57E-06	0.99(0.95-1.03)	0.01	0.02

chr8:129209155:D	129209155	A/ATATT	<0.01/0.53	0.269	0.945	1.05(1.03-1.08)	2.81E-06	1.07(1.04-1.09)	1.66E-06	1.03(0.99-1.08)	1.11E-01	4.54E-02
c8_pos129279361	129210179	T/C	<0.01/0.84	0.186	0.999	1.06(1.04-1.09)	4.83E-07	1.07(1.04-1.11)	1.07E-06	1.05(1-1.1)	5.28E-02	1.03E-01
rs7836152	129211415	A/G	<0.01/0.84	0.184	0.982	1.07(1.04-1.09)	4.61E-07	1.07(1.04-1.11)	1.13E-06	1.05(1-1.1)	5.50E-02	9.97E-02
rs12550618	129212443	T/C	<0.01/0.54	0.260	0.982	1.05(1.03-1.08)	2.59E-06	1.07(1.04-1.09)	1.34E-06	1.04(0.99-1.08)	1.03E-01	5.13E-02
rs11776408	129215220	C/G	<0.01/0.54	0.260	0.982	1.05(1.03-1.08)	2.51E-06	1.07(1.04-1.09)	1.27E-06	1.04(0.99-1.08)	1.02E-01	5.11E-02
rs11776569	129215700	T/G	<0.01/0.84	0.186	0.999	1.07(1.04-1.09)	4.23E-07	1.07(1.04-1.11)	9.62E-07	1.05(1-1.1)	5.11E-02	1.04E-01
rs1902787	129217854	C/T	<0.01/0.54	0.262	0.990	1.05(1.03-1.08)	2.25E-06	1.07(1.04-1.09)	9.67E-07	1.04(0.99-1.08)	1.01E-01	4.92E-02
rs11989994	129217909	T/C	<0.01/0.54	0.261	0.987	1.05(1.03-1.08)	2.37E-06	1.07(1.04-1.09)	1.09E-06	1.04(0.99-1.08)	1.01E-01	5.13E-02
rs11997192	129218127	G/A	<0.01/0.84	0.187	1.000	1.06(1.04-1.09)	4.39E-07	1.07(1.04-1.11)	8.95E-07	1.05(1-1.1)	5.19E-02	1.02E-01
rs72722788	129219611	A/C	<0.01/0.84	0.185	0.986	1.07(1.04-1.09)	4.95E-07	1.07(1.04-1.11)	1.08E-06	1.05(1-1.1)	5.28E-02	1.04E-01
rs9283955	129219805	C/G	<0.01/0.54	0.263	0.998	1.05(1.03-1.08)	2.44E-06	1.07(1.04-1.09)	1.07E-06	1.04(0.99-1.08)	9.92E-02	5.21E-02
rs1967315	129224182	A/G	<0.01/0.53	0.267	0.962	0.96(0.94-1.08)	1.21E-06	1.07(1.04-1.09)	1.26E-06	1.04(0.99-1.08)	8.77E-02	5.49E-02
rs2909242	129224680	A/C	<0.01/0.34	0.644	0.995	0.98(0.98-1.08)	9.05	0.95(0.93-0.97)	7.11E-05	0.98(0.95-1.02)	3.69E-01	3.02E-02
c8_pos129294070	129224888	C/G	<0.01/0.77	0.190	1.000	1.07(1.04-1.09)	1.94E-07	1.07(1.04-1.11)	7.11E-07	1.05(1-1.1)	3.04E-02	9.68E-02
rs16902734	129225868	T/C	<0.01/0.32	0.215	0.992	1.05(1.02-1.07)	7.04E-05	1.06(1.03-1.09)	2.89E-05	1.03(0.99-1.08)	1.78E-01	7.21E-02
rs17383047	129227763	A/G	<0.01/0.33	0.211	0.985	1.05(1.02-1.07)	6.26E-05	1.06(1.03-1.09)	1.98E-05	1.03(0.98-1.08)	2.04E-01	6.12E-02
rs56161112	129227921	G/C	<0.01/0.33	0.211	0.984	1.05(1.02-1.07)	6.28E-05	1.06(1.03-1.09)	1.89E-05	1.03(0.98-1.08)	2.54E-01	4.88E-02
c8_pos129303491	129234309	C/G	<0.01/0.32	0.214	1.000	1.05(1.02-1.07)	5.67E-05	1.06(1.03-1.09)	1.41E-05	1.03(0.98-1.07)	2.31E-01	5.98E-02
rs12541578	129238347	G/C	<0.01/0.32	0.212	0.981	1.05(1.02-1.07)	6.34E-05	1.06(1.03-1.09)	2.02E-05	1.03(0.98-1.07)	2.40E-01	5.86E-02
rs12541389	129243389	T/C	<0.01/0.32	0.212	0.986	1.05(1.02-1.07)	6.08E-05	1.06(1.03-1.09)	1.86E-05	1.03(0.98-1.07)	2.41E-01	5.79E-02
rs72724706	129244551	G/C	<0.01/0.32	0.212	0.988	1.05(1.02-1.07)	5.73E-05	1.06(1.03-1.09)	1.78E-05	1.03(0.98-1.07)	2.36E-01	5.82E-02
rs12542862	129245387	T/G	<0.01/0.32	0.211	0.985	1.05(1.02-1.07)	6.03E-05	1.06(1.03-1.09)	1.60E-05	1.03(0.98-1.07)	2.57E-01	5.06E-02
rs10492294	129246415	C/T	<0.01/0.32	0.214	0.999	1.05(1.02-1.07)	6.03E-05	1.06(1.03-1.09)	1.60E-05	1.03(0.98-1.07)	2.57E-01	5.06E-02

rs4733851	129264420	G/A	<0.01/0.19	0.577	0.981	1.07) 0.96(0.94- 0.98)	05 7.60E- 05	05 0.96(0.93-0.98)	05 1.02E- 04	01 0.99(0.96-1.03)	01 6.43E- 01	02 3.01E- 02
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^a SNP identification number from the 1000 Genomes Project.

^b Base position on chromosome 8 is based on the NCBI human genome build 37 from the 1000 Genomes Project.

^c Risk/reference alleles are based on forward positive strand of the NCBI human genome build 37 from the 1000 Genomes Project.

^d r^2 for linkage disequilibrium with the index SNPs rs13281615 and rs11780156 computed with data of European ancestry women controls.

^e Effect allele frequency (EAF) is calculated with combined women controls of European ancestry.

^f Per allele odds ratio (OR), 95% confidence interval (CI) and significance were estimated from logistic regression, adjusted for age, study site and principal components.

^g Adjusted for age, study site and principal components.

^h Breast cancer risk estimated for ER-positive disease, adjusted for age, study site and principal components..

ⁱ Breast cancer risk estimated for ER-negative disease, adjusted for age, study site and principal components.

^j Heterogeneity test between ER-positive and ER-negative disease.

Supplementary Table 3. Association of top SNPs with breast cancer risk (combined *P* value <0.01) in women of non-European ancestry.

Ancestry	SNP ^a	Base position ^b	Alleles ^c	EAF ^d	Imputation (r ₂)	OR(95%CI) ^e	<i>P</i> _overall ^e
Asian							
	rs76382129	127934959	C/T	0.2	0.89	1.12(1.05-1.19)	8.3E-04
	rs60712131	128056174	A/T	0.15	0.99	0.89(0.82-0.95)	1.3E-03
	rs974451	127708294	G/A	0.23	1.00	0.91(0.85-0.96)	1.4E-03
	rs13272700	127734691	C/T	0.22	1.00	0.91(0.85-0.96)	1.5E-03
	rs6982887	127730075	A/C	0.22	1.00	0.91(0.85-0.96)	1.5E-03
	rs7000457	127726729	G/A	0.22	1.00	0.91(0.85-0.96)	1.6E-03
	rs16901917	128055813	C/T	0.14	1.00	0.89(0.82-0.96)	1.7E-03
	rs55708623	127751476	A/G	0.33	0.98	0.92(0.87-0.97)	1.7E-03
	rs2101518	127716187	T/C	0.22	0.99	0.91(0.85-0.96)	1.9E-03
	rs117117537	128032297	G/T	0.12	0.90	0.88(0.81-0.95)	2.0E-03
	rs6470466	127739184	A/G	0.22	1.00	0.91(0.85-0.97)	2.3E-03
	rs56005245	128113426	T/C	0.25	0.98	1.09(1.03-1.16)	2.5E-03
	chr8:127928795:D	127928795	A/AG	0.24	0.98	1.09(1.03-1.16)	2.6E-03
	rs149356055	128489905	G/A	0.02	0.70	1.33(1.10-1.60)	2.8E-03
	c8_pos128691265	128622083	C/T	0.09	1.00	0.87(0.79-0.95)	2.9E-03
	chr8:128272219:I	128272219	AG/A	0.03	0.53	1.32(1.10-1.59)	2.9E-03
	rs6470471	127783480	G/A	0.62	0.97	0.92(0.88-0.97)	2.9E-03
	rs12549369	128059230	A/T	0.15	0.98	0.89(0.83-0.96)	3.0E-03
	rs7815605	128590946	G/A	0.12	1.00	0.89(0.82-0.96)	3.1E-03
	rs76324084	129148523	C/T	0.06	0.93	1.17(1.05-1.30)	3.1E-03
	rs75846588	127929528	G/C	0.24	1.00	1.09(1.03-1.16)	3.2E-03
	rs76891459	127929542	T/G	0.24	1.00	1.09(1.03-1.16)	3.2E-03
	rs13259479	127675332	T/G	0.27	0.99	1.09(1.03-1.15)	3.4E-03
	rs12548654	127932874	G/T	0.24	0.99	1.09(1.03-1.16)	3.6E-03
	rs4733807	128592256	G/A	0.12	0.98	0.89(0.82-0.96)	3.6E-03
	rs2129544	127936351	A/G	0.24	0.99	1.09(1.03-1.15)	4.1E-03
	rs12550197	127935661	C/T	0.24	0.99	1.09(1.03-1.15)	4.1E-03
	rs35686742	128613878	T/C	0.09	0.95	0.87(0.79-0.96)	4.4E-03
	rs55971392	128598784	A/G	0.1	0.97	0.88(0.80-0.96)	4.5E-03
	rs983592	127808949	A/G	0.35	0.91	0.92(0.87-0.98)	4.6E-03
	c8_pos128711250	128642068	C/T	0.11	1.00	0.88(0.81-0.96)	4.7E-03
	rs77269231	127934542	C/T	0.24	0.98	1.09(1.03-1.15)	4.9E-03
	rs2171769	127798919	G/A	0.35	0.91	0.92(0.87-0.98)	5.0E-03
	rs12542598	127935518	T/A	0.24	0.99	1.09(1.03-1.15)	5.1E-03
	rs117981446	127916735	C/T	0.06	0.50	1.20(1.06-1.36)	5.3E-03
	rs143740159	128037636	T/C	0.13	0.97	0.89(0.83-0.97)	5.4E-03
	rs79831056	129148701	T/C	0.06	0.98	1.15(1.04-1.27)	5.4E-03
	rs116088171	129148896	A/T	0.06	0.98	1.15(1.04-1.27)	5.4E-03
	rs116343249	129149049	G/A	0.06	0.98	1.15(1.04-1.27)	5.4E-03
	rs11996839	128631622	C/T	0.11	0.98	0.89(0.82-0.97)	5.5E-03

rs75742348	129148352	T/C	0.06	0.98	1.15(1.04-1.27)	5.7E-03
rs79983962	129145314	C/G	0.06	0.97	1.15(1.04-1.27)	5.7E-03
rs79352355	129145353	T/C	0.06	0.97	1.15(1.04-1.27)	5.7E-03
rs16901905	128036579	T/C	0.14	0.98	0.90(0.83-0.97)	5.8E-03
rs11985853	128631524	T/A	0.11	1.00	0.89(0.82-0.97)	5.8E-03
rs11993113	128631530	T/G	0.11	1.00	0.89(0.82-0.97)	5.9E-03
rs75304215	128635589	C/T	0.1	0.87	0.88(0.80-0.96)	5.9E-03
rs10101587	128635755	C/T	0.1	0.87	0.88(0.80-0.96)	6.0E-03
rs10086191	128635476	G/A	0.1	0.87	0.88(0.80-0.96)	6.0E-03
rs10085933	128635230	G/A	0.1	0.87	0.88(0.80-0.96)	6.0E-03
rs12546164	127903238	T/C	0.21	0.88	1.10(1.03-1.17)	6.1E-03
rs7815310	128062896	C/T	0.15	1.00	0.90(0.84-0.97)	6.5E-03
rs16901629	127672507	A/G	0.13	0.69	1.12(1.03-1.22)	6.6E-03
rs16901857	127925789	A/G	0.24	0.99	1.08(1.02-1.15)	6.6E-03
chr8:127754893:D	127754893	G/GTT	0.56	0.90	0.93(0.88-0.98)	6.7E-03
rs76875214	128037747	G/A	0.14	0.98	0.90(0.83-0.97)	6.9E-03
rs74418064	128636558	A/G	0.1	0.87	0.88(0.80-0.97)	7.0E-03
rs76777631	128637525	A/G	0.1	0.87	0.88(0.80-0.97)	7.0E-03
chr8:127754898:D	127754898	T/TTG	0.56	0.89	0.93(0.88-0.98)	7.0E-03
rs28392817	128272220	G/T	0.17	1.00	1.10(1.03-1.18)	7.1E-03
rs77446604	128635036	A/G	0.1	0.88	0.88(0.80-0.97)	7.3E-03
rs78338326	128633750	A/T	0.1	0.88	0.88(0.80-0.97)	7.6E-03
rs11992514	128632636	C/T	0.1	0.95	0.89(0.81-0.97)	7.6E-03
rs60208962	128632585	A/C	0.1	0.95	0.89(0.81-0.97)	7.7E-03
rs11774427	128593690	G/C	0.1	0.98	0.89(0.81-0.97)	7.7E-03
rs79170863	128633858	G/A	0.1	0.88	0.88(0.80-0.97)	7.9E-03
rs1873186	127837111	T/G	0.93	1.00	1.16(1.04-1.29)	8.0E-03
rs979200	127923720	T/C	0.45	1.00	1.07(1.02-1.13)	8.2E-03
rs79941908	128640038	C/T	0.09	0.82	0.88(0.79-0.97)	8.3E-03
chr8:128153727:I	128153727	CT/C	0.05	0.93	1.17(1.04-1.32)	8.4E-03
rs35813501	128235083	A/C	0.13	1.00	0.90(0.84-0.97)	8.7E-03
c8_pos129122927	129053745	A/G	0.19	0.99	0.92(0.86-0.98)	8.8E-03
rs76020024	128051923	G/A	0.13	0.97	0.90(0.83-0.97)	8.8E-03
rs7003877	127760670	C/T	0.28	1.00	0.93(0.88-0.98)	8.8E-03
rs75127456	128008134	C/A	0.1	0.98	0.89(0.81-0.97)	8.9E-03
rs111814509	128019180	C/A	0.11	0.98	0.90(0.82-0.97)	9.2E-03
chr8:128011837:D	128011837	T/TAA	0.11	0.99	0.90(0.82-0.97)	9.5E-03
rs4282527	128630497	T/G	0.11	0.99	0.89(0.82-0.97)	9.6E-03
rs7014860	127905188	A/C	0.22	0.36	1.14(1.03-1.25)	9.8E-03
rs4314620	128630589	A/C	0.11	0.99	0.89(0.82-0.97)	9.8E-03
rs10956329	127841932	C/T	0.93	1.00	1.15(1.03-1.28)	1.0E-02
rs13257258	127842198	C/T	0.93	1.00	1.15(1.03-1.28)	1.0E-02

African American

rs73361922	129266860	A/G	0.03	0.93	1.94(1.38-2.74)	1.6E-04
rs10092526	129274507	C/G	0.38	0.99	0.78(0.68-0.89)	1.9E-04
rs7846242	129268140	T/C	0.39	1	0.78(0.68-0.89)	2.1E-04
rs73361926	129267034	T/G	0.03	0.94	1.84(1.32-2.57)	3.2E-04
rs73361943	129271296	G/A	0.05	0.97	1.59(1.21-2.10)	9.6E-04
rs73361919	129266001	A/G	0.04	0.98	1.61(1.21-2.13)	1.0E-03
rs73361928	129268062	G/A	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs73361920	129266479	C/T	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs78400768	129268242	G/A	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs73361936	129269253	A/C	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs112193671	129269199	C/T	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs73361937	129270710	G/A	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs73361940	129270736	T/A	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs73361942	129270812	G/A	0.04	0.98	1.60(1.21-2.12)	1.1E-03
chr8:129270768:D	129270768	C/CT	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs73361944	129272494	T/C	0.04	0.98	1.60(1.21-2.12)	1.1E-03
rs2142199	129266826	C/T	0.31	0.99	0.79(0.69-0.91)	1.1E-03
rs4733601	129269466	G/A	0.26	1	0.79(0.68-0.91)	1.5E-03
rs9642881	129324232	C/T	0.19	0.97	1.29(1.10-1.51)	1.6E-03
rs73710038	128866506	A/G	0.21	0.74	0.75(0.63-0.90)	1.6E-03
rs73361910	129260466	A/T	0.02	0.97	1.85(1.26-2.72)	1.8E-03
rs112416472	129226925	A/C	0.02	0.99	1.84(1.25-2.71)	2.1E-03
rs9643233	129322437	T/C	0.39	1	1.22(1.07-1.38)	2.2E-03
rs1120501	129274183	T/A	0.31	0.99	0.80(0.70-0.92)	2.2E-03
rs73356180	129228944	A/G	0.02	0.99	1.84(1.24-2.71)	2.2E-03
rs73356190	129230788	A/G	0.02	0.99	1.83(1.24-2.70)	2.3E-03
rs73356192	129230991	T/C	0.02	0.99	1.83(1.24-2.70)	2.3E-03
rs7842861	129325699	C/G	0.39	0.99	1.21(1.07-1.37)	2.7E-03
rs73356177	129224821	G/A	0.1	0.95	1.36(1.11-1.67)	2.8E-03
rs4733851	129264420	G/A	0.56	0.93	0.83(0.73-0.94)	3.2E-03
rs4311631	129312530	A/T	0.39	0.99	1.21(1.06-1.37)	3.3E-03
rs11778971	129318011	C/G	0.39	0.99	1.20(1.06-1.36)	3.5E-03
rs6996426	129312741	G/T	0.39	0.99	1.20(1.06-1.37)	3.5E-03
rs7818334	128630216	A/G	0.07	0.94	0.67(0.52-0.88)	3.5E-03
rs10103510	127761312	T/C	0.03	0.75	0.51(0.32-0.80)	3.5E-03
rs150846373	128647523	T/C	0.03	0.79	0.56(0.37-0.83)	3.8E-03
c8_pos129054328	128985146	A/T	0.05	0.52	0.62(0.45-0.86)	4.0E-03
rs79746025	128628074	T/G	0.07	0.95	0.68(0.52-0.89)	4.2E-03
rs116635531	128646495	A/G	0.04	0.77	0.57(0.38-0.84)	5.0E-03
rs73710037	128866252	G/C	0.09	0.68	0.68(0.52-0.89)	5.5E-03
rs75603024	127791799	T/C	0.03	0.8	0.50(0.31-0.82)	5.6E-03
rs75082286	129019522	C/T	0.02	0.43	0.41(0.22-0.77)	5.7E-03
rs79638788	129310119	T/A	0.27	0.91	1.22(1.06-1.40)	5.8E-03

rs1516964	129493657	T/C	0.08	0.69	0.67(0.51-0.89)	6.1E-03
rs11786536	129000416	A/G	0.04	1	0.60(0.42-0.87)	6.5E-03
rs73361950	129276057	T/C	0.04	0.96	1.49(1.12-1.99)	6.8E-03
rs11777546	129311776	A/G	0.35	0.98	1.19(1.05-1.36)	6.9E-03
rs59367394	129328032	T/C	0.16	0.97	1.26(1.06-1.49)	6.9E-03
rs4559211	129328365	T/C	0.16	0.97	1.26(1.06-1.49)	7.0E-03
rs10101587	128635755	C/T	0.2	0.83	1.25(1.06-1.47)	7.3E-03
rs12680661	128827465	A/G	0.15	0.89	0.77(0.64-0.93)	7.4E-03
rs75304215	128635589	C/T	0.2	0.83	1.25(1.06-1.47)	7.4E-03
rs11786459	129331091	T/G	0.16	0.97	1.26(1.06-1.48)	7.4E-03
rs7819582	128597214	T/C	0.49	0.96	1.19(1.05-1.36)	7.4E-03
rs10086191	128635476	G/A	0.2	0.83	1.25(1.06-1.47)	7.4E-03
rs36121174	129170290	T/C	0.23	0.99	0.82(0.70-0.95)	7.5E-03
rs10085933	128635230	G/A	0.2	0.83	1.25(1.06-1.47)	7.6E-03
rs60990950	128640649	G/C	0.44	0.76	0.82(0.71-0.95)	7.7E-03
rs138554988	128449097	A/G	0.12	0.68	1.34(1.08-1.67)	8.0E-03
chr8:128441225:D	128441225	A/AC	0.04	0.69	0.54(0.34-0.85)	8.3E-03
rs143643635	128644345	T/C	0.03	0.81	0.57(0.38-0.87)	8.7E-03
rs11779126	128987768	T/C	0.03	1	0.54(0.35-0.86)	8.7E-03
rs12056931	129357876	C/T	0.17	0.98	1.24(1.06-1.45)	8.8E-03
rs7841519	128217961	C/A	0.1	0.69	0.72(0.56-0.92)	8.9E-03
rs76437407	129360494	T/C	0.17	0.97	1.24(1.06-1.45)	8.9E-03
rs115907016	127705838	C/T	0.03	0.63	0.50(0.30-0.84)	9.1E-03
rs6988558	128773207	C/G	0.48	0.82	0.83(0.73-0.96)	9.6E-03
rs6651248	129023645	C/T	0.81	1	0.81(0.70-0.95)	9.7E-03
rs74431944	129089033	A/G	0.03	0.79	1.64(1.13-2.38)	9.8E-03
rs4733590	129027695	T/C	0.81	1	0.81(0.70-0.95)	9.8E-03
rs55738171	128669298	C/A	0.07	0.53	1.46(1.10-1.94)	9.8E-03
c8_pos129641585	129572403	A/G	0.2	1	1.22(1.05-1.42)	9.8E-03
rs74623761	129363670	G/A	0.15	0.97	1.25(1.05-1.47)	9.9E-03
rs113669912	129356053	A/G	0.15	0.97	1.25(1.05-1.47)	9.9E-03

^a SNP identification number from the 1000 Genomes Project.

^b Base position on chromosome 8 is based on the NCBI human genome build 37 from the 1000 Genomes Project.

^c Risk/reference alleles are based on forward positive strand of the NCBI human genome build 37 from the 1000 Genomes Project.

^d Effect allele frequency (EAF) is calculated with combined women controls of European ancestry.

^e Per allele odds ratio (OR), 95% confidence interval (CI) and significance were estimated from logistic regression, adjusted for age, study site and principal components.

Supplementary Table 4. Details of 154 SNPs correlated with rs13281615 at $r^2 > 0.2$.

SNP	Base position	Allele1	Allele2	LD ^a (r^2)	Beta ^b	se ^b	P ^b	logLikelihood ^c	RegulomeDB score ^d	Functional Annotation ^e
rs283727	128313360	A	G	0.24	0.0688	0.0097	1.44E-12	60131.075	2b	enhancer
rs283728	128313500	A	T	0.26	0.0716	0.0097	1.89E-13	60130.7	4	enhancer
rs4871015	128314516	G	A	0.24	-0.0774	0.0098	3.49E-15	60128.34	3a	Weak transcription
rs34882299	128314913	G	A	0.23	0.0639	0.0097	3.91E-11	60131.92	4	Weak transcription
rs283704	128315582	G	A	0.25	0.0726	0.0098	1.38E-13	60130.41	4	Weak transcription
rs283705	128317450	T	C	0.22	0.0749	0.0097	1.19E-14	60128.34	2b	Weak transcription
rs10107982	128318755	C	T	0.25	0.0551	0.0108	3.09E-07	60133.935	5	enhancer
rs7838810	128321202	C	T	0.4	0.0665	0.0101	5.08E-11	60133.92	5	Quiescent/Low
rs453875	128321411	A	G	0.42	0.0728	0.0098	1.05E-13	60133.385	5	Quiescent/Low
rs445114	128323181	C	T	0.37	0.0614	0.0100	8.56E-10	60133.94	5	Quiescent/Low
rs378854	128323819	T	C	0.36	0.0573	0.0101	1.25E-08	60133.84	5	Quiescent/Low
rs421094	128323874	A	G	0.37	0.0597	0.0100	2.62E-09	60133.89	5	Quiescent/Low
rs382434	128324147	T	C	0.3	0.0574	0.0102	2.10E-08	60133.94	5	Quiescent/Low
rs618477	128327641	G	C	0.36	0.0614	0.0102	2.03E-09	60133.925	5	Quiescent/Low
rs112175013	128327800	A	G	0.26	-0.0848	0.0099	1.12E-17	60126.31	5	Quiescent/Low
rs79297161	128328709	T	C	0.28	0.0582	0.0106	3.97E-08	60133.93	5	Quiescent/Low
rs11781932	128330178	T	C	0.26	-0.0853	0.0099	7.74E-18	60126.15	5	Quiescent/Low
rs11785664	128330424	C	T	0.26	-0.0854	0.0099	7.14E-18	60126.125	5	Quiescent/Low
rs56154314	128330748	A	C	0.26	-0.0876	0.0100	2.90E-18	60125.48	5	Quiescent/Low
rs13272693	128332975	A	G	0.24	0.0698	0.0098	1.26E-12	60130.775	6	Quiescent/Low
rs13272305	128333116	G	A	0.21	0.0723	0.0103	2.18E-12	60130.21	5	Quiescent/Low
rs622856	128333180	T	C	0.36	0.0679	0.0104	6.12E-11	60133.81	5	Quiescent/Low
rs622853	128333181	A	G	0.37	0.0680	0.0104	6.39E-11	60133.82	5	Quiescent/Low
rs622556	128333197	C	T	0.22	0.0670	0.0097	4.42E-12	60130.81	5	Quiescent/Low
rs452529	128333259	C	G	0.22	0.0659	0.0097	1.03E-11	60131.15	5	Quiescent/Low
rs444318	128333513	G	A	0.22	0.0656	0.0097	1.26E-11	60131.225	3a	Quiescent/Low
rs606677	128334485	C	T	0.21	0.0643	0.0097	3.46E-11	60131.41	5	Quiescent/Low
rs606345	128334499	A	T	0.22	0.0659	0.0097	1.04E-11	60131.155	5	Quiescent/Low
rs2691039	128334662	G	A	0.22	0.0659	0.0097	1.05E-11	60131.155	5	Quiescent/Low

rs13256367	128334900	C	A	0.41	0.0664	0.0102	5.93E-11	60133.935	5	Quiescent/Low
rs594154	128334911	A	G	0.22	0.0659	0.0097	1.06E-11	60131.165	5	Quiescent/Low
rs594076	128334966	C	G	0.22	0.0659	0.0097	1.06E-11	60131.16	5	Quiescent/Low
rs373701	128334992	A	C	0.22	0.0659	0.0097	1.06E-11	60131.16	5	Quiescent/Low
rs437980	128335246	C	A	0.22	0.0658	0.0097	1.07E-11	60131.165	5	Quiescent/Low
rs62516012	128335526	G	C	0.27	0.0536	0.0107	5.68E-07	60133.895	4	Quiescent/Low
rs620861	128335673	A	G	0.38	0.0623	0.0100	4.67E-10	60133.935	4	Quiescent/Low
rs620808	128335714	T	C	0.22	0.0697	0.0100	3.39E-12	60130.65	3a	Quiescent/Low
rs590574	128335715	G	A	0.21	0.0667	0.0101	3.60E-11	60131.505	3a	Quiescent/Low
rs443053	128335796	T	G	0.38	0.0626	0.0100	4.01E-10	60133.94	5	Quiescent/Low
rs11775799	128336236	G	A	0.28	-0.0880	0.0099	5.23E-19	60125.285	5	Quiescent/Low
rs400818	128336546	C	T	0.23	0.0684	0.0097	1.57E-12	60130.85	5	Quiescent/Low
rs78015822	128336740	G	A	0.24	0.0732	0.0100	3.12E-13	60130.26	5	Quiescent/Low
rs74588857	128336741	T	C	0.24	0.0732	0.0100	3.12E-13	60130.26	5	Quiescent/Low
rs34628978	128336744	A	G	0.23	0.0687	0.0097	1.38E-12	60130.76	5	Quiescent/Low
rs386883	128336871	A	G	0.23	0.0686	0.0097	1.42E-12	60130.81	5	Quiescent/Low
rs377649	128337241	T	G	0.24	0.0691	0.0097	9.42E-13	60130.675	5	Quiescent/Low
rs432523	128337927	T	A	0.23	0.0686	0.0097	1.41E-12	60130.81	5	Quiescent/Low
rs430693	128338594	T	G	0.23	0.0686	0.0097	1.45E-12	60130.825	5	Quiescent/Low
rs684254	128338693	A	G	0.23	0.0686	0.0097	1.36E-12	60130.8	5	Quiescent/Low
rs1395287	128338702	G	C	0.41	0.0670	0.0102	4.14E-11	60133.93	5	Quiescent/Low
rs631845	128338760	A	G	0.23	0.0691	0.0097	1.04E-12	60130.665	3a	Quiescent/Low
rs653605	128338847	T	G	0.23	0.0686	0.0097	1.41E-12	60130.81	2c	Quiescent/Low
rs432470	128339044	T	C	0.33	0.0835	0.0097	1.02E-17	60128.44	3a	Quiescent/Low
rs424281	128339426	A	G	0.33	0.0838	0.0097	8.46E-18	60128.355	5	Quiescent/Low
rs1668875	128341103	C	G	0.51	0.0789	0.0099	1.18E-15	60133.46	5	enhancer
rs7002712	128341612	T	A	0.28	-0.0876	0.0099	7.84E-19	60125.62	5	enhancer
rs587948	128341680	G	T	0.51	0.0774	0.0099	4.08E-15	60133.61	5	enhancer
rs623401	128341727	G	C	0.51	0.0773	0.0099	4.45E-15	60133.62	5	enhancer
rs35049703	128342114	A	C	0.4	0.0672	0.0101	3.03E-11	60133.895	5	enhancer
rs10956359	128342154	C	T	0.28	0.0560	0.0106	1.35E-07	60133.935	5	enhancer

rs17464492	128342866	G	A	0.29	0.0612	0.0107	9.44E-09	60133.88	4	enhancer
rs35603878	128343341	C	G	0.27	0.0502	0.0118	2.23E-05	60133.28	5	enhancer
rs420101	128343879	A	G	0.93	0.0971	0.0099	1.27E-22	60133.93	5	enhancer
rs7838714	128343948	C	T	0.48	-0.1077	0.0099	1.18E-27	60119.735	5	enhancer
rs389143	128344380	T	C	0.94	0.0971	0.0099	1.21E-22	60133.91	2b	enhancer
rs688201	128344402	T	G	0.93	0.0970	0.0099	1.20E-22	60133.93	4	enhancer
rs595821	128344410	A	G	0.94	0.0975	0.0099	7.80E-23	60133.93	4	enhancer
rs687324	128344591	C	T	0.94	0.0974	0.0099	8.55E-23	60133.925	3a	enhancer
rs594869	128344601	C	T	0.91	0.1013	0.0102	3.18E-23	60133.74	5	enhancer
rs594868	128344602	A	G	0.92	0.0994	0.0101	5.40E-23	60133.885	5	enhancer
rs687279	128344624	T	C	0.62	0.0790	0.0106	7.19E-14	60133.625	4	enhancer
rs436238	128345028	T	C	0.94	0.0973	0.0099	9.94E-23	60133.91	4	enhancer
rs581761	128345231	T	G	0.94	0.0975	0.0099	8.66E-23	60133.93	3a	Quiescent/Low
rs673745	128345269	T	C	0.94	0.0988	0.0099	2.20E-23	60133.865	5	Quiescent/Low
rs688937	128345381	A	T	0.94	0.0980	0.0099	5.00E-23	60133.94	5	Quiescent/Low
rs672888	128345463	G	A	0.94	0.0980	0.0099	4.69E-23	60133.94	5	Quiescent/Low
rs7826557	128345731	A	C	0.47	-0.1057	0.0099	1.34E-26	60121.125	5	Quiescent/Low
rs419018	128346259	G	A	0.94	0.0979	0.0099	5.03E-23	60133.94	5	Quiescent/Low
rs418269	128346358	A	G	0.94	0.0980	0.0099	4.90E-23	60133.94	5	Quiescent/Low
rs385278	128347017	C	T	0.94	0.0978	0.0099	5.55E-23	60133.94	5	Quiescent/Low
rs391640	128347124	G	A	0.36	0.0526	0.0121	1.41E-05	60131.83	5	Quiescent/Low
rs670725	128347157	C	A	0.94	0.0978	0.0099	5.79E-23	60133.94	5	Quiescent/Low
rs382824	128347724	G	T	0.94	0.0978	0.0099	5.58E-23	60133.94	4	Quiescent/Low
rs383205	128347977	A	G	0.94	0.0976	0.0099	6.74E-23	60133.935	5	Quiescent/Low
rs373616	128348062	C	T	0.94	0.0975	0.0099	7.94E-23	60133.93	5	Quiescent/Low
rs400772	128348298	T	G	0.94	0.0972	0.0099	1.13E-22	60133.9	5	Quiescent/Low
rs13275275	128349727	G	A	0.94	0.0978	0.0099	5.92E-23	60133.935	5	Quiescent/Low
rs13248140	128349888	A	G	0.94	0.0977	0.0099	6.49E-23	60133.935	5	Quiescent/Low
rs10956360	128349970	A	G	0.94	0.0979	0.0099	5.32E-23	60133.94	5	Quiescent/Low
rs10956361	128350106	A	G	0.94	0.0972	0.0099	1.08E-22	60133.895	5	Quiescent/Low
rs10956362	128350386	G	A	0.94	0.0976	0.0099	7.00E-23	60133.93	5	Quiescent/Low

rs13249993	128350515	A	G	0.54	0.1035	0.0098	3.48E-26	60123.33	5	Quiescent/Low
rs11777532	128350608	C	G	0.41	-0.0975	0.0100	2.55E-22	60125.41	5	Quiescent/Low
rs10956363	128351773	A	G	0.94	0.0969	0.0099	1.51E-22	60133.83	5	Quiescent/Low
rs36024485	128352205	C	T	0.52	0.0670	0.0109	9.13E-10	60132.48	3a	enhancer
rs4871782	128352234	A	G	0.94	0.0971	0.0099	1.22E-22	60133.86	3a	enhancer
rs28759353	128352363	T	G	0.64	0.0780	0.0105	1.01E-13	60133.265	4	enhancer
rs10087810	128352730	T	C	0.82	-0.0953	0.0098	2.18E-22	60133.2	3a	enhancer
rs12541832	128353171	A	C	0.64	0.0781	0.0105	9.73E-14	60133.275	5	enhancer
rs13262406	128353739	G	A	0.65	0.0792	0.0105	4.17E-14	60133.455	5	enhancer
rs17465052	128354080	A	G	0.48	-0.1083	0.0099	5.72E-28	60119.345	4	enhancer
rs13270266	128354086	G	A	0.65	0.0789	0.0105	5.03E-14	60133.41	4	enhancer
rs10098985	128355019	T	G	0.47	-0.1063	0.0099	6.23E-27	60120.755	5	enhancer
rs13281615	128355618	G	A	-	0.1004	0.0098	2.04E-24	60133.94	5	Quiescent/Low
rs17465283	128355824	A	G	0.47	-0.1062	0.0099	7.44E-27	60120.865	5	Quiescent/Low
rs13256275	128356226	A	G	0.4	0.0887	0.0097	6.85E-20	60127.65	5	Quiescent/Low
rs17465317	128356670	T	C	0.52	0.1028	0.0098	8.37E-26	60123.575	5	Quiescent/Low
rs13267780	128357817	A	G	0.48	0.0737	0.0112	3.91E-11	60133.78	5	Quiescent/Low
rs10447995	128357924	A	G	0.52	0.1028	0.0098	8.07E-26	60123.56	5	Quiescent/Low
rs6999578	128358795	T	C	0.47	-0.1067	0.0099	3.98E-27	60120.29	6	Quiescent/Low
rs7014657	128361241	G	A	0.47	-0.1069	0.0099	3.58E-27	60120.195	5	Quiescent/Low
rs56110209	128361928	G	T	0.47	-0.1069	0.0099	3.44E-27	60120.15	5	Quiescent/Low
rs13272866	128363367	G	A	0.45	-0.1027	0.0099	2.75E-25	60122.4	5	Quiescent/Low
rs10097200	128363652	C	T	0.44	-0.1033	0.0099	1.15E-25	60121.51	5	Quiescent/Low
rs7002826	128364271	C	G	0.45	-0.1061	0.0099	6.11E-27	60120.105	5	Quiescent/Low
rs7007568	128364906	C	G	0.45	-0.1058	0.0099	8.49E-27	60120.33	5	Quiescent/Low
rs7842494	128366570	A	C	0.39	-0.0991	0.0100	3.78E-23	60123.78	5	Quiescent/Low
rs5022926	128366829	C	A	0.45	-0.1059	0.0099	8.01E-27	60120.25	4	Quiescent/Low
rs10112674	128367454	G	T	0.38	0.0868	0.0097	5.08E-19	60128.2	5	Quiescent/Low
rs9693995	128368513	T	C	0.82	-0.1006	0.0098	6.45E-25	60130.775	4	Quiescent/Low
rs35440286	128369973	A	G	0.82	0.0895	0.0100	5.15E-19	60133.66	5	Quiescent/Low
rs35904426	128370183	T	G	0.97	0.1010	0.0099	1.43E-24	60133.315	6	Quiescent/Low

rs35112951	128370271	A	G	0.81	0.0871	0.0101	5.22E-18	60133.325	5	Quiescent/Low
rs10110330	128370755	A	G	0.97	0.1019	0.0099	5.83E-25	60132.665	5	Quiescent/Low
rs12550713	128370949	G	C	0.97	0.1019	0.0099	6.00E-25	60132.695	3a	Quiescent/Low
rs10096351	128372172	G	A	0.52	0.1049	0.0098	9.86E-27	60122.225	5	Quiescent/Low
rs2121629	128373027	T	C	0.8	-0.0970	0.0098	3.30E-23	60132.395	5	Quiescent/Low
rs12541305	128373756	C	T	0.45	-0.1049	0.0099	2.46E-26	60120.98	5	Quiescent/Low
rs978683	128374117	G	A	0.68	-0.0829	0.0099	5.56E-17	60133.935	3a	Quiescent/Low
rs9297753	128375270	T	C	0.45	-0.1056	0.0099	1.17E-26	60120.505	5	Quiescent/Low
rs9283954	128375370	T	C	0.4	-0.0981	0.0100	1.05E-22	60124.405	5	Quiescent/Low
rs7831303	128376732	A	C	0.45	-0.1057	0.0099	1.06E-26	60120.44	5	Quiescent/Low
rs7815100	128376801	C	T	0.45	-0.1055	0.0099	1.22E-26	60120.505	5	Quiescent/Low
rs7835046	128376926	T	C	0.39	-0.0645	0.0105	6.95E-10	60133.915	5	Quiescent/Low
rs4143118	128377468	G	A	0.8	-0.0967	0.0098	4.24E-23	60132.485	5	Quiescent/Low
rs6988647	128377656	C	T	0.45	-0.1053	0.0099	1.58E-26	60120.705	5	Quiescent/Low
rs7006882	128377667	T	G	0.8	-0.0976	0.0098	1.83E-23	60132.08	5	Quiescent/Low
rs9692890	128377774	A	G	0.4	-0.0985	0.0100	6.30E-23	60124.135	5	Quiescent/Low
rs9693143	128378025	T	C	0.45	-0.1053	0.0099	1.48E-26	60120.67	5	enhancer
rs28524866	128378191	C	T	0.82	-0.0946	0.0098	3.99E-22	60133.455	4	enhancer
rs2060775	128378626	C	T	0.25	-0.0486	0.0114	2.09E-05	60133.515	3a	Weak transcription
rs10956364	128378883	T	C	0.82	-0.1005	0.0098	6.96E-25	60130.805	6	enhancer
rs11776330	128378963	T	G	0.8	-0.0972	0.0098	2.66E-23	60132.285	5	no data
rs7845452	128379409	C	G	0.44	-0.1028	0.0099	2.09E-25	60121.815	5	Weak transcription
rs16902126	128382357	G	A	0.43	-0.1016	0.0099	6.97E-25	60122.43	5	Weak transcription
rs7815245	128383597	T	C	0.45	-0.1076	0.0099	1.33E-27	60118.935	5	enhancer
rs2121631	128386556	G	A	0.36	-0.0680	0.0107	2.02E-10	60133.895	5	Quiescent/Low
rs9643220	128386926	G	A	0.23	-0.0505	0.0115	1.19E-05	60133.78	5	Quiescent/Low
rs1562430	128387852	C	T	0.45	-0.1064	0.0099	4.50E-27	60119.68	5	Quiescent/Low
rs2392780	128388025	G	A	0.43	-0.1031	0.0099	1.42E-25	60121.435	5	Quiescent/Low
rs7015780	128389507	T	C	0.44	-0.1074	0.0101	1.55E-26	60120.21	5	Quiescent/Low
rs4871017	128389765	T	A	0.23	-0.0499	0.0115	1.53E-05	60133.77	5	Quiescent/Low
rs1949810	128394313	T	C	0.25	0.0498	0.0119	2.87E-05	60133.455	6	Quiescent/Low

rs7820981	128400176	C	T	0.28	-0.0456	0.0098	3.54E-06	60133.61	5	Quiescent/Low
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^a r^2 for linkage disequilibrium with the index SNP rs13281615 (Signal 2 in text) computed with data of European ancestry women controls.

^b Per allele effect (beta), standard error (se) and significance were estimated from univariate logistic regression, adjusted for age, study site and principal components.

^c Results from likelihood test under a glm model which includes covariates age, study site, principal components and the signal or its correlated SNP.

^d Score from the estimates in the Regulome database. 2b:TF binding + any motif + DNase Footprint + DNase peak; 2c: TF binding + matched TF motif + DNase peak; 3a: TF binding + any motif + DNase peak; 4: TF binding + DNase peak; 5: TF binding or DNase peak; 6: other functional support data. For details, see <http://www.regulomedb.org/index>.

^e Implied regulatory chromatin state from ENCODE data, for details see HaploReg database website
<http://www.broadinstitute.org/mammals/haploreg/haploreg.php>.

Supplementary Table 5. Details of 170 SNPs correlated with rs7815245 at $r^2 > 0.2$.

SNP	Base position	Allele1	Allele2	LD ^a (r^2)	Beta ^b	se ^b	P ^b	logLikelihood ^c	RegulomeDB score ^d	Functional Annotation ^e
rs55753707	128285968	G	T	0.25	-0.0444	0.0097	5.15E-06	60126.175	5	Quiescent/Low
rs283718	128307082	T	C	0.28	-0.0423	0.0098	1.55E-05	60125.555	4	enhancer
rs12549518	128309591	A	G	0.35	-0.0601	0.0098	7.57E-10	60126.64	5	enhancer
rs6996866	128310155	T	C	0.35	-0.0604	0.0098	6.31E-10	60126.645	3a	enhancer
rs283727	128313360	A	G	0.42	0.0688	0.0097	1.44E-12	60126.685	2b	enhancer
rs283728	128313500	A	T	0.44	0.0716	0.0097	1.89E-13	60126.655	4	enhancer
rs4871015	128314516	G	A	0.58	-0.0774	0.0098	3.49E-15	60126.525	3a	Weak transcription
rs34882299	128314913	G	A	0.43	0.0639	0.0097	3.91E-11	60126.455	4	Weak transcription
rs283704	128315582	G	A	0.42	0.0726	0.0098	1.38E-13	60126.59	4	Weak transcription
rs56983490	128316676	G	A	0.52	-0.0778	0.0098	2.08E-15	60126.675	5	Weak transcription
rs283705	128317450	T	C	0.43	0.0749	0.0097	1.19E-14	60126.38	2b	Weak transcription
rs7006593	128317585	T	A	0.52	-0.0757	0.0098	8.58E-15	60126.69	2b	Weak transcription
rs7838810	128321202	C	T	0.24	0.0665	0.0101	5.08E-11	60125.6	5	Quiescent/Low
rs453875	128321411	A	G	0.23	0.0728	0.0098	1.05E-13	60123.47	5	Quiescent/Low
chr8:128322698:D	128322698	T	TA	0.53	-0.0822	0.0100	2.45E-16	60126.655	5	Quiescent/Low
rs445114	128323181	C	T	0.23	0.0614	0.0100	8.56E-10	60126.11	5	Quiescent/Low
rs378854	128323819	T	C	0.22	0.0573	0.0101	1.25E-08	60126.475	5	Quiescent/Low
rs421094	128323874	A	G	0.23	0.0597	0.0100	2.62E-09	60126.34	5	Quiescent/Low
rs382434	128324147	T	C	0.19	0.0574	0.0102	2.10E-08	60126.265	5	Quiescent/Low
rs618477	128327641	G	C	0.23	0.0614	0.0102	2.03E-09	60126.24	5	Quiescent/Low
rs112175013	128327800	A	G	0.62	-0.0848	0.0099	1.12E-17	60126.69	5	Quiescent/Low
rs617894	128327828	G	A	0.44	0.0654	0.0099	3.46E-11	60126.45	5	Quiescent/Low
rs79297161	128328709	T	C	0.28	0.0582	0.0106	3.97E-08	60126.655	5	Quiescent/Low
rs11781932	128330178	T	C	0.62	-0.0853	0.0099	7.74E-18	60126.685	5	Quiescent/Low
rs11785664	128330424	C	T	0.62	-0.0854	0.0099	7.14E-18	60126.685	5	Quiescent/Low
rs56154314	128330748	A	C	0.61	-0.0876	0.0100	2.90E-18	60126.625	5	Quiescent/Low
rs13271897	128332878	T	C	0.43	0.0617	0.0099	4.48E-10	60126.095	6	Quiescent/Low
rs13272693	128332975	A	G	0.44	0.0698	0.0098	1.26E-12	60126.68	6	Quiescent/Low
rs13272305	128333116	G	A	0.43	0.0723	0.0103	2.18E-12	60126.68	5	Quiescent/Low

rs622856	128333180	T	C	0.24	0.0679	0.0104	6.12E-11	60125.63	5	Quiescent/Low
rs622853	128333181	A	G	0.24	0.0680	0.0104	6.39E-11	60125.615	5	Quiescent/Low
rs622556	128333197	C	T	0.45	0.0670	0.0097	4.42E-12	60126.6	5	Quiescent/Low
rs452529	128333259	C	G	0.45	0.0659	0.0097	1.03E-11	60126.515	5	Quiescent/Low
rs444318	128333513	G	A	0.45	0.0656	0.0097	1.26E-11	60126.49	3a	Quiescent/Low
chr8:128334141:D	128334141	C	CCT	0.4	0.0671	0.0101	3.25E-11	60126.57	5	Quiescent/Low
chr8:128334150:D	128334150	C	CTT	0.44	0.0655	0.0098	2.25E-11	60126.43	5	Quiescent/Low
rs606677	128334485	C	T	0.46	0.0643	0.0097	3.46E-11	60126.195	5	Quiescent/Low
rs606345	128334499	A	T	0.45	0.0659	0.0097	1.04E-11	60126.515	5	Quiescent/Low
rs2691039	128334662	G	A	0.45	0.0659	0.0097	1.05E-11	60126.515	5	Quiescent/Low
rs13256367	128334900	C	A	0.24	0.0664	0.0102	5.93E-11	60125.73	5	Quiescent/Low
rs594154	128334911	A	G	0.45	0.0659	0.0097	1.06E-11	60126.51	5	Quiescent/Low
rs594076	128334966	C	G	0.45	0.0659	0.0097	1.06E-11	60126.515	5	Quiescent/Low
rs373701	128334992	A	C	0.45	0.0659	0.0097	1.06E-11	60126.515	5	Quiescent/Low
rs437980	128335246	C	A	0.45	0.0658	0.0097	1.07E-11	60126.51	5	Quiescent/Low
rs620861	128335673	A	G	0.24	0.0623	0.0100	4.67E-10	60126.09	4	Quiescent/Low
rs620808	128335714	T	C	0.43	0.0697	0.0100	3.39E-12	60126.67	3a	Quiescent/Low
rs590574	128335715	G	A	0.42	0.0667	0.0101	3.60E-11	60126.56	3a	Quiescent/Low
rs443053	128335796	T	G	0.24	0.0626	0.0100	4.01E-10	60126.06	5	Quiescent/Low
rs11775799	128336236	G	A	0.65	-0.0880	0.0099	5.23E-19	60126.645	5	Quiescent/Low
rs400818	128336546	C	T	0.47	0.0684	0.0097	1.57E-12	60126.585	5	Quiescent/Low
rs78015822	128336740	G	A	0.45	0.0732	0.0100	3.12E-13	60126.685	5	Quiescent/Low
rs74588857	128336741	T	C	0.45	0.0732	0.0100	3.12E-13	60126.685	5	Quiescent/Low
rs34628978	128336744	A	G	0.47	0.0687	0.0097	1.38E-12	60126.595	5	Quiescent/Low
rs386883	128336871	A	G	0.47	0.0686	0.0097	1.42E-12	60126.59	5	Quiescent/Low
rs377649	128337241	T	G	0.47	0.0691	0.0097	9.42E-13	60126.62	5	Quiescent/Low
rs432523	128337927	T	A	0.47	0.0686	0.0097	1.41E-12	60126.595	5	Quiescent/Low
rs430693	128338594	T	G	0.47	0.0686	0.0097	1.45E-12	60126.59	5	Quiescent/Low
rs684254	128338693	A	G	0.47	0.0686	0.0097	1.36E-12	60126.595	5	Quiescent/Low
rs1395287	128338702	G	C	0.24	0.0670	0.0102	4.14E-11	60125.64	5	Quiescent/Low
rs631845	128338760	A	G	0.47	0.0691	0.0097	1.04E-12	60126.615	3a	Quiescent/Low

rs653605	128338847	T	G	0.47	0.0686	0.0097	1.41E-12	60126.595	2c	Quiescent/Low
rs432470	128339044	T	C	0.54	0.0835	0.0097	1.02E-17	60126.345	3a	Quiescent/Low
rs424281	128339426	A	G	0.54	0.0838	0.0097	8.46E-18	60126.32	5	Quiescent/Low
rs1668875	128341103	C	G	0.30	0.0789	0.0099	1.18E-15	60123.61	5	enhancer
rs7002712	128341612	T	A	0.65	-0.0876	0.0099	7.84E-19	60126.66	5	enhancer
rs587948	128341680	G	T	0.29	0.0774	0.0099	4.08E-15	60123.97	5	enhancer
rs623401	128341727	G	C	0.29	0.0773	0.0099	4.45E-15	60124	5	enhancer
rs35049703	128342114	A	C	0.24	0.0672	0.0101	3.03E-11	60125.52	5	enhancer
rs420101	128343879	A	G	0.42	0.0971	0.0099	1.27E-22	60120.15	5	enhancer
rs7838714	128343948	C	T	0.94	-0.1077	0.0099	1.18E-27	60125.625	5	enhancer
rs389143	128344380	T	C	0.42	0.0971	0.0099	1.21E-22	60120.175	2b	enhancer
rs688201	128344402	T	G	0.42	0.0970	0.0099	1.20E-22	60120.24	4	enhancer
rs595821	128344410	A	G	0.42	0.0975	0.0099	7.80E-23	60119.99	4	enhancer
rs687324	128344591	C	T	0.42	0.0974	0.0099	8.55E-23	60120.03	3a	enhancer
rs594869	128344601	C	T	0.42	0.1013	0.0102	3.18E-23	60119.44	4	enhancer
rs594868	128344602	A	G	0.42	0.0994	0.0101	5.40E-23	60119.825	4	enhancer
rs687279	128344624	T	C	0.27	0.0790	0.0106	7.19E-14	60124.34	4	enhancer
rs436238	128345028	T	C	0.42	0.0973	0.0099	9.94E-23	60120.11	4	enhancer
rs581761	128345231	T	G	0.42	0.0975	0.0099	8.66E-23	60120.01	3a	Quiescent/Low
rs673745	128345269	T	C	0.42	0.0988	0.0099	2.20E-23	60119.35	5	Quiescent/Low
rs688937	128345381	A	T	0.42	0.0980	0.0099	5.00E-23	60119.79	5	Quiescent/Low
rs672888	128345463	G	A	0.42	0.0980	0.0099	4.69E-23	60119.77	5	Quiescent/Low
rs7826557	128345731	A	C	0.95	-0.1057	0.0099	1.34E-26	60126.645	5	Quiescent/Low
chr8:128345939:I	128345939	CCTT	C	0.43	0.0980	0.0099	4.97E-23	60119.8	5	Quiescent/Low
rs419018	128346259	G	A	0.42	0.0979	0.0099	5.03E-23	60119.79	5	Quiescent/Low
rs418269	128346358	A	G	0.42	0.0980	0.0099	4.90E-23	60119.785	5	Quiescent/Low
chr8:128346646:D	128346646	A	AT	0.43	0.0983	0.0099	4.05E-23	60119.69	5	Quiescent/Low
rs385278	128347017	C	T	0.42	0.0978	0.0099	5.55E-23	60119.845	5	Quiescent/Low
rs670725	128347157	C	A	0.42	0.0978	0.0099	5.79E-23	60119.865	5	Quiescent/Low
rs382824	128347724	G	T	0.42	0.0978	0.0099	5.58E-23	60119.85	4	Quiescent/Low
rs383205	128347977	A	G	0.42	0.0976	0.0099	6.74E-23	60119.945	5	Quiescent/Low

rs373616	128348062	C	T	0.42	0.0975	0.0099	7.94E-23	60119.985	5	Quiescent/Low
rs400772	128348298	T	G	0.42	0.0972	0.0099	1.13E-22	60120.175	5	Quiescent/Low
rs13275275	128349727	G	A	0.42	0.0978	0.0099	5.92E-23	60119.885	5	Quiescent/Low
rs13248140	128349888	A	G	0.42	0.0977	0.0099	6.49E-23	60119.93	5	Quiescent/Low
rs10956360	128349970	A	G	0.42	0.0979	0.0099	5.32E-23	60119.835	5	Quiescent/Low
rs10956361	128350106	A	G	0.42	0.0972	0.0099	1.08E-22	60120.185	5	Quiescent/Low
rs10956362	128350386	G	A	0.42	0.0976	0.0099	7.00E-23	60119.965	5	Quiescent/Low
rs13249993	128350515	A	G	0.80	0.1035	0.0098	3.48E-26	60124.935	5	Quiescent/Low
rs11777532	128350608	C	G	0.83	-0.0975	0.0100	2.55E-22	60126.545	5	Quiescent/Low
chr8:128350707:D	128350707	C	CA	0.44	0.0973	0.0099	1.16E-22	60120.235	5	Quiescent/Low
c8_pos128420230	128351048	T	A	0.42	0.0977	0.0099	6.43E-23	60119.92	5	enhancer
c8_pos128420624	128351442	C	A	0.42	0.0978	0.0099	5.59E-23	60119.865	5	enhancer
rs10956363	128351773	A	G	0.42	0.0969	0.0099	1.51E-22	60120.345	5	enhancer
c8_pos128421136	128351954	T	C	0.28	0.0779	0.0105	1.09E-13	60124.725	5	enhancer
rs36024485	128352205	C	T	0.25	0.0670	0.0109	9.13E-10	60126.27	3a	enhancer
rs4871782	128352234	A	G	0.42	0.0971	0.0099	1.22E-22	60120.265	3a	enhancer
rs28759353	128352363	T	G	0.28	0.0780	0.0105	1.01E-13	60124.705	4	enhancer
rs10087810	128352730	T	C	0.49	-0.0953	0.0098	2.18E-22	60122.2	3a	enhancer
chr8:128352967:D	128352967	C	CA	0.48	-0.0951	0.0098	2.72E-22	60122.26	5	enhancer
rs12541832	128353171	A	C	0.28	0.0781	0.0105	9.73E-14	60124.695	5	enhancer
rs13262406	128353739	G	A	0.28	0.0792	0.0105	4.17E-14	60124.44	5	enhancer
rs17465052	128354080	A	G	0.94	-0.1083	0.0099	5.72E-28	60125.305	4	enhancer
rs13270266	128354086	G	A	0.28	0.0789	0.0105	5.03E-14	60124.505	4	enhancer
rs10095860	128354785	A	C	0.32	-0.0546	0.0104	1.40E-07	60126.275	5	enhancer
rs10098985	128355019	T	G	0.96	-0.1063	0.0099	6.23E-27	60126.575	5	enhancer
rs13281615	128355618	G	A	0.45	0.1004	0.0098	2.04E-24	60118.935	5	Quiescent/Low
rs17465283	128355824	A	G	0.96	-0.1062	0.0099	7.44E-27	60126.62	5	Quiescent/Low
c8_pos128425122	128355940	A	G	0.41	-0.0872	0.0097	2.19E-19	60123.21	5	Quiescent/Low
rs13256275	128356226	A	G	0.74	0.0887	0.0097	6.85E-20	60126.625	5	Quiescent/Low
rs17465317	128356670	T	C	0.83	0.1028	0.0098	8.37E-26	60125.66	5	Quiescent/Low
c8_pos128426042	128356860	C	T	0.84	0.1046	0.0098	1.27E-26	60125.165	5	Quiescent/Low

rs13267780	128357817	A	G	0.23	0.0737	0.0112	3.91E-11	60125.405	5	Quiescent/Low
rs10447995	128357924	A	G	0.83	0.1028	0.0098	8.07E-26	60125.665	5	Quiescent/Low
rs6999578	128358795	T	C	0.97	-0.1067	0.0099	3.98E-27	60126.6	6	Weak transcription
rs7014657	128361241	G	A	0.97	-0.1069	0.0099	3.58E-27	60126.6	5	Quiescent/Low
rs56110209	128361928	G	T	0.97	-0.1069	0.0099	3.44E-27	60126.595	6	Quiescent/Low
chr8:128362790:I	128362790	TTTC	T	0.24	-0.0676	0.0108	4.05E-10	60126.465	5	Quiescent/Low
rs13272866	128363367	G	A	0.96	-0.1027	0.0099	2.75E-25	60125.97	5	Quiescent/Low
rs10097200	128363652	C	T	0.97	-0.1033	0.0099	1.15E-25	60125.9	5	Quiescent/Low
rs7002826	128364271	C	G	0.99	-0.1061	0.0099	6.11E-27	60126.59	5	Quiescent/Low
rs7007568	128364906	C	G	0.98	-0.1058	0.0099	8.49E-27	60126.47	5	Quiescent/Low
rs7842494	128366570	A	C	0.86	-0.0991	0.0100	3.78E-23	60126.5	5	Quiescent/Low
rs5022926	128366829	C	A	0.99	-0.1059	0.0099	8.01E-27	60126.38	5	Quiescent/Low
rs10112674	128367454	G	T	0.73	0.0868	0.0097	5.08E-19	60126.45	5	Quiescent/Low
rs9693995	128368513	T	C	0.55	-0.1006	0.0098	6.45E-25	60121.16	4	Quiescent/Low
rs35440286	128369973	A	G	0.40	0.0895	0.0100	5.15E-19	60123.185	5	Quiescent/Low
rs35904426	128370183	T	G	0.47	0.1010	0.0099	1.43E-24	60119.39	5	Quiescent/Low
rs35112951	128370271	A	G	0.39	0.0871	0.0101	5.22E-18	60123.855	5	Quiescent/Low
rs10110330	128370755	A	G	0.47	0.1019	0.0099	5.83E-25	60118.965	5	Quiescent/Low
rs12550713	128370949	G	C	0.47	0.1019	0.0099	6.00E-25	60118.985	3a	Quiescent/Low
rs10096351	128372172	G	A	0.86	0.1049	0.0098	9.86E-27	60125.445	5	Quiescent/Low
rs2121629	128373027	T	C	0.55	-0.0970	0.0098	3.30E-23	60122.705	4	Quiescent/Low
rs12541305	128373756	C	T	0.99	-0.1049	0.0099	2.46E-26	60125.145	6	Quiescent/Low
rs978683	128374117	G	A	0.46	-0.0829	0.0099	5.56E-17	60125.635	3a	Quiescent/Low
rs9297753	128375270	T	C	0.99	-0.1056	0.0099	1.17E-26	60125.695	5	Quiescent/Low
rs9283954	128375370	T	C	0.87	-0.0981	0.0100	1.05E-22	60126.21	5	Quiescent/Low
rs7831303	128376732	A	C	0.99	-0.1057	0.0099	1.06E-26	60125.97	5	Quiescent/Low
rs7815100	128376801	C	T	0.99	-0.1055	0.0099	1.22E-26	60125.98	5	Quiescent/Low
rs7835046	128376926	T	C	0.31	-0.0645	0.0105	6.95E-10	60126.675	5	Quiescent/Low
rs4143118	128377468	G	A	0.55	-0.0967	0.0098	4.24E-23	60122.8	5	Quiescent/Low
rs6988647	128377656	C	T	0.99	-0.1053	0.0099	1.58E-26	60125.46	5	Quiescent/Low
rs7006882	128377667	T	G	0.54	-0.0976	0.0098	1.83E-23	60122.4	5	Quiescent/Low

rs9692890	128377774	A	G	0.87	-0.0985	0.0100	6.30E-23	60126.36	5	Quiescent/Low
rs9693143	128378025	T	C	0.99	-0.1053	0.0099	1.48E-26	60125.735	5	enhancer
rs28524866	128378191	C	T	0.53	-0.0946	0.0098	3.99E-22	60123.4	4	enhancer
rs10956364	128378883	T	C	0.56	-0.1005	0.0098	6.96E-25	60121.255	5	Weak transcription
rs11776330	128378963	T	G	0.55	-0.0972	0.0098	2.66E-23	60122.64	5	Weak transcription
rs7845452	128379409	C	G	0.98	-0.1028	0.0099	2.09E-25	60124.575	5	Weak transcription
rs16902126	128382357	G	A	0.98	-0.1016	0.0099	6.97E-25	60123.33	5	enhancer
rs7815245	128383597	T	C	-	-0.1076	0.0099	1.33E-27	60126.69	5	Quiescent/Low
rs2121631	128386556	G	A	0.28	-0.0680	0.0107	2.02E-10	60126.4	5	Quiescent/Low
chr8:128387062:D	128387062	T	TTA	0.78	-0.1005	0.0106	1.60E-21	60126.2	5	Quiescent/Low
chr8:128387063:D	128387063	T	TATA	0.85	-0.1026	0.0102	5.48E-24	60126.68	5	Quiescent/Low
chr8:128387067:D	128387067	A	ATAC	0.85	-0.1039	0.0102	3.14E-24	60126.655	5	Quiescent/Low
rs1562430	128387852	C	T	0.99	-0.1064	0.0099	4.50E-27	60126.505	5	Quiescent/Low
rs2392780	128388025	G	A	0.98	-0.1031	0.0099	1.42E-25	60125.325	5	Quiescent/Low
rs7015780	128389507	T	C	0.97	-0.1074	0.0101	1.55E-26	60126.59	5	Quiescent/Low
rs2166690	128394475	G	T	0.49	-0.0876	0.0103	2.02E-17	60125.95	5	Quiescent/Low
rs6986543	128396316	A	C	0.43	-0.0840	0.0102	2.06E-16	60125.645	5	Quiescent/Low

^a r^2 for linkage disequilibrium with SNP rs7815245 (Signal 3 in text) computed with data of European ancestry women controls.

^b Per allele effect (beta), standard error (se) and significance were estimated from univariate logistic regression, adjusted for age, study site and principal components.

^c Results from likelihood test under a glm model which includes covariates age, study site, principal components and the signal or its correlated SNP.

^d Score from the estimates in the Regulome database. 2b:TF binding + any motif + DNase Footprint + DNase peak; 2c: TF binding + matched TF motif + DNase peak; 3a: TF binding + any motif + DNase peak; 4: TF binding + DNase peak; 5: TF binding or DNase peak; 6: other functional support data. For details, see <http://www.regulomedb.org/index>.

^e Implied regulatory chromatin state from ENCODE data, for details see HaploReg database website <http://www.broadinstitute.org/mammals/haploreg/haploreg.php>.

Supplementary Table 6. Details of 62 SNPs correlated with rs11780156 at $r^2 > 0.2$.

SNP	Base position	Allele1	Allele2	LD ^a (r^2)	Beta ^b	se ^b	P ^b	logLikelihood ^c	RegulomeDB score ^d	Functional Annotation ^e
rs12542995	129145022	T	C	0.68	0.0675	0.0147	4.36E-06	60170.94	5	Quiescent/Low
rs12676630	129145876	T	C	0.68	0.0670	0.0146	4.50E-06	60170.94	5	Quiescent/Low
rs2648829	129147911	C	T	0.35	0.0634	0.0120	1.42E-07	60167.8	5	Quiescent/Low
rs12680075	129148524	C	T	0.67	0.0691	0.0147	2.71E-06	60170.88	6	Quiescent/Low
rs2542418	129149638	C	T	0.49	0.0627	0.0132	2.13E-06	60170.13	6	Quiescent/Low
rs2648832	129150668	C	A	0.26	0.0560	0.0113	6.60E-07	60167.73	3a	Quiescent/Low
rs7814495	129161453	C	G	0.71	0.0690	0.0147	2.60E-06	60170.94	5	Quiescent/Low
rs10956412	129162497	C	A	0.75	0.0666	0.0135	7.58E-07	60170.86	4	enhancer
rs12676304	129163295	C	A	0.63	0.0606	0.0116	1.68E-07	60169.92	4	Quiescent/Low
rs759651	129164288	C	T	0.63	0.0603	0.0116	1.76E-07	60169.92	5	Quiescent/Low
rs1121948	129165056	G	A	0.77	0.0635	0.0122	2.01E-07	60170.61	5	Quiescent/Low
rs1121946	129165198	G	T	0.81	0.0718	0.0140	2.71E-07	60170.84	3a	Quiescent/Low
rs12675643	129165692	A	T	0.63	0.0608	0.0116	1.69E-07	60169.92	2b	Quiescent/Low
rs10956413	129167185	A	C	0.56	0.0518	0.0113	4.29E-06	60170.69	4	Quiescent/Low
rs7001706	129169758	C	G	0.56	0.0507	0.0112	6.08E-06	60170.75	2b	Quiescent/Low
rs16893186	129170026	C	T	0.56	0.0522	0.0112	3.43E-06	60170.64	4	enhancer
rs2608029	129170126	G	C	0.37	0.0521	0.0103	4.04E-07	60168.57	5	enhancer
rs10956414	129172633	A	G	0.82	0.0708	0.0138	3.12E-07	60170.88	5	Weak transcription
rs1875028	129173675	C	G	0.56	0.0518	0.0112	3.98E-06	60170.68	3a	Weak transcription
rs7002044	129177370	A	C	0.56	0.0518	0.0112	3.96E-06	60170.68	5	Weak transcription
rs10956415	129179621	A	C	0.56	0.0522	0.0112	3.34E-06	60170.63	4	enhancer
rs1499364	129179926	G	A	0.59	0.0558	0.0114	8.74E-07	60170.35	2a	enhancer
rs12546580	129180513	A	G	0.59	0.0560	0.0114	8.16E-07	60170.34	4	enhancer
rs7006455	129181367	T	C	0.6	0.0567	0.0113	5.73E-07	60170.25	5	enhancer
rs11778142	129183417	C	T	0.9	0.0704	0.0135	1.99E-07	60170.95	5	Weak transcription
rs12542202	129184555	A	G	0.9	0.0696	0.0134	2.24E-07	60170.94	2b	enhancer
rs1902789	129185104	G	A	0.62	0.0577	0.0113	3.62E-07	60170.17	6	enhancer
rs72722756	129186110	C	T	0.99	0.0720	0.0131	4.14E-08	60170.92	2b	enhancer
rs7825555	129186266	T	A	0.62	0.0576	0.0113	3.73E-07	60170.18	5	Weak transcription

rs28597394	129190148	G	A	0.61	0.0544	0.0113	1.46E-06	60170.59	5	enhancer
rs10956416	129190290	C	T	0.62	0.0579	0.0113	3.06E-07	60170.11	5	enhancer
rs6999335	129192584	G	A	0.62	0.0574	0.0113	3.73E-07	60170.19	5	enhancer
rs6999897	129192710	A	G	0.62	0.0575	0.0113	3.67E-07	60170.19	5	enhancer
rs10808567	129192961	T	G	0.62	0.0580	0.0113	2.76E-07	60170.07	5	enhancer
rs11780156	129194641	T	C	-	0.0714	0.0130	4.07E-08	60170.95	5	enhancer
rs56152647	129195921	A	G	0.62	0.0577	0.0113	3.48E-07	60170.18	4	enhancer
rs6470608	129196570	G	C	0.62	0.0578	0.0113	2.92E-07	60170.1	5	enhancer
rs6992491	129197903	G	C	0.62	0.0575	0.0113	3.62E-07	60170.2	4	enhancer
rs55929956	129199261	A	G	0.62	0.0576	0.0113	3.53E-07	60170.18	5	Quiescent/Low
rs56354710	129199352	A	T	0.55	0.0633	0.0124	2.98E-07	60169.72	5	Quiescent/Low
rs1016578	129199566	A	G	1	0.0718	0.0131	4.37E-08	60170.91	4	Quiescent/Low
rs3802173	129199914	T	G	0.62	0.0577	0.0113	2.98E-07	60170.1	5	Quiescent/Low
rs3802172	129199915	T	C	0.62	0.0577	0.0113	2.99E-07	60170.1	5	Quiescent/Low
rs992241	129203312	C	A	0.61	0.0570	0.0113	4.48E-07	60170.25	3a	Quiescent/Low
rs16902714	129203826	T	C	0.61	0.0571	0.0113	4.18E-07	60170.21	5	Quiescent/Low
rs16902715	129203857	T	C	0.61	0.0573	0.0113	3.78E-07	60170.15	5	Quiescent/Low
rs10106296	129205610	A	G	0.54	0.0516	0.0110	2.86E-06	60170.49	4	Quiescent/Low
rs7836152	129211415	A	G	0.84	0.0634	0.0126	4.61E-07	60170.95	6	Weak transcription
rs12550618	129212443	T	C	0.54	0.0522	0.0111	2.59E-06	60170.49	6	Weak transcription
rs11776408	129215220	C	G	0.54	0.0522	0.0111	2.51E-06	60170.48	6	enhancer
rs11776569	129215700	T	G	0.84	0.0630	0.0125	4.23E-07	60170.95	5	enhancer
rs11989994	129217909	T	C	0.54	0.0523	0.0111	2.37E-06	60170.45	4	Quiescent/Low
rs11997192	129218127	G	A	0.84	0.0629	0.0124	4.39E-07	60170.95	4	Quiescent/Low
rs72722788	129219611	A	C	0.84	0.0631	0.0125	4.95E-07	60170.95	5	Quiescent/Low
rs9283955	129219805	C	G	0.54	0.0520	0.0110	2.44E-06	60170.44	5	Quiescent/Low
rs1967315	129224182	A	G	0.53	0.0523	0.0111	2.60E-06	60170.43	6	Quiescent/Low
rs2909242	129224680	A	C	0.34	-0.0443	0.0101	1.21E-05	60169.94	6	Quiescent/Low
rs16902734	129225868	T	C	0.32	0.0470	0.0118	7.04E-05	60170.4	4	Quiescent/Low
rs56161112	129227921	G	C	0.33	0.0478	0.0119	6.28E-05	60170.38	6	Quiescent/Low
rs12541578	129238347	G	C	0.32	0.0477	0.0119	6.34E-05	60170.37	5	Quiescent/Low

rs12541389	129243389	T	C	0.32	0.0477	0.0119	6.23E-05	60170.36	4	Quiescent/Low
rs10492294	129246415	C	T	0.32	0.0475	0.0118	6.03E-05	60170.35	5	Quiescent/Low

^a r² for linkage disequilibrium with the index SNP rs11780156 (Signal 5 in text) computed with data of European ancestry women controls.

^b Per allele effect (beta), standard error (se) and significance were estimated from univariate logistic regression, adjusted for age, study site and principal components.

^c Results from likelihood test under a glm model which includes covariates age, study site, principal components and the signal or its correlated SNP.

^d Score from the estimates in the Regulome database. 2a: TF binding + matched TF motif + matched DNase Footprint + DNase peak; 2b: TF binding + any motif + DNase Footprint + DNase peak; 3a: TF binding + any motif + DNase peak; 4: TF binding + DNase peak; 5: TF binding or DNase peak; 6: other functional support data. For details, see <http://www.regulomedb.org/index>.

^e Implied regulatory chromatin state from ENCODE data, for details see HaploReg database website <http://www.broadinstitute.org/mammals/haploreg/haploreg.php>.