

Detection and replication of epistasis influencing transcription in humans

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Abstract

Epistasis is the phenomenon whereby one polymorphism’s effect on a trait depends on other polymorphisms present in the genome. The extent to which epistasis influences complex traits¹ and contributes to their variation^{2,3} is a fundamental question in evolution and human genetics. Though epistasis has been demonstrated in artificial gene manipulation studies in model organisms,^{4,5} and some examples have been reported in other species,⁶ few convincing examples exist for epistasis amongst natural polymorphisms in human traits.^{7,8} Its absence from empirical findings may simply be due to its low incidence in the genetic control of complex traits,^{2,3} but an alternative view is that it has previously been too technically challenging to detect due to statistical power and computational issues.⁹ Here we show that, using advanced computation techniques¹⁰ and a gene expression study design, many instances of epistasis are found between common single nucleotide polymorphisms (SNPs). In a cohort of 846 individuals with data on 7339 gene expression levels in peripheral blood, we found 501 significant pairwise epistatic interactions between common SNPs acting on the expression levels of 238 genes ($p < 2.91 \times 10^{-16}$). We tested the discovery interactions for replication in two independent data sets.^{11,12} Three hundred and forty-five interactions had replication interaction p -values that were more extreme than the 2.5% confidence interval of the distribution under the null hypothesis of no epistasis, with 30 significant at a conservative $p < 0.05$ Bonferroni level. There was evidence of functional enrichment for the interacting SNPs, for instance 44 of the genetic interactions are located within 2Mb of regions of known intra-cellular chromosome interactions¹³ ($p = 1.8 \times 10^{-10}$). Epistatic networks of three SNPs or more influence the expression levels of 129 genes, whereby one *cis*-acting SNP is modulated by several *trans*-acting SNPs. For example MBNL1 is influenced by an additive effect at rs13069559 which itself is masked by *trans*-SNPs on 14 different chromosomes, with nearly identical genotype-phenotype (GP) maps for each *cis-trans* interaction. This study presents the first evidence for multiple instances of epistatic genetic effects emerging from natural genetic variation in humans.

1 Main text

In the genetic analysis of complex traits it is usual for SNP effects to be estimated using an additive model where they are assumed to contribute independently and cumulatively to the mean of a trait. This framework has been successful in identifying thousands of associations,¹⁴ but to date there is little empirical exploration of the role that epistasis plays in the architecture of complex traits in humans,^{7,8} though its contribution to phenotypic variance is frequently the subject of debate.¹⁻³ Outside the prism of human association studies there is evidence for epistasis, not only at the molecular scale from artificially induced mutations⁴ but also at the evolutionary scale in fitness adaptation¹⁵ and speciation.¹⁶

Methods are now available to overcome the computational problems involved in searching for epistasis, but its detection still remains problematic due to reduced statistical power. For example increased dependence on linkage disequilibrium (LD) between causal SNPs and observed SNPs,^{17,18} increased model complexity in fitting interaction terms,¹⁹ and more extreme significance thresholds to account for increased multiple testing⁹ all make it more difficult to detect epistasis in comparison to additive effects. Thus, when combined with small genetic effect sizes, as is expected in most complex traits of interest,¹⁴ the power to detect epistasis diminishes rapidly. There are two simple ways to overcome this problem. One is by using extremely large sample sizes;²⁰ another is by analysing traits that are likely to have large effect sizes among common variants. Because our focus was to ascertain the extent to which instances of epistasis occur amongst natural genetic variation we designed a study around the latter approach and searched for epistatic genetic effects that influence gene expression levels. Transcription levels can be measured for thousands of genes. These traits are largely heritable but on average less polygenic than high level phenotypes,²¹ thus it is expected that many genetic effects will be relatively large, maximising the chance at detecting epistasis, should it exist.

In our discovery dataset (Brisbane Systems Genetics Study, BSGS²²) of 846 individuals genotyped at 528,509 SNPs, we exhaustively tested every pair of SNPs for genetic interactions against each of 7339 expression traits in peripheral blood. After stringent filtering and multiple testing correction (Methods) we identified 501 putative genetic interactions influencing the expression levels of 238 genes (Supplementary Table 5). Of the 501 discovery interactions, 434 had available data and passed filtering (Methods) in two independent replication datasets, Fehrmann¹² and the Estonian Genomics Centre University of Tartu (EGCUT),¹¹ in which we saw convincing evidence for replication. We used the summary statistics from the replication datasets to perform a meta analysis to obtain an independent p -value for the putative interactions, and 30 were significant after applying a Bonferroni correction for multiple testing (Table 1). These significant interactions exhibited remarkable similarity in GP maps between all three datasets (Figure 2).

In addition, using the meta analysis from the replication samples only, we observed that 316 of the remaining 404 discovery SNPs had replication interaction p -values more extreme than the 2.5% confidence interval of the distribution under the null distribution of no epistatic effects ($p < 1.0 \times 10^{-16}$, Figure 3 and Supplementary Figure S1). The congruence of the epistatic networks in discovery and replication datasets is shown in Figure 1, demonstrating that these complex genetic patterns are common even across independent datasets. A further replication was attempted using the Centre for Health Discovery and Wellbeing (CHDWB) dataset,²³ but only 27 of the SNP pairs passed filtering because the sample size was small ($n = 139$), and likely due to insufficient power we found no evidence for replication. It should be noted that although it is a necessary step to establish the veracity of the signals from the discovery set, replication of epistasis is theoretically difficult because the dependence on LD between observed SNPs and causal variants is up to three orders of magnitude

higher than it is for independent additive effects.^{17,18} Therefore these results are encouraging with regards to the detection and replication of epistasis.

Though seldom the focus of association studies, SNPs with known main effects are often tested for additive \times additive genetic interactions,⁹ but our analysis shows that this is unlikely to be the most effective strategy for its detection. The majority of our discovery interactions comprised of one SNP that was significantly associated with the gene expression level in the discovery dataset, and one SNP that had no previous association²¹ (439 out of 501, Methods). Only nine interactions were between SNPs that both had known main effects while 64 were between SNPs that had no known main effects. Additionally, we observed that the largest epistatic variance component for the 501 interactions was equally divided amongst additive \times additive, additive \times dominance, dominance \times additive and dominance \times dominance at the discovery stage ($p = 0.22$ for departure from expectation). This is not surprising because the patterns of epistasis used for statistical decomposition are not designed to resemble biological function.²⁴

Of the discovery interactions, 47 were *cis-cis* acting (both SNPs were on the same chromosome as the expression gene), 441 were *cis-trans*-acting, and 13 were *trans-trans*-acting. We observed a wide range of significant GP maps (Figure 2) but the most common pattern of epistasis that we detected involved a *trans*-SNP masking the effect of an additive *cis*-SNP. For example, MBNL1 (involved in RNA modification and regulation of splicing²⁵) has a *cis* effect at rs13069559 which in turn is controlled by 13 *trans*-SNPs and one *cis*-SNP that each exhibit a masking pattern, such that when the *trans*-SNP is homozygous for the masking allele the decreasing allele of the *cis*-SNP no longer has an effect (Supplementary Figure S5). Each of these interactions have evidence for replication in at least one dataset and six are significant at the Bonferroni level (Supplementary Figure S2). We see similar epistatic networks involving multiple *trans*-acting SNPs for other gene expression levels too, for example TMEM149 (Supplementary Figure S6), NAPRT1 (Supplementary Figure S7), TRAPPC5 (Supplementary Figure S8), and CAST (Supplementary Figure S9).

In total the 501 interactions comprised 781 unique SNPs, which we analysed for functional enrichment (Methods). We tested the SNPs for cell-type specific overlap with transcriptionally active chromatin regions, tagged by histone-3-lysine-4,3-methylation (H3K4me3) chromatin marks, in 34 cell types²⁶ (Supplementary Figure S4). There was significant enrichment for *cis*-acting SNPs in haematopoietic cell types only ($p < 1 \times 10^{-4}$ for the three tissues with the strongest enrichment after adjusting for multiple testing). However *trans*-acting SNPs did not show any tissue specific enrichment ($p > 0.1$ for all tissues). This difference between *cis* and *trans* SNPs suggests different roles in which epistasis might arise where the *cis*-SNPs provide tissue specificity in these interactions. There is also strong enrichment for SNPs to be localised in enhancer regions,²⁷ consistent for both *cis* and *trans* SNPs ($p < 1 \times 10^{-6}$).

We also demonstrate spacial organisation of interacting loci suggesting a mechanism by which biological function can lead to epistatic genetic variance. It has been shown that different chromosomal regions spatially colocalise in the

cell through chromatin interactions.¹³ We cross-referenced our epistatic SNPs with a map of chromosome interacting regions ($n = 96,139$) in K562 blood cell lines²⁸ (Methods) and found that 44 epistatic interactions mapped to within 2Mb ($p < 1.8 \times 10^{-10}$), (Supplementary Figure S10). Interaction of distant loci may occur through physical proximity in transcriptional factories that organise across different chromosome regions and can regulate transcription of related genes.^{29,30}

Though we present many instances of epistasis, quantifying its relative importance to complex traits in humans remains an open question. In this study we are able to identify 238 gene expression traits with at least one significant interaction given our experiment-wide threshold. How does this compare to the number of traits influenced by additive effects? The BSGS dataset has been previously analysed for additive effects at all expression traits,²² and if we take all the additive eQTLs that were significant at the epistatic threshold of $p < 2.91 \times 10^{-16}$ we find that 453 gene expression levels out of the 7339 analysed had at least one significant expression quantitative trait locus (eQTL). Therefore it can be argued that the number of instances of detectable epistasis are substantial.

However in terms of their contribution to complex traits a more important metric might be the proportion of the variance that the epistatic loci explain.² Ideally one would approach this question from a whole genome perspective³¹ but this is intractable for non-additive variance components. Nevertheless, some inference can be made from the ascertained effects in these analyses and it is evident that additive variance is overall a larger component than epistatic variance, as has been argued previously.^{2,3} Taking the additive effects detected in Powell *et al* (2012) at the $p < 2.91 \times 10^{-16}$ threshold, we calculate that on average they explain 1.73% of the phenotypic variance of each of the 7339 probes. By contrast, the epistatic variance from the interacting SNPs detected in this study on average explain 0.25% of phenotypic variance, approximately seven times lower than the additive variance (Methods). There are several caveats to this comparison. Firstly, the ratio of additive to epistatic variance may differ at different effect sizes, and our estimate is determined by the threshold used. Secondly, the power of a 1 *d.f.* test exceeds that of an 8 *d.f.* test. And thirdly, the non-additive variance at causal variants is expected to be underestimated by observed SNPs in comparison to estimates for additive variance, due to differences in the rate of decay of the estimate of the genetic variance of the causal SNPs as LD decreases with the observed SNPs.

Overall, we have demonstrated that it is possible to identify and replicate epistasis in complex traits amongst common human variants. The bioinformatic analysis of the significant epistatic loci suggests that there are a large number of possible mechanisms that can lead to non-additive genetic variation. Further research into such epistatic effects may provide a useful framework to understanding molecular mechanisms and complex trait variation in greater detail. With computational techniques and data now widely available the search for epistasis in larger datasets for traits of broader interest is warranted.

1.1 Methods Summary

We searched for pairwise epistasis exhaustively in the BSGS discovery dataset,²² which comprises 846 individuals who are genotyped at 528,509 autosomal SNPs and who have gene expression levels measured in peripheral blood samples for 7,339 probes representing 6,158 RefSeq genes. Recent hardware and software¹⁰ advances made it possible to perform the 1.03×10^{15} statistical tests to complete this analysis. We used permutation analysis³² to calculate an experiment-wide significance threshold of $T_e = 2.91 \times 10^{-16}$ at the 5% family-wise error rate (FWER). SNP pairs were modelled for full genetic effects, including marginal additive and dominance at both SNPs plus four interaction terms. Though we could have used a less complex model to improve statistical efficiency, we deemed it important to be agnostic about the type of epistasis that might exist, and therefore chose not to over-parameterise the test.^{18,19} Because there are many large marginal effects present in these data it was necessary to perform several filtering steps to exclude SNP pairs that were significant due to marginal effects alone. All SNP pairs with LD $r^2 > 0.1$ and $D'^2 > 0.1$ were removed to minimise the possibility of haplotype effects. All SNP pairs were required to have at least five data points in all nine genotype classes. If multiple SNP pairs were present on the same chromosomes for a particular expression trait then only the sentinel SNP pair was retained. Finally, a nested test contrasting the full genetic model against the marginal additive and dominance model was performed for each remaining SNP pair (Methods), resulting in 501 significant interactions after Bonferroni correction for multiple testing of the filtered SNPs. The significant SNP pairs were carried forward for replication in two independent datasets that used the same expression assays for analysing transcription in peripheral blood, the Fehrmann dataset¹² ($n = 1240$) and the Estonian Genome Centre University of the University of Tartu (EGCUT) dataset¹¹ ($n = 891$). Of these, 434 passed filtering in both replication datasets. A meta analysis on the interaction p -values from each replication dataset was performed to provide an overall replication statistic for each putative interaction.

1.2 Acknowledgements

We are grateful to the volunteers for their generous participation in these studies. We thank Bill Hill, Chris Haley and Lars Ronnegard for helpful discussions and comments.

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2 Tables

Table 1: Epistatic interactions significant at the Bonferroni level in two replication sets

	Gene (chr.)	SNP 1 (chr.)	SNP 2 (chr.)	BSGS ²	Fehrmann ³	EGCUT ³	Meta ⁴
1	ADK (10)	rs2395095 (10)	rs10824092 (10)	6.69 ¹	18.33 ¹	21.21 ¹	39.82 ¹
2	ATP13A1 (19)	rs4284750 (19)	rs873870 (19)	5.30	12.18	3.25	14.23
3	C21ORF57 (21)	rs9978658 (21)	rs11701361 (21)	9.42	6.08	16.36	21.67
4	CSTB (21)	rs9979356 (21)	rs3761385 (21)	11.99	25.20	16.72	42.27
5	CTSC (11)	rs7930237 (11)	rs556895 (11)	7.16	18.76	15.06	33.53
6	FN3KRP (17)	rs898095 (17)	rs9892064 (17)	16.16	28.24	29.39	59.95
7	GAA (17)	rs11150847 (17)	rs12602462 (17)	13.91	19.98	12.99	32.60
8	HNRPH1 (5)	rs6894268 (5)	rs4700810 (5)	15.38	8.55	3.01	10.37
9	LAX1 (1)	rs1891432 (1)	rs10900520 (1)	19.16	18.60	11.22	29.24
10	MBNL1 (3)	rs16864367 (3)	rs13079208 (3)	13.49	16.25	24.74	41.56
11	MBNL1 (3)	rs7710738 (5)	rs13069559 (3)	7.92	2.55	7.89	9.28
12	MBNL1 (3)	rs2030926 (6)	rs13069559 (3)	7.10	0.91	5.80	5.53
13	MBNL1 (3)	rs2614467 (14)	rs13069559 (3)	5.74	4.13	2.22	5.30
14	MBNL1 (3)	rs218671 (17)	rs13069559 (3)	7.63	0.62	5.82	5.23
15	MBNL1 (3)	rs11981513 (7)	rs13069559 (3)	7.71	0.43	5.36	4.58
16	MBP (18)	rs8092433 (18)	rs4890876 (18)	5.40	7.06	21.91	28.73
17	NAPRT1 (8)	rs2123758 (8)	rs3889129 (8)	8.45	15.12	16.08	30.77
18	NCL (2)	rs7563453 (2)	rs4973397 (2)	7.31	7.51	6.33	12.70
19	PRMT2 (21)	rs2839372 (21)	rs11701058 (21)	4.81	0.69	4.47	4.06
20	RPL13 (16)	rs352935 (16)	rs2965817 (16)	4.98	3.79	14.41	17.24
21	SNORD14A (11)	rs2634462 (11)	rs6486334 (11)	7.31	13.11	10.96	23.22
22	TMEM149 (19)	rs807491 (19)	rs7254601 (19)	12.16	81.55	45.78	145.78
23	TMEM149 (19)	rs8106959 (19)	rs6926382 (6)	5.80	3.06	8.80	10.72
24	TMEM149 (19)	rs8106959 (19)	rs914940 (1)	6.22	3.36	6.96	9.20
25	TMEM149 (19)	rs8106959 (19)	rs2351458 (4)	7.30	0.04	9.61	8.00
26	TMEM149 (19)	rs8106959 (19)	rs6718480 (2)	8.55	3.31	5.15	7.36
27	TMEM149 (19)	rs8106959 (19)	rs1843357 (8)	6.21	3.72	3.33	6.00
28	TMEM149 (19)	rs8106959 (19)	rs9509428 (13)	9.44	0.10	5.75	4.47
29	TRA2A (7)	rs7776572 (7)	rs11770192 (7)	8.23	3.19	1.89	4.09
30	VASP (19)	rs1264226 (19)	rs2276470 (19)	5.09	0.94	5.14	4.95

¹ $-\log_{10} p$ -values for 4 *d.f.* interaction tests

² Discovery dataset

³ Independent replication dataset

⁴ Meta analysis of interaction terms between replication datasets only

3 Figures

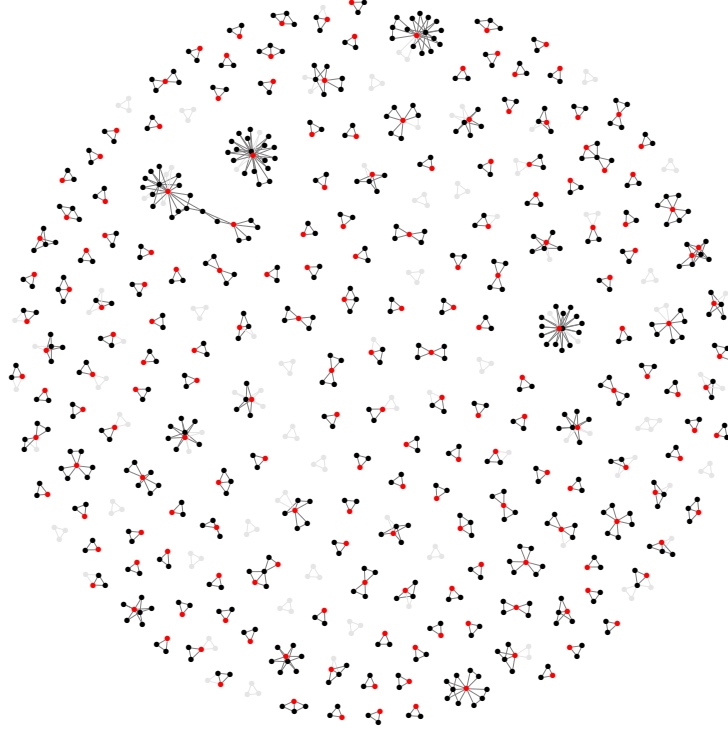


Figure 1: **Discovery and replication of epistatic networks** All 434 putative genetic interactions (edges) with data common to discovery and replication sets is shown, where black nodes represent SNPs and red nodes represent traits (gene expression probes). Three hundred and forty-five interactions had p -values exceeding the 2.5% confidence interval following meta analysis of the replication data, but the remaining 89 interactions that did not replicate are depicted in grey. It is evident that a large proportion of the complex networks identified in the discovery set also exist in independent populations.

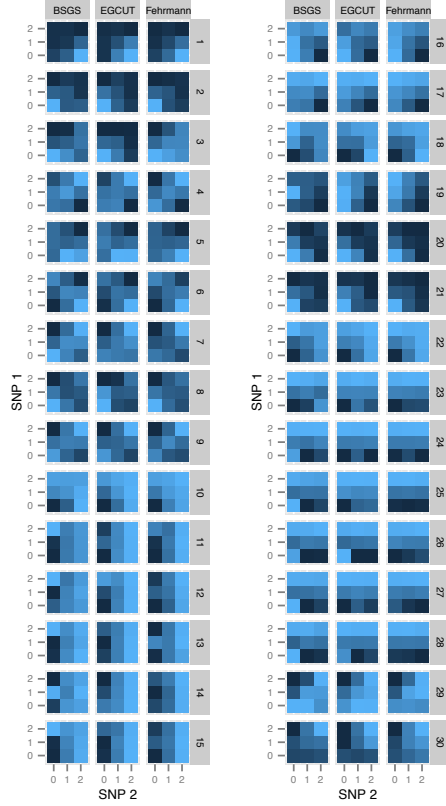


Figure 2: Replication of GP maps in two independent populations The GP maps for each epistatic interaction that is significant at the Bonferroni level in both replication datasets are shown. Each GP map consists of nine tiles where each tile represents the expression level for that two-locus genotype class. Phenotypes are for gene transcript levels (dark coloured tiles = low expression, light coloured tiles = high expression). Columns of GP maps are for each independent population. Rows of GP maps are for each of 30 significantly replicated interactions at the Bonferroni level, corresponding to the rows in Table 1. There is a clear trend of the GP maps replicating across all three datasets.

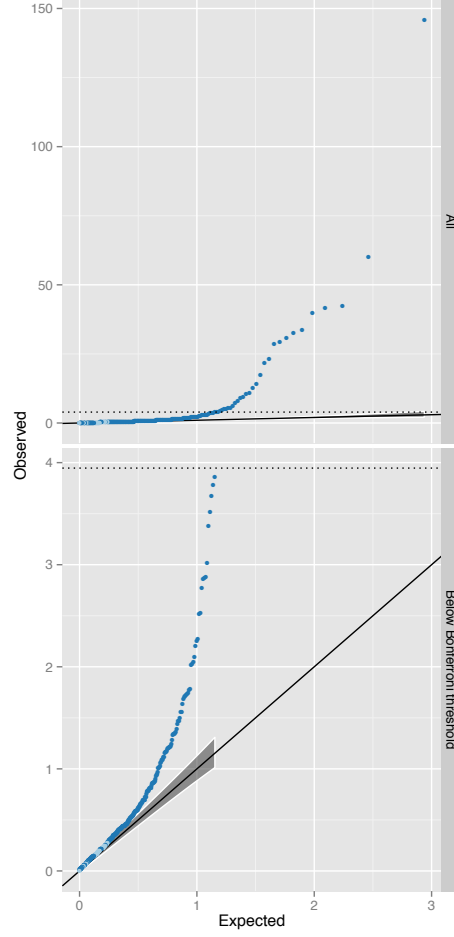


Figure 3: **Q-Q plots of interaction p -values from replication datasets** The top panel shows all 434 discovery SNPs that were tested for interactions. Observed p -values (y -axis, $-\log_{10}$ scale) are plotted against the expected p -values (x -axis, $-\log_{10}$ scale). The multiple testing correction threshold for significance following Bonferroni correction is denoted by a dotted line. The bottom panel shows the same data as the top panel but excluding the 30 interactions that were significant at the Bonferroni level in the replication datasets. The shaded grey area represents the 5% confidence interval for the expected distribution of p -values. Dark blue points represent p -values that exceed the confidence interval, light blue are within the confidence interval.

4 Supplementary Figures

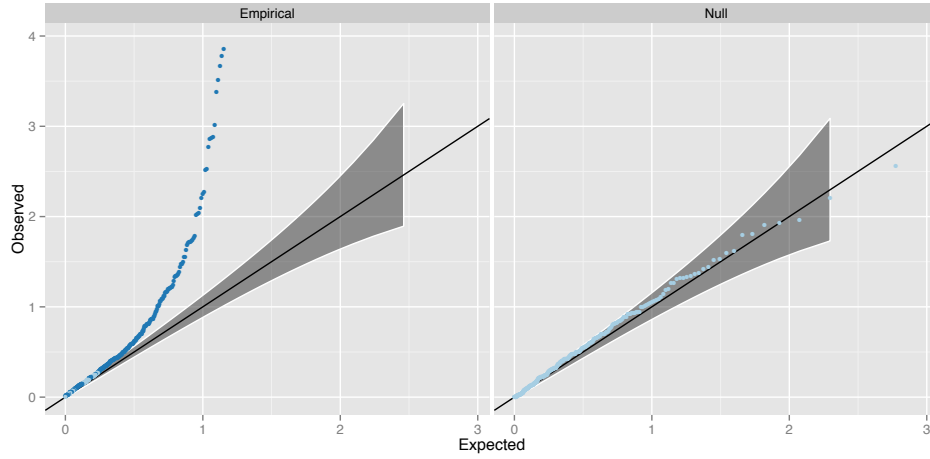


Figure S1: **Q-Q plots of interaction p -values from replication datasets, excluding the 30 points significant at the Bonferroni level** The right panel (Null) shows the interaction p -values from a meta analysis across two independent datasets on 434 randomly drawn SNP pairs. The left panel (Empirical) shows the interaction p -values from the 404 putative interactions that were not significant at the Bonferroni correction threshold. Dark blue points represent p -values that surpass the 2.5% FDR level, as in Figure 3.

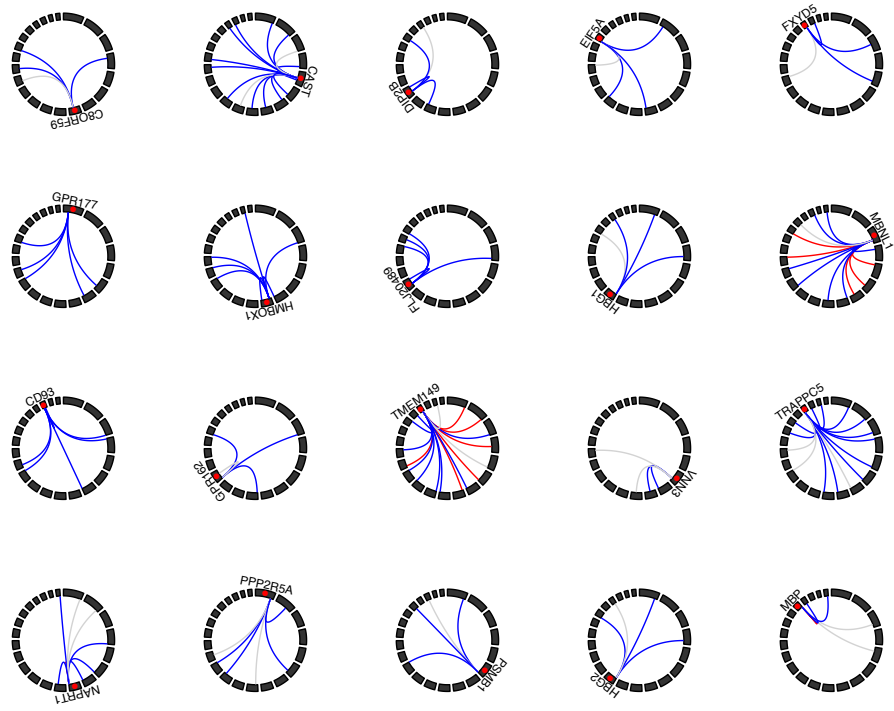


Figure S2: **Gene expression traits with four or more genetic interactions** Circle plots represent the genomic positions for SNPs (linking lines) and expression probes (red points). Chromosomes are represented by black blocks and ordered from 1 to 22 clockwise, starting from the top. Grey lines represent no evidence for replication, blue lines denote interactions that are outside the 97.5% confidence interval or the Q-Q plot (Figure 3), and red lines denote replication at the Bonferroni correction level. Most interactions are characterised as being *cis-trans* to the expression probe.

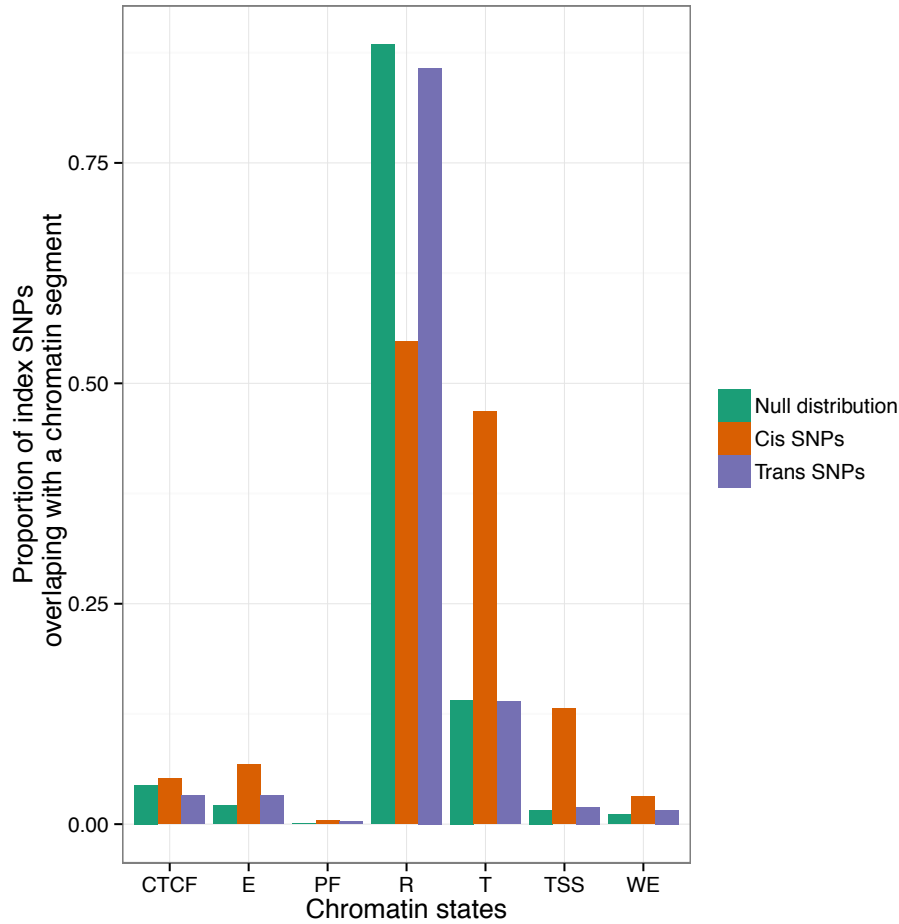


Figure S3: Location of SNPs relative to genomic features All SNPs within 1Mb and $r^2 > 0.8$ of each *cis*- and *trans*-SNP were taken to find which genomic features (x -axis) were covered by the SNPs that compose the 501 significant interactions. Green bars represent the proportion (y -axis) of the 528,509 SNPs used in the analysis that fall within the range of the different genomic features. There is enrichment for *cis*-acting SNPs (red bars) in promotor regions, but *trans*-acting SNPs (blue bars) are not enriched for genomic features. The labels on the x -axis are as follows: TSS = Predicted promoter region including TSS, PF = Predicted promoter flanking region, E = Predicted enhancer, WE = Predicted weak enhancer or open chromatin cis regulatory element, CTCF = CTCF enriched element, T = Predicted transcribed region, R = Predicted Repressed or Low Activity region

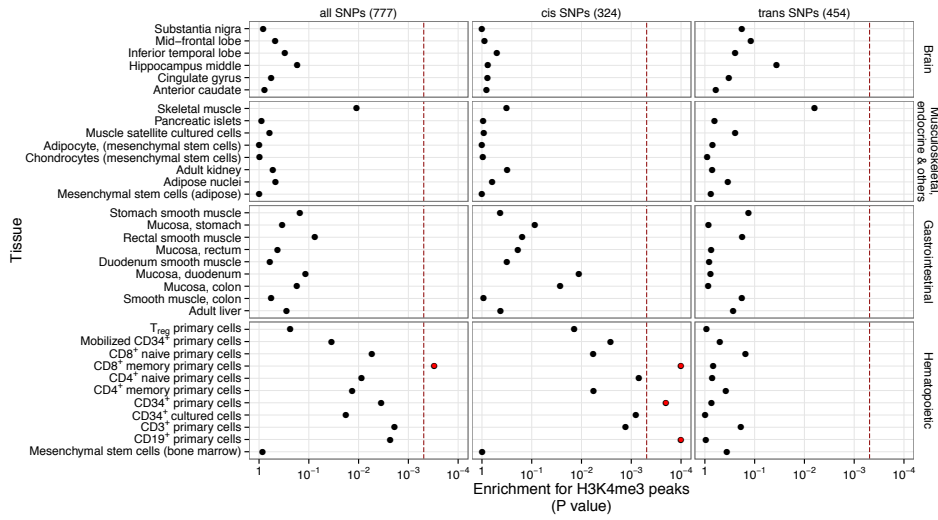


Figure S4: Tissue specific enrichment of SNPs in transcriptionally active regions The locations of transcriptional activity can be predicted by chromatin marks, assayed by H3K4me3.²⁶ Enrichment p -values are calculated using permutation analysis for 34 different cell types (y -axis) in four tissue types (Rows of boxes). There is enrichment for *cis*-acting SNPs in Haematopoietic tissue types only. *Trans*-acting SNPs have no tissue specificity.

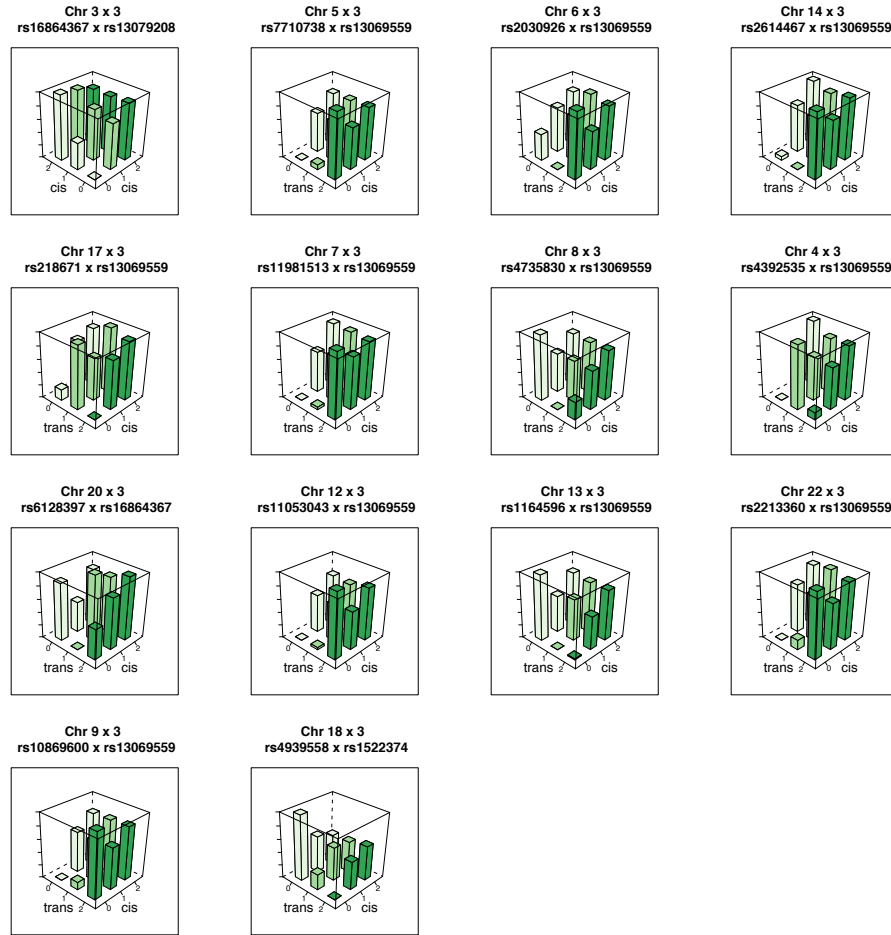


Figure S5: **Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions the *cis* effect is masked when the *trans* SNP is homozygous.

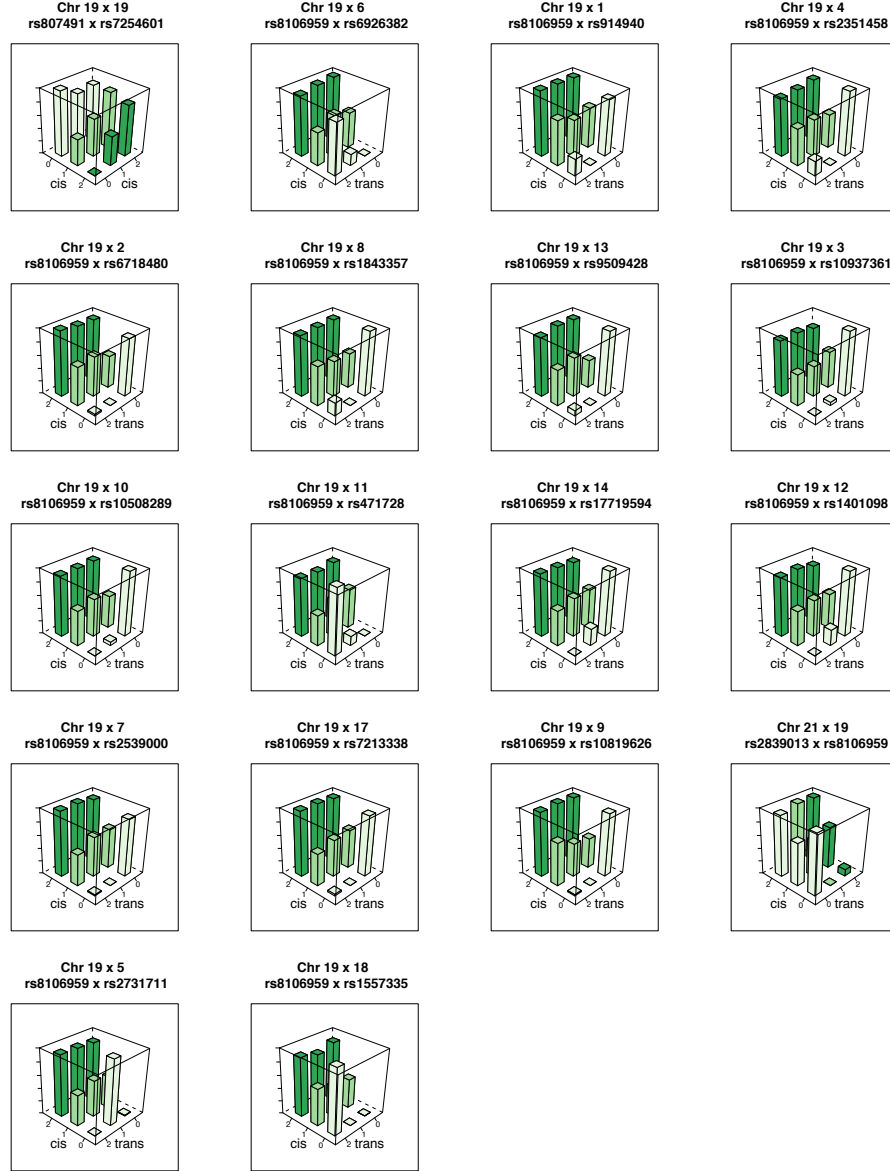


Figure S6: **Genotype-phenotype maps for 19 interactions influencing the expression of TMEM149** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of TMEM149, but in many of these interactions the *cis* effect is masked when the *trans* SNP is homozygous.

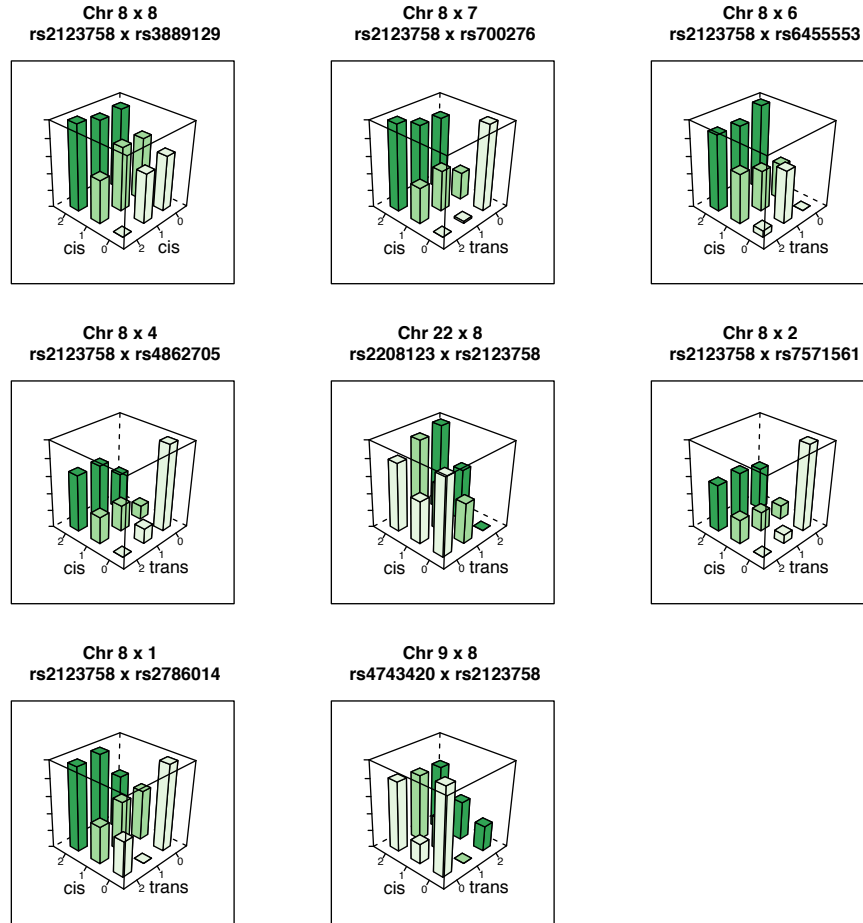


Figure S7: **Genotype-phenotype maps for 8 interactions influencing the expression of NAPRT1** Each bar represents the mean phenotypic value for individuals in that genotype class.

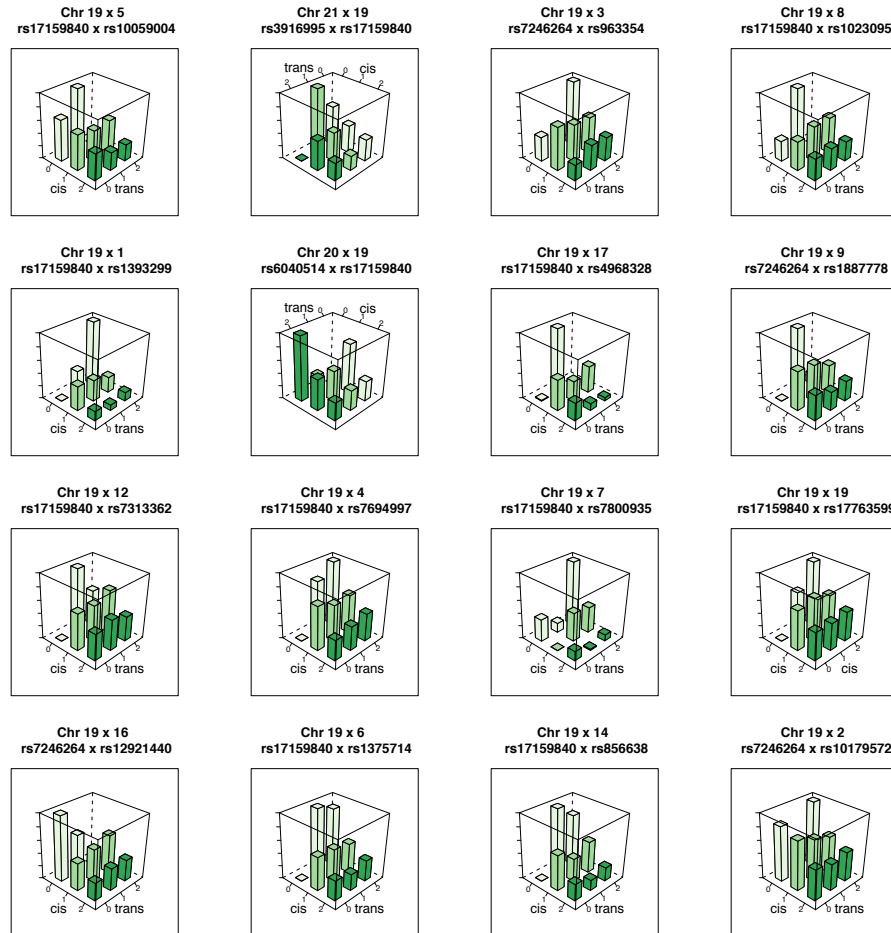


Figure S8: **Genotype-phenotype maps for 16 interactions influencing the expression of TRAPPC5** Each bar represents the mean phenotypic value for individuals in that genotype class.

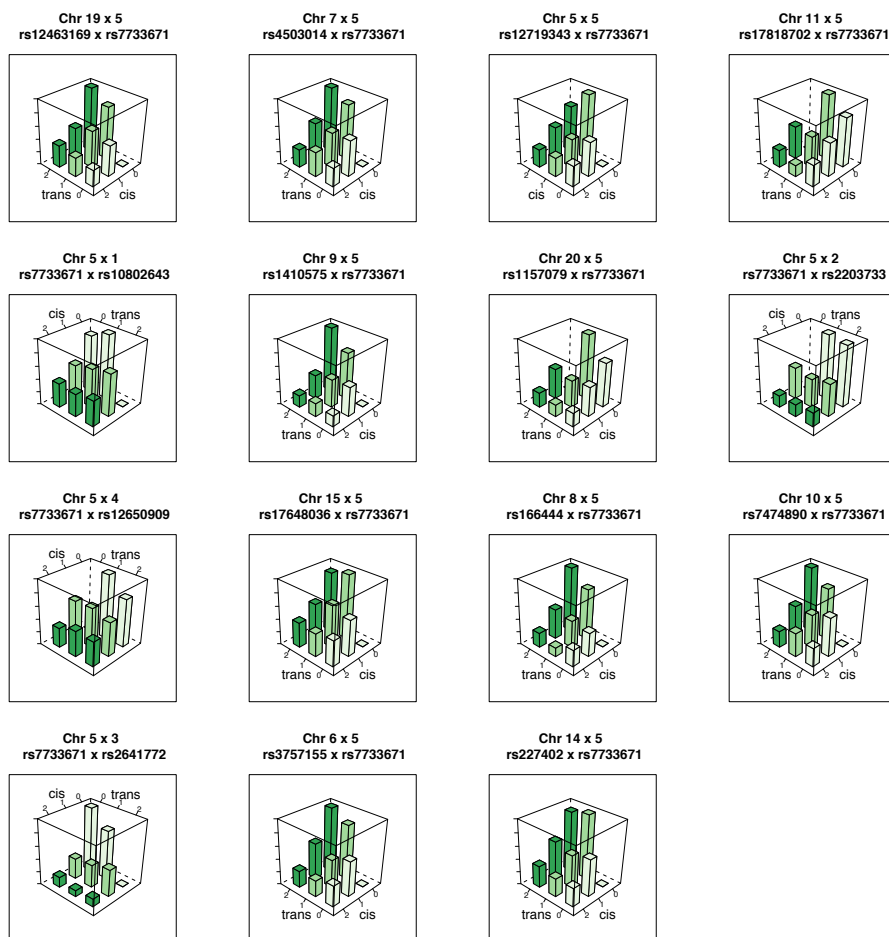


Figure S9: **Genotype-phenotype maps for 15 interactions influencing the expression of CAST** Each bar represents the mean phenotypic value for individuals in that genotype class.

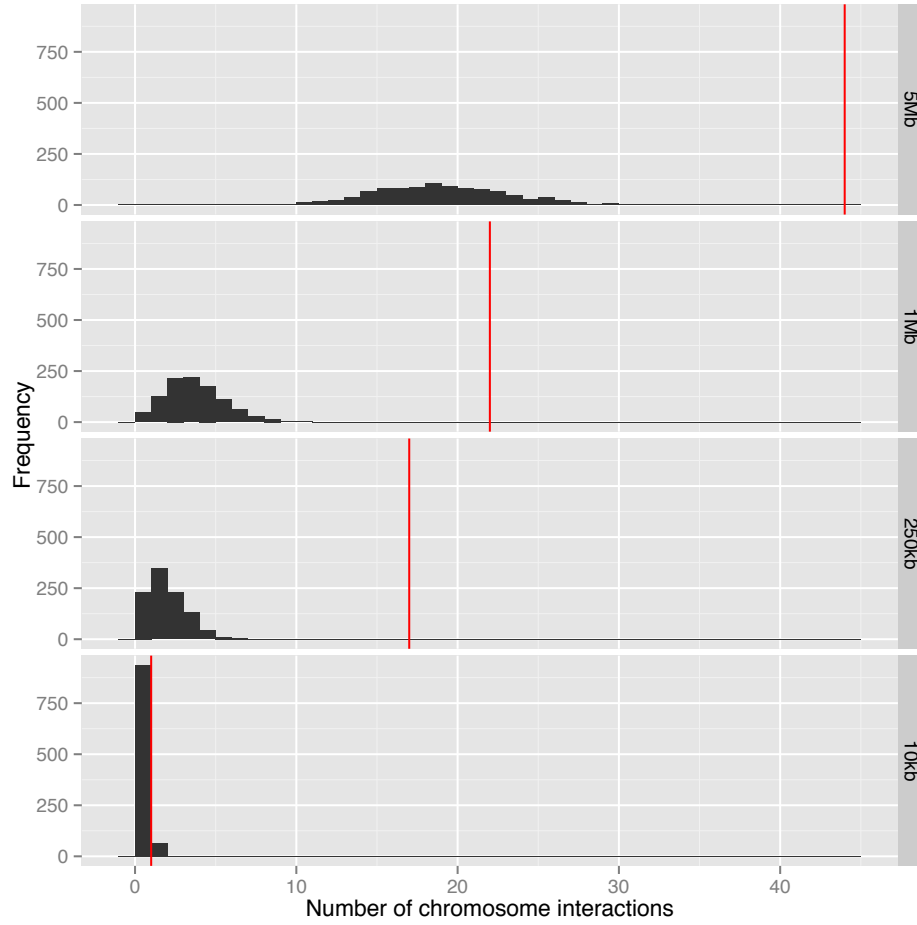


Figure S10: Number of overlaps between chromosome interactions and epistatic interactions Interacting chromosome regions may be a possible mechanism underlying epistatic interactions. The number of epistatic interactions within 20kb, 500kb, 2Mb and 10Mb of known chromosome interacting regions are shown by red vertical lines. The histograms represent the null distribution based on random sampling of 10,000 datasets for each window size.

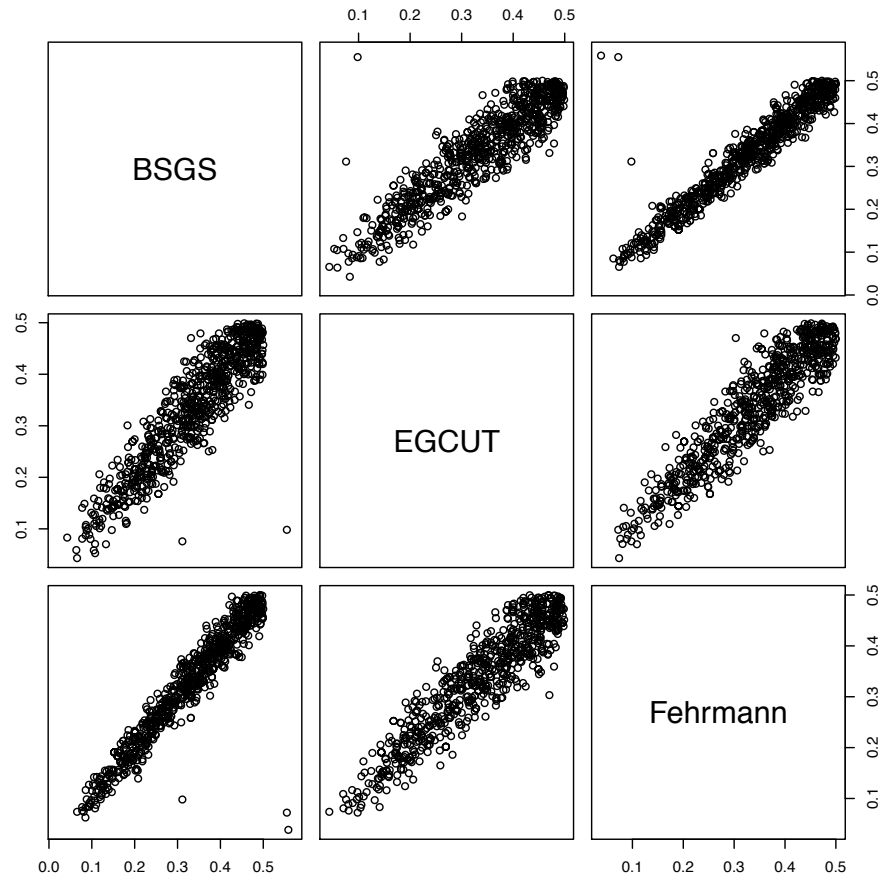


Figure S11: **Comparison of allele frequencies for 781 SNPs involved in genetic interactions across independent populations** Outliers were removed from the analysis as part of the filtering stage during replication.

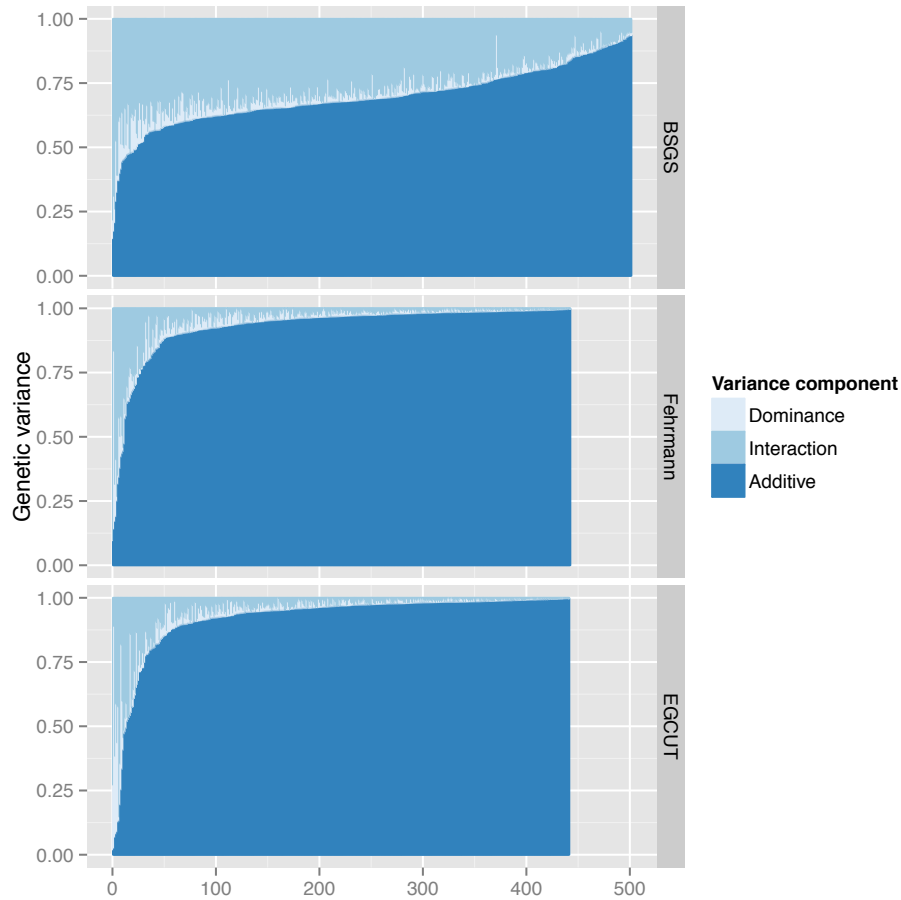


Figure S12: Comparison of variance distribution from different cohorts
How does the estimated variance decomposition change in different cohorts? The cumulative proportion of the genetic variance that is additive, dominant, or epistatic for each putative interaction is shown on the y -axis. BSGS has 501 interactions whereas Fehrmann and EGCUT have 434 (x -axis). The variance estimates are ordered from lowest additive to highest additive proportion. This is done independently for each cohort to depict the distribution of estimated effects.

5 Supplementary Tables

Table S1: Details on 501 interactions discovered in BSGS dataset

Expression trait			SNP 1				SNP 2				Interaction statistic / - log ₁₀ p-values				Distance / Mb ^h
Gene ID ^a	Probe ID ^b	Chr.	rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c	Association ^d	BSGS ^e	Fehrmann ^f	EGCUT ^g	Meta ^g	
ABCA7	ILMN.1743205	19	rs3752237	19	1047161	ABCA7	rs596183	6	158100199		5.82	0.38	0.02	0.09	0.517
ABCA7	ILMN.1743205	19	rs3752237	19	1047161	ABCA7	rs914737	9	139522101		5.50				
ABCC3	ILMN.1677814	17	rs9455	17	48771135	ABCC3	rs4732202	7	136057883		6.10	0.02	1.81	0.95	
ACAT1	ILMN.1800008	11	rs227064	11	108207393	ACAT1	rs4744894	9	72001517		6.59	1.04	1.78	2.02	
ADCK1	ILMN.1698777	14	rs12431896	14	78088813	ADCK1	rs4833241	4	122933691		5.59	0.36	1.14	0.87	
ADCK1	ILMN.1698777	14	rs8058066	16	88462550		rs12431896	14	78088813	ADCK1	6.58	2.04	0.83	2.05	
ADK	ILMN.2358626	10	rs2395095	10	76446305	ADK	rs10824092	10	75929517		6.69	18.33	21.21	39.82	
AGAP6	ILMN.3239130	10	rs2611512	10	51515534	AGAP8	rs2547996	5	95174319		6.22				
AHSA2	ILMN.1798308	2	rs10881585	9	137112421		rs842647	2	61119471		7.15	1.83	1.93	2.88	
AHSA2	ILMN.1798308	2	rs2523971	6	29938258	HLA-G	rs1177303	2	61388355	AHSA2	5.45	0.92	0.64	0.94	
AKTIP	ILMN.1665982	16	rs2896940	16	57721127		rs13332406	16	53489705	AKTIP	6.91	0.16	0.99	0.57	4.231
AKTIP	ILMN.1665982	16	rs7189819	16	53536345	AKTIP	rs1362032	7	125543391		5.93	0.71	0.20	0.42	
AKTIP	ILMN.1665982	16	rs7189819	16	53536345	AKTIP	rs1473017	4	179323762		6.18	0.27	0.30	0.23	
ALDH3A2	ILMN.2401641	17	rs3760489	17	19581009	ALDH3A2	rs11720112	3	161996349		6.26	0.33	1.37	1.01	
ANG	ILMN.1760727	14	rs9322855	14	21153299	ANG	rs4866516	5	3032625		5.75	0.02	0.20	0.04	
ANPEP	ILMN.1763837	15	rs11073891	15	90363995	ANPEP	rs3823523	7	154511163		5.85	0.44	1.09	0.90	
ANPEP	ILMN.1763837	15	rs11073891	15	90363995	ANPEP	rs6846031	4	178019148		6.31	0.47	0.17	0.26	
AP3B1	ILMN.1768867	5	rs6453374	5	77508159	AP3B1	rs4684443	3	4818792		5.94	0.05			
APPL2	ILMN.1765076	12	rs935251	12	105580918	APPL2	rs2769594	9	87918528		5.60	0.80	1.02	1.16	
ARL17B	ILMN.3231952	17	rs12947580	17	75768225		rs8079215	17	44064851	ARL17B	5.96				31.703
ARL17B	ILMN.3231952	17	rs2834541	21	35932619		rs8079215	17	44064851	ARL17B	6.65				
ARL17B	ILMN.3231952	17	rs8079215	17	44064851	ARL17B	rs1950646	14	94722497		7.64				
ARL17B	ILMN.3231952	17	rs8079215	17	44064851	ARL17B	rs2197777	12	125831219		6.26				
ARL17B	ILMN.3231952	17	rs8079215	17	44064851	ARL17B	rs2684789	15	99492045		5.98				
ARL17B	ILMN.3231952	17	rs8079215	17	44064851	ARL17B	rs9834627	3	191203546		5.72				
ATP13A1	ILMN.2134224	19	rs4284750	19	19810050		rs873870	19	19738554		5.30	12.18	3.25	14.23	
BID	ILMN.1763386	22	rs8919	22	18213057	BID	rs9804943	12	129906275		5.84	0.06	0.40	0.14	
BID	ILMN.2372413	22	rs181405	22	18233000		rs10888267	1	248059423		6.60	0.87	0.16	0.50	
C11ORF17	ILMN.1752988	11	rs2568061	11	8886260	C11ORF17	rs6553184	4	189150656		5.66	1.15	0.04	0.54	0.071
C13ORF18	ILMN.2196550	13	rs2110603	16	6259852		rs674754	13	46913416	C13ORF18	6.66	0.28	0.28	0.22	
C13ORF18	ILMN.2196550	13	rs674754	13	46913416	C13ORF18	rs6857876	4	153610164		3.87	0.38	0.50	0.43	
C14ORF173	ILMN.2393450	14	rs11089825	22	37575398		rs4983382	14	105189504	C14ORF173	6.02	0.60	0.84	0.85	
C14ORF173	ILMN.2393450	14	rs3935344	15	92276674		rs4983382	14	105189504	C14ORF173	5.98	0.31	0.28	0.24	
C14ORF173	ILMN.2393450	14	rs4983382	14	105189504	C14ORF173	rs10754644	1	238724741		7.15	0.42	0.34	0.35	
C14ORF4	ILMN.1804396	14	rs1293455	18	13819673		rs2655991	14	77574438		4.87				
C14ORF4	ILMN.1804396	14	rs2655991	14	77574438		rs10972462	9	35427324		4.32				
C14ORF4	ILMN.1804396	14	rs2655991	14	77574438		rs6445340	3	63371601		4.40				
C14ORF4	ILMN.1804396	14	rs2655991	14	77574438		rs9787151	1	63179138		4.05				
C14ORF4	ILMN.1804396	14	rs4793445	17	70416307		rs2655991	14	77574438		3.85				0.263
C14ORF4	ILMN.1804396	14	rs6010061	22	51151724		rs2655991	14	77574438		4.61				
C14ORF4	ILMN.1804396	14	rs7245800	19	52083552		rs2655991	14	77574438		4.69				
C17ORF60	ILMN.1747347	17	rs9907897	17	63502633		rs7405659	17		C17ORF60	6.79	0.53	0.05	0.19	
C1ORF86	ILMN.1726989	1	rs2334323	6	110577257		rs2257182	1	2082566	C1ORF86	5.90	0.01	0.50	0.13	
C1ORF86	ILMN.2097790	1	rs2279474	18	46384412		rs2460002	1	2119833	C1ORF86	5.65		0.03		
C1ORF86	ILMN.2097790	1	rs7188668	16	25711358		rs2460002	1	2119833	C1ORF86	5.59	0.29	0.50	0.37	
C21ORF57	ILMN.1795836	21	rs4819271	21	48052838		rs901964	12	48676038	ZNF641	4.91	0.65	0.08	0.28	
C21ORF57	ILMN.1795836	21	rs9978658	21	48027084		rs11701361	21	47764477		9.42	6.08	16.36	21.67	
C5ORF4	ILMN.1728742	5	rs1122762	18	45866512		rs286595	5	154348552	C5ORF4	5.55	0.72	0.04	0.27	
C8ORF59	ILMN.1653205	8	rs12429804	13	36577930		rs2896452	8	86102223	C8ORF59	5.49	0.29	0.02	0.07	0.263
C8ORF59	ILMN.1653205	8	rs12454561	18	31272238		rs2896452	8	86102223	C8ORF59	5.45	0.31			
C8ORF59	ILMN.1653205	8	rs2896452	8	86102223	C8ORF59	rs1004564	4	55242625		7.62	0.38	0.18	0.21	
C8ORF59	ILMN.1653205	8	rs7152284	14	52273663		rs2896452	8	86102223	C8ORF59	5.67	2.18	0.07	1.33	

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Table S1 – continued from previous page

Gene ID ^a	Expression trait	Probe ID ^b	Chr.	rs ID	Chr.	SNP 1	Pos/Mb ^c	Association ^d	rs ID	Chr.	SNP 2	Pos/Mb ^c	Association ^d	BSGS ^e	Interaction statistic ^f	EGCUT ^g	Distance / Mb ^h
C8ORF59	ILMN-1653205	8	rs8051751	16	7188323	16	7188323	rs2890452	rs2890452	8	86102223	86102223	C8ORF59	5.79	1.39	0.18	0.87
C9ORF72	ILMN-1741881	9	rs10122902	9	27556780	9	27556780	rs2526068	rs2526068	1	242029101	242029101	CABC1	6.36	0.96	0.01	0.37
CABC1	ILMN-1731064	1	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.00	0.34
CAD9	ILMN-1712532	9	rs4266763	9	139289825	9	139289825	rs6540410	rs6540410	1	82128660	82128660	INPP5E	5.81	0.81	0.00	0.86
CAD9	ILMN-1712532	9	rs4573661	11	6076661	11	6076661	rs4077315	rs4077315	9	139266496	139266496	INPP5E	7.61	0.09	0.86	0.42
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs12765847	10	4353808	10	4353808	rs3758725	rs3758725	1	227174210	227174210	CABC1	6.36	0.94	0.01	0.37
CAD9	ILMN-1712532	9	rs1														

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Table S1 – continued from previous page

Gene ID ^a	Expression trait	Probe ID ^b	Chr.	rs ID	Chr.	SNP 1	Pos/Mb ^c	Association ^d	rs ID	Chr.	SNP 2	Pos/Mb ^c	Association ^d	BSGS ^e	Interaction statistic ^f	-log ₁₀ p-values	MetaSig	Distance / Mb ^g
CPVL	ILMN-1682928	7	rs2835998	21	39202070	7	29188475	CPVL	rs2835884	7	29188475	0.19	0.03	5.55	0.19	0.03	0.04	
CRPT1	ILMN-1813256	20	rs2131290	4	188859908	2	46843651	CRPT1	rs1531133	2	46843651	0.28	0.10	5.47	0.28	0.10	0.12	
CRPT2	ILMN-1737685	2	rs6139887	20	5986234		62406408		rs1473927	21	2320	0.36	0.15	6.18	0.36	0.15		
CTSB	ILMN-1761797	17	rs8979356	18	43250974				rs3761385	21	15199	16.72	42.27	11.99	25.20	16.72	42.27	0.033
CTNNA1	ILMN-1804834	1	rs2949034	18	6920090305				rs1763882	5	13824268735				5.74	0.02	0.41	0.11
CTNNA1	ILMN-1606347	11	rs2457684	18	8829983				rs1793264	10	108670392	0.32	0.4	7.16	0.32	0.4	0.33	
CTSC	ILMN-1722433	22	rs2955557	22	2955557				rs1793264	10	108670392	0.32	0.4	7.16	0.32	0.4	0.33	
CTSC	ILMN-2242463	11	rs7049237	11	88117965				rs5568982	11	880774179	18.76	15.06	7.16	18.76	15.06	33.53	0.040
GWFL19L1	ILMN-1651886	10	rs7108734	11	11456927				rs12784396	10	102027407	0.21	0.03	5.42	0.21	0.03		
CYBRD1	ILMN-1721305	2	rs25092948	4	129994690				rs888427	2	172368120	0.23	0.53	5.89	0.23	0.53	0.34	
CYBRD1	ILMN-1712905	2	rs7852475	9	14698856				rs888427	2	172368120	0.20	0.02	5.68	0.20	0.02	0.04	
CYBRD1	ILMN-2087692	2	rs11257679	10	12318284				rs888427	2	172368120	0.39	1.87	5.81	0.39	1.87	1.47	
CYBRD1	ILMN-2087692	2	rs6137908	20	23344590				rs888427	2	172368120	0.05	0.83	5.53	0.05	0.83	0.36	
CYBRD1	ILMN-2087692	2	rs888427	20	23344590				rs7591849	2	160112881	0.87	0.10	5.85	0.87	0.10	0.44	
CYP27A1	ILMN-1704985	2	rs6021982	20	36571928				rs933994	2	219650616	0.29	0.86	5.42	0.29	0.86	0.60	
DAB2	ILMN-2128428	5	rs7778910	7	110451383				rs352523	5	39381357	0.48	0.44	5.44	0.48	0.44	0.44	
DDT	ILMN-1811648	17	rs9900173	17	43111688				rs1343244	6	82076988	0.64	0.00	5.62	0.64	0.00	0.58	0.14
DDT	ILMN-1690982	22	rs5767102	22	2448761				rs2378341	3	187475208	0.92	0.25	5.62	0.92	0.25	0.42	
DDX58	ILMN-1797001	9	rs4937097	11	125962645				rs7042042	9	32451144	0.61	0.29	5.41	0.61	0.29	0.41	
DEM1	ILMN-1783996	1	rs10120023	9	137810259				rs2519515	9	88204888	0.08	0.49	5.47	0.08	0.49	0.16	
DEM1	ILMN-1783996	1	rs12363827	11	106703727				rs10120023	9	137810259	0.77	0.02	6.39	0.77	0.02	0.29	
DHRS9	ILMN-173998	2	rs1519956	12	89468283				rs7566044	2	169960422	0.06	1.17	6.00	0.06	1.17	0.58	
DHRS9	ILMN-173998	2	rs1528529	9	147132505				rs7566044	2	169960422	0.37	0.34	6.48	0.37	0.34	0.32	
DHRS9	ILMN-2384181	21	rs2831914	21	29959453				rs2161037	2	169893419	0.88	0.04	5.51	0.88	0.04	0.37	
DHRS9	ILMN-2384181	21	rs7661304	4	187776431				rs2161037	2	169893419	0.77	0.02	6.39	0.77	0.02	0.29	
DIP2B	ILMN-1755589	12	rs11080134	17	29161503				rs11169322	12	50610976	0.32	0.05	4.65	0.32	0.05	0.10	
DIP2B	ILMN-1755589	12	rs1169335	12	50636364				rs2872008	7	153134888	0.58	0.58	4.87	0.58	0.58		
DIP2B	ILMN-1755589	12	rs338585	19	41711815				rs1734595	12	50730458	0.30	0.22	5.31	0.30	0.22	0.19	
DIP2B	ILMN-1755589	12	rs134595	12	50730458				rs1808634	8	61971140	0.37	0.02	4.40	0.37	0.02	0.01	
DIP2B	ILMN-1755589	12	rs731252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	66.920
DIP2B	ILMN-1755589	12	rs871252	12	50744171				rs4532958	10	115214154	0.09	0.00	5.03	0.09	0.00	0.11	

0.23 Continued on next page

Table S1 – continued from previous page

Gene ID ^a	Expression trait ^b	Chr.	rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c	Association ^d	BSGS ^e	Fehrmann ^f	-log ₁₀ p-values	EGCUT ^g	Meta ^g	Distance / Mb ^h
FEZ2	ILMN-1739586	2	rs2366400	19	44321776		rs13406184	2	36791226	FEZ2	5.78	0.14	0.33	0.16		
FEZ2	ILMN-1739586	2	rs969010	4	139963132		rs11691600	2	36810133	FEZ2	6.59	0.14	0.28	0.14		
FGD2	ILMN-2115005	6	rs4803848	19	46205050		rs831486	6	37001267	FGD2	5.69	0.12	0.25	0.11		
FGD2	ILMN-2115005	12	rs902634	10	133943951		rs831486	6	36999652	FGD2	5.49	1.20	0.11	0.06		68.867
FLJ20489	ILMN-1778144	12	rs17615703	12	117036766	FLJ20489	rs83782908	12	48169526	FLJ20489	5.81	0.06	0.70	0.29		
FLJ20489	ILMN-1778144	12	rs3782908	12	48169526	FLJ20489	rs875111	4	167695601	FLJ20489	5.53	0.03	0.11	0.02		
FLJ20489	ILMN-1778144	12	rs4792199	17	7992118		rs3782908	12	48169526	FLJ20489	5.74	0.19	0.02	0.04		
FLJ20489	ILMN-1778144	12	rs4984440	15	97033126		rs3782908	12	48169526	FLJ20489	6.49	0.31	0.47	0.36		
FLJ20489	ILMN-1778144	12	rs7204135	16	50626195		rs2287197	16	50106594	FLJ20489	6.90	0.38	0.17	0.21		
FLJ20718	ILMN-1763663	16	rs9325634	21	43818790		rs2287197	16	50106594	FLJ20718	6.04	0.14	0.95	0.53		
FLJ43093	ILMN-2123450	6	rs11712712	14	107276627	FLJ43093	rs6906101	6	36667610	FLJ43093	5.48	0.39	0.06	0.13		3.962
FLJ43093	ILMN-2123450	6	rs6906101	6	36667610		rs13214069	6	32705248	FLJ43093	5.48	0.39	0.06	0.13		3.962
FN3KRP	ILMN-1652333	17	rs898095	17	80890638		rs9892064	17	80827903		16.16	28.24	29.39	59.95		0.063
FUCA1	ILMN-1752728	1	rs4971478	2	1346063		rs12744386	1	24168019	FUCA1	6.41	0.01	0.30	0.06		
FXD5	ILMN-2309848	19	rs1633921	19	35695200		rs2285515	13	98328559		3.70	0.09	0.41	0.17		
FXD5	ILMN-2309848	19	rs17395183	20	35609148	FXD5	rs2285515	13	98328559	FXD5	6.58	0.03	0.48	0.15		
FXD5	ILMN-2309848	19	rs2285515	19	35660450	FXD5	rs11739594	3	141709563		5.70	0.07	0.17	0.05		
FXD5	ILMN-2309848	19	rs2285515	19	35660450	FXD5	rs13067700	3	95331048		6.00	0.09	0.51	0.22		
G3BP2	ILMN-2309848	4	rs2285515	19	35660450	FXD5	rs17036504	2	47567329		6.10	0.28	0.08	0.37		0.14
G3BP2	ILMN-2381758	4	rs10230232	7	29390239		rs1553985	4	76554604		5.19	0.08	0.37	0.14		
GAA	ILMN-2410783	17	rs11150847	17	78153130	GAA	rs12602462	17	78146016		13.91	19.98	12.99	32.60		0.007
GAA	ILMN-2410783	17	rs8068856	17	75100731	GAPT	rs1092506	12	132678089		5.95	0.11	0.39	0.17		
GAPT	ILMN-1675191	5	rs10070522	5	57786110	GAPT	rs7605821	2	235695238		5.85	0.01	0.78	0.28		
GAPT	ILMN-1675191	7	rs7082031	10	128038717		rs10070522	5	57786110	GAPT	5.72	0.26	0.11	0.11		
GATS	ILMN-1699631	7	rs11147447	14	6640742	GATS	rs2950520	7	99827148	GATS	5.47	0.83	0.63	0.87		
GATS	ILMN-1699631	7	rs2423256	7	33555572		rs2950520	7	99827148	GATS	6.22	0.42	0.35	0.33		
GDPD3	ILMN-1774901	16	rs3809624	16	30102802	GDPD3	rs2197465	14	18572632		6.57	0.38	0.35	0.24		
GDPD3	ILMN-1774901	16	rs7204270	16	30156963	GDPD3	rs1015111	4	128972357		5.86	0.55	0.09	0.24		
GDPD3	ILMN-1790692	12	rs4145072	13	110899955	GDPD3	rs7577293	4	128972357	GDPD3	5.78	0.55	0.09	0.24		
GPR162	ILMN-3239426	12	rs7198464	16	26084476		rs7577293	4	128972357	GPR162	5.72	0.02	0.45	0.13		
GPR162	ILMN-1730816	12	rs1860563	16	6478898		rs7577293	4	128972357	GPR162	5.72	0.02	0.45	0.13		
GPR162	ILMN-1730816	12	rs2972500	12	79685913		rs2707210	12	6902002	GPR162	5.49	0.36	0.46	0.39		
GPR162	ILMN-1730816	12	rs2707210	12	6902002	GPR162	rs2707210	12	6902002	GPR162	5.07	0.25	0.03	0.06		
GPR162	ILMN-1730816	12	rs2707210	12	6902002	GPR162	rs4740848	9	6554558		5.47	0.25	0.06	0.07		
GPR177	ILMN-1660549	1	rs10527383	12	124369421		rs9827054	3	188880113		6.21	0.96	0.06	0.44		
GPR177	ILMN-1660549	1	rs12527241	6	120468039		rs12065581	1	68732819	GPR177	5.45	0.72	0.67	0.81		
GPR177	ILMN-1660549	1	rs12532999	7	127939793		rs12065581	1	68732819	GPR177	5.76	0.17	0.40	0.22		
GPR177	ILMN-1660549	1	rs12532999	7	127939793		rs12065581	1	68732819	GPR177	5.43	0.79	1.43	1.50		
GPR177	ILMN-1660549	1	rs725613	16	11169683		rs12065581	1	68732819	GPR177	6.04	0.95	0.21	0.60		
GPR177	ILMN-1660549	1	rs9575097	13	82986268		rs12065581	1	68732819	GPR177	5.43	0.31	0.11	0.13		
GPR177	ILMN-2283325	1	rs6566669	18	70506011		rs12065581	1	68732819	GPR177	5.86	0.24	0.24	0.23		
GPR177	ILMN-2283325	1	rs9290426	3	171399321		rs12065581	1	68732819	GPR177	6.50	0.01	0.24	0.04		
GSDMB	ILMN-2347193	17	rs11557467	17	38028634	GSDMB	rs4965745	15	101508261		5.88	0.68	0.20	0.41		
GSTM1	ILMN-2391861	1	rs12248673	10	53192833		rs11101992	1	110266754	GSTM1	6.11	0.27	0.19	0.16		
GSTM1	ILMN-2391861	1	rs1547574	13	85344527		rs11101992	1	110266754	GSTM1	5.91	0.27	1.14	0.79		
GSTM2	ILMN-2201580	1	rs6492807	13	96150560		rs3754446	1	110253241		6.77	0.52	0.66	0.65		
H1FO	ILMN-1757467	22	rs139898	22	38399979		rs453333	2	77919015		6.36	0.32	0.27	0.27		
H1FO	ILMN-1757467	22	rs139898	22	38399979		rs6497007	15	85877017		6.52	0.27	0.31	0.23		
H1FO	ILMN-1757467	22	rs139898	22	38399979		rs9983949	21	19532546		5.70	0.25	0.48	0.32		
H1FO	ILMN-1757467	22	rs139898	22	38399979		rs2855039	11	5271671	HBC2	5.47	0.00	0.66	0.19		
HBC1	ILMN-1796678	11	rs11078523	17	4523167		rs2855039	11	5271671	HBC2	5.98	0.15	0.52	0.21		
HBC1	ILMN-1796678	11	rs12975066	19	35723501		rs2855039	11	5271671	HBC2	6.78	0.08	0.52	0.21		
HBC1	ILMN-1796678	11	rs2855039	11	5271671	HBC2	rs12042181	1	213088494	LQK1	6.42	0.01	0.46	0.11		
HBC1	ILMN-1796678	11	rs2855039	11	5271671	HBC2	rs12503379	4	14153832		6.06	0.01	0.41	0.10		

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Table S1 – continued from previous page

Gene ID ^a	Probe ID ^b	Chr.	rs ID	Chr.	SNP 1	Pos/Mb ^c	Association ^d	rs ID	Chr.	SNP 2	Pos/Mb ^c	Association ^d	BSGS ^e	Interaction statistic ^f	EGCUT ^g	Meta ^g	Distance / Mb ^h
MBNL1	ILMN_2313158	3	rs4392935	4	41513423			rs13069559	3	152187431		MBNL1	8.39	0.02	4.33	3.02	
MBNL1	ILMN_2313158	3	rs4735850	8	895841			rs15069559	3	152187431		MBNL1	6.74	0.32	4.21	3.38	
MBNL1	ILMN_2313158	18	rs46278091	18	46278091			rs1522374	3	15223530		MBNL1	7.72	0.03	4.27	0.07	
MBNL1	ILMN_2313158	3	rs6128397	20	57263132			rs10804367	7	152234166		MBNL1	7.22	1.34	1.15	1.73	
MBNL1	ILMN_2313158	3	rs7110738	20	57263132			rs13069559	18	152187431		MBNL1	7.92	2.55	7.89	9.28	
MBNL1	ILMN_2313158	18	rs4735850	18	895841			rs10804367	18	152234166		MBNL1	7.22	0.03	4.27	0.07	
MBP	ILMN_2398939	22	rs395684	22	43210981			rs2051344	18	74715653		MBP	5.56	0.02	0.23	0.02	
MBP	ILMN_2398939	18	rs2051344	18	74715653		MBP	rs1125539	3	155204939		MBP	5.79	0.02	0.76	0.27	
MBP	ILMN_2398939	18	rs2051344	18	74715653		MBP	rs20519046	5	55097534		MBP	6.03	0.15	0.50	0.26	
MBP	ILMN_2398939	18	rs4805021	19	33436367			rs2051344	18	74715653		MBP	5.82	0.03	0.47	0.14	
MBP	ILMN_2398939	18	rs8092433	18	74747424			rs48090876	18	74732087		MEGF9	5.40	7.06	3.03	0.14	
MBP	ILMN_2398939	18	rs13039689	18	51922071			rs966396	9	123453281		MEGF9	4.63	1.13	1.33	1.71	
MBP	ILMN_2398939	13	rs7989895	13	109401737			rs4846085	1	12050634		MFN2	5.76	0.61	0.25	0.41	
MGC13057	ILMN_1675385	2	rs12718598	7	50428445			rs11725347	4	171860973		MGC13057	5.81	1.02	0.30	0.14	
MGC13057	ILMN_1787526	2	rs674608	18	69070772			rs12718598	7	50428445		MGC13057	5.07	0.07	1.03	0.50	
MGC13057	ILMN_1787526	2	rs8028318	16	82628245			rs12718598	7	50428445		MGC13057	7.05	0.11	1.02	0.05	
MGC72104	ILMN_1688318	20	rs845787	20	26197931			rs2660608	8	137526799		MGC72104	4.17	0.05	0.08	0.02	
MGC72104	ILMN_1751956	1	rs740441	17	55796644			rs4147592	1	165600146		MGC72104	5.45	0.57	0.27	0.40	
MGC72104	ILMN_1751956	1	rs740441	17	55796644			rs11771552	2	115070609		MGC72104	5.64	0.01	0.23	0.04	
MP2L2	ILMN_1752932	11	rs7316716	12	19953193			rs1805	11	118076069		MP2L2	5.91	0.97	1.08	1.35	
MP2L2	ILMN_1752932	11	rs7316716	12	19953193			rs750495	5	1782046		MP2L2	6.89	0.34	0.18	0.19	
MP2L2	ILMN_1752932	11	rs7316716	12	19953193			rs2863095	10	102746503		MP2L2	5.71	0.26	0.14	0.14	
MRPL36	ILMN_1800197	5	rs17469061	16	8436432			rs3811188	14	42194916		MRPL36	6.56	0.14	0.44	0.22	
MRPL43	ILMN_2258774	14	rs10950857	16	80641040			rs222269	6	42194916		MRPL43	7.48	0.46	0.70	0.64	
MRPL52	ILMN_1713966	14	rs1950857	8	110202230			rs2395803	6	42158596		MRPL52	6.85	0.31	0.63	0.46	
MRPS10	ILMN_1663664	6	rs11698155	20	15063214			rs13217993	6	42164041		MRPS10	6.21	0.41	0.25	0.28	
MRPS10	ILMN_1663664	6	rs1420537	16	52453567			rs12431444	14	42068689		MRPS10	5.18	1.87	1.87	2.86	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596		MTMR15	6.31	0.46	0.52	0.50	
MTMR15	ILMN_2152178	15	rs7178375	15	31215935		MTMR10	rs11160227	14	95514596							

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Table S1 – continued from previous page

Gene ID ^a	Expression trait	SNP 1			SNP 2			Interaction statistic / -log ₁₀ p-values		
		rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c	Association ^d	Meta ^g
NRBF2	ILMN-3237385	rs6025645	20	56157341		rs7923609	10	65133822	NRBF2	5.45
NRBF2	ILMN-3237385	rs6517815	21	19819016		rs7923609	10	65133822	NRBF2	6.11
NRBF2	ILMN-1800897	rs4852124	2	240080022		rs6588415	1	52334037	NRBF2	3.44
NUDT18	ILMN-1787885	rs5017351	11	25453442		rs1005901	8	21964378	NUDT18	6.13
OAS1	ILMN-1658247	rs11613438	12	113480510		rs1047944	6	163994607	OAS1	1.55
OAS1	ILMN-1658247	rs13311	12	113480510		rs2072133	12	113409200	OAS1	4.13
OAS1	ILMN-1675640	rs2892233	19	49160255		rs3741981	12	3149249	OAS1	4.38
OPIN	ILMN-2381899	rs7192613	16	74286646		rs17312962	10	13169066	OPIN	0.46
OSBPL5	ILMN-2307032	rs2829679	21	26652543		rs998639	11	3149249	OSBPL5	0.14
OSTF1	ILMN-1742456	rs17780195	9	77755469	OSTF1	rs2273770	9	77755469	OSTF1	0.07
OSTF1	ILMN-1742456	rs2273770	9	77755469	OSTF1	rs1264898	5	1179690952	OSTF1	0.16
OSTF1	ILMN-17434542	rs10802822	1	240132968		rs1264898	5	1179690952	OSTF1	0.08
OSTF1	ILMN-17434542	rs347351	3	140148107	PAM	rs1264898	5	1179690952	OSTF1	1.21
PAM	ILMN-2313901	rs28092	5	102149795	PAM	rs7846000	1	40138553	PAM	0.66
PAM	ILMN-1815931	rs2438490	5	14826162	PCYOX1L	rs2731939	3	21395959	PCYOX1L	0.26
PAM	ILMN-1602332	rs10444467	12	128052636		rs4328748	12	7364442	PCYOX1L	0.19
PEX5	ILMN-1602332	rs7495797	13	27240462		rs4328748	12	7364442	PEX5	0.71
PEX5	ILMN-1797893	rs131969	22	49151303		rs7325733	13	33126737	PEX5	0.09
PGLYRP1	ILMN-1704870	rs12982533	19	46229456	PGLYRP1	rs1263806	14	76708086	PGLYRP1	0.34
PGLYRP1	ILMN-1812532	rs493642	11	123097386		rs10736812	11	61728397	PGLYRP1	0.36
PIK3P1	ILMN-1719986	rs4141464	22	31675185	PIK3P1	rs2065841	1	61728397	PIK3P1	0.90
PIK3P1	ILMN-1719986	rs47072	22	32263151	PISD	rs10498313	14	30398876	PISD	0.70
PISD	ILMN-1739934	rs61872	22	33230327	PISD	rs1465754	1	8240551	PISD	0.91
PISD	ILMN-1739934	rs715372	22	33230327	PISD	rs657574	22	3209775	PISD	0.02
PISD	ILMN-1739934	rs6666666	1	158751604		rs4982884	2	21918248	PISD	0.19
PISD	ILMN-1739934	rs11638998	16	48251604		rs4982884	2	21918248	PISD	0.05
PISD	ILMN-1739934	rs91019	20	4865255		rs4758046	9	14048768	PISD	0.16
PISD	ILMN-1739934	rs1291403	15	5830805		rs4758046	9	14048768	PISD	0.31
PISD	ILMN-1739934	rs10430170	2	16399967		rs13156875	14	3569830	PISD	0.78
PISD	ILMN-1739934	rs1488083	13	16322094		rs12130009	1	21247107	PISD	0.29
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.72
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.42
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.95
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.13
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.28
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.36
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.06
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.16
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.34
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.14
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.11
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.47
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.04
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.26
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.78
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.42
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.19
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.44
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.14
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.47
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.04
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.26
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.78
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.42
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.19
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.44
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.14
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.26
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.78
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.42
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.19
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.44
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.14
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.26
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.78
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.42
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.19
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.44
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.14
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.26
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.78
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.42
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.19
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.44
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.14
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.26
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.78
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.33
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.42
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.19
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.44
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.14
PISD	ILMN-1739934	rs75233	11	10747238		rs12130009	1	21247107	PISD	0.03
PISD	ILMN-1739934	rs75233	11	1074723						

	SNP 2	Interaction statistic /	— og ₁₀ p-values

Continued on next page

Table S1 – continued from previous page

Expression trait			SNP 1			SNP 2			Interaction statistic / -log ₁₀ p-values			Distance / Mb ^h		
Gene ID ^a	Probe ID ^b	Chr.	rs ID	Chr.	Pos /Mb ^c	Association ^d	rs ID	Chr.	Pos /Mb ^c	Association ^d	BSGS ^e		Fehrmann ^f	EGCUT ^g
UBASH3A	ILMN-2338348	21	rs1893592	21	43855067	UBASH3A	rs7201194	16	83600397		5.91	0.59	0.42	0.52
UBASH3A	ILMN-2338348	21	rs1893592	21	43855067	UBASH3A	rs7512594	1	214514361		6.01	0.48	1.29	1.10
USP36	ILMN-1697227	17	rs2279308	17	76794981	USP36	rs7225546	17	75151717		5.71	0.03	0.14	0.03
VASP	ILMN-1743646	19	rs1264226	19	40663167		rs2276470	19	45974668		5.09	0.94	5.14	4.95
VNN2	ILMN-1678939	6	rs10435352	7	103252718		rs1883613	6	133077063	VNN2	5.64	0.84	0.15	0.46
VNN2	ILMN-1678939	6	rs13044386	20	9116155		rs1883617	6	133072650	VNN2	5.44	0.39	0.69	0.57
VNN2	ILMN-1678939	6	rs134447	22	49927332		rs1883617	6	133072650	VNN2	5.72			
VNN3	ILMN-1678939	6	rs216495	11	16834510		rs1883617	6	133072650	VNN2	5.77	0.33	0.19	0.19
VNN3	ILMN-1604935	6	rs10278073	7	151662184		rs2267932	6	133067782	VNN3	6.44	0.16	0.74	0.41
VNN3	ILMN-1604935	6	rs1443946	8	73006453		rs2267932	6	133067782	VNN3	5.74	0.23	0.48	0.31
VNN3	ILMN-1604935	6	rs348462	9	75547169		rs2267952	6	133067782	VNN3	6.44	0.31	0.17	0.17
VNN3	ILMN-1604935	6	rs7157055	14	83262064		rs2267952	6	133067782	VNN3	5.82	0.03	0.19	0.04
VNN3	ILMN-2387680	6	rs2823165	21	5694253		rs2267952	6	133067782	VNN3	6.12	0.73	1.15	1.21
VNN3	ILMN-2387680	6	rs9596457	13	51692548		rs2267952	6	133067782	VNN3	4.83	0.46	0.05	0.16
VSTM1	ILMN-1763455	19	rs10500316	19	54553697	VSTM1	rs4552100	18	71024750		5.60	0.53	0.54	0.57
VSTM1	ILMN-1763455	19	rs10500316	19	54553697	VSTM1	rs7895870	10	123095249		5.71	0.48	0.17	0.26
VSTM1	ILMN-1763455	19	rs9625870	22	30261219		rs10500316	19	54553697	VSTM1	5.88	0.81	1.38	1.47
WDR48	ILMN-1762103	3	rs1388935	4	18892782		rs6778963	3	39091812	WDR48	5.88	0.09	0.33	0.09
WDR48	ILMN-1762103	3	rs1887778	9	134635088	RAPGEF1	rs853349	3	39067925	WDR48	6.34	0.57	1.35	1.22
WDR48	ILMN-1762103	3	rs9554833	13	102624790		rs7619193	3	39044116	WDR48	5.85	0.18	0.61	0.35
WDR6	ILMN-1669484	3	rs12362253	11	123571708		rs7619193	3	39044116	WDR6	4.86	1.64	1.43	2.25
XAF1	ILMN-2330953	17	rs1533031	17	9673170	XAF1	rs12591171	15	93119799		5.78	2.38	0.17	1.63
ZFP90	ILMN-1684628	16	rs909446	16	37040648		rs182968	16	68573945	ZFP90	5.79	0.09	0.36	0.15
ZNF500	ILMN-1700238	16	rs4823723	22	48283177		rs2290560	16	4799041	ZNF500	5.29	0.67	0.27	0.46
ZYX	ILMN-1701875	7	rs6056281	20	8935312		rs2242601	7	143093824	ZYX	6.04	0.26	0.01	0.05

^a Phenotypes are expression levels of RefSeq Genes^b Illumina probe ID used to measure gene expression^c Physical SNP position in base pairs (HG19)^d RefSeq Gene ID of gene expression level that is influenced by the SNP (BSGS discovery dataset, significance threshold = 1.29 × 10⁻¹¹)^e Interaction - log₁₀ p-value from discovery dataset^f Interaction - log₁₀ p-value from replication dataset^g Interaction - log₁₀ p-value from meta analysis of replication datasets only^h Distance in Mb between interacting SNPs for *cis-cis* acting SNP pairs

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