

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

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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

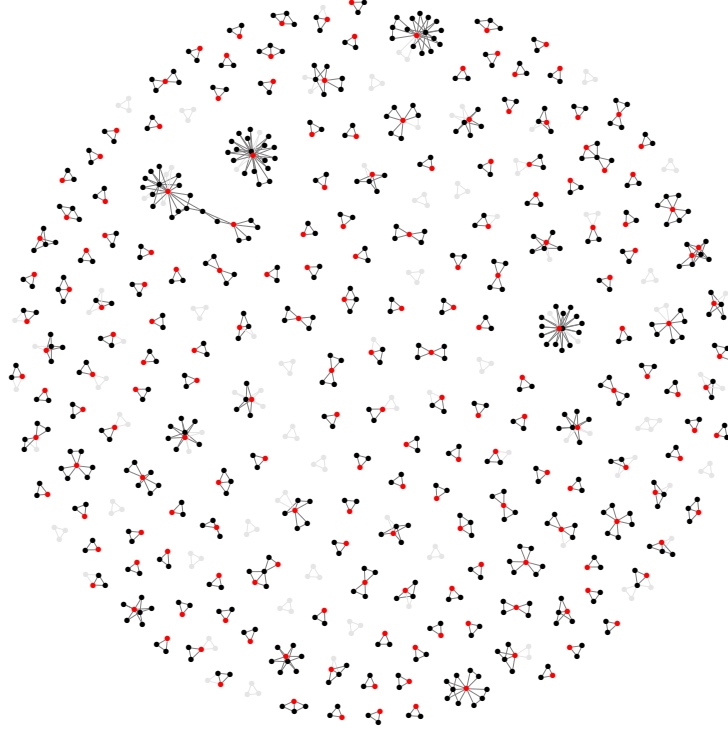


Figure 1: **Discovery and replication of epistatic networks** All 434 putative genetic interactions (edges) with data common to discovery and replication sets is shown, where black nodes represent SNPs and red nodes represent traits (gene expression probes). Three hundred and forty-five interactions 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.

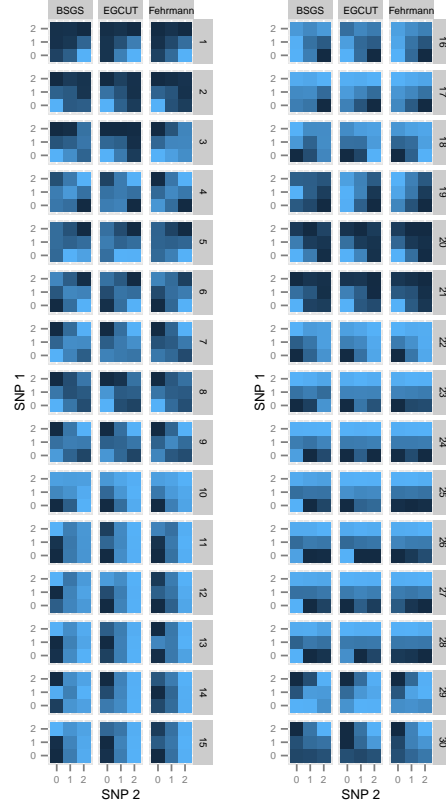


Figure 2: Replication of GP maps in two independent populations The GP maps for each epistatic interaction that is significant at the Bonferroni level in both replication datasets are shown. Each GP map consists of nine tiles where each tile represents the expression level for that two-locus genotype 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.

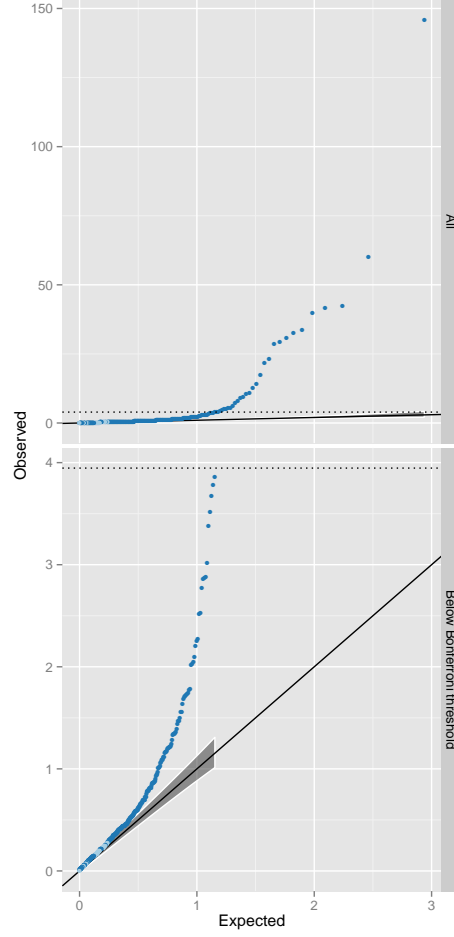


Figure 3: **Q-Q plots of interaction p -values from replication datasets**
The top panel shows all 434 discovery SNPs that were tested for interactions. Observed p -values (y -axis, $-\log_{10}$ scale) are plotted against the expected p -values (x -axis, $-\log_{10}$ scale). The multiple testing correction 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

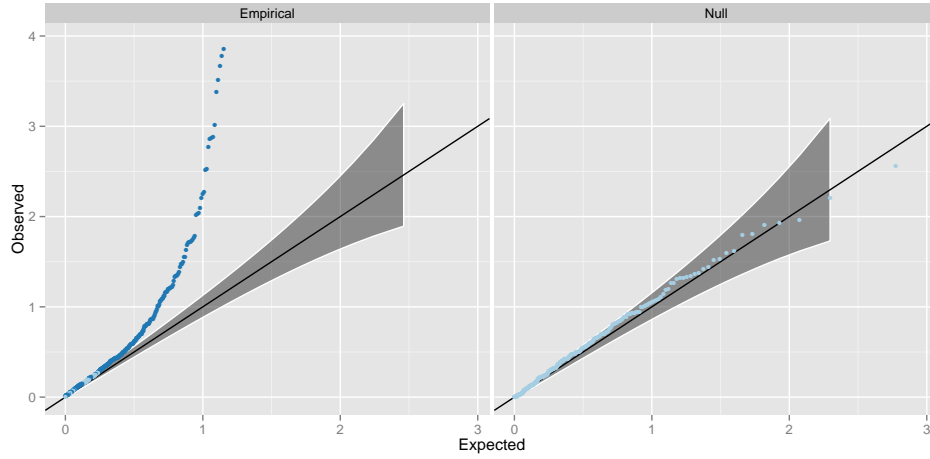


Figure S1: **Q-Q plots of interaction p -values from replication datasets, excluding the 30 points significant at the Bonferroni level** The right panel (Null) shows the interaction p -values from a meta analysis across two independent datasets on 434 randomly drawn SNP pairs. The left panel (Empirical) 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.

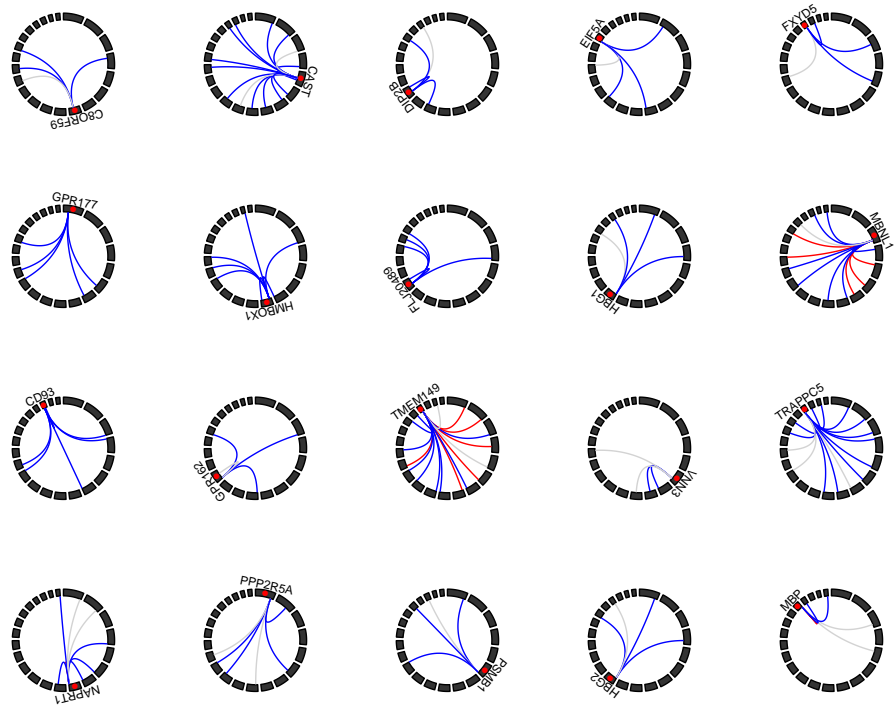


Figure S2: **Gene expression traits with four or more genetic interactions** Circle plots represent the genomic positions for SNPs (linking lines) and expression probes (red points). Chromosomes are represented by black blocks and ordered from 1 to 22 clockwise, starting from the top. Grey lines represent 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.

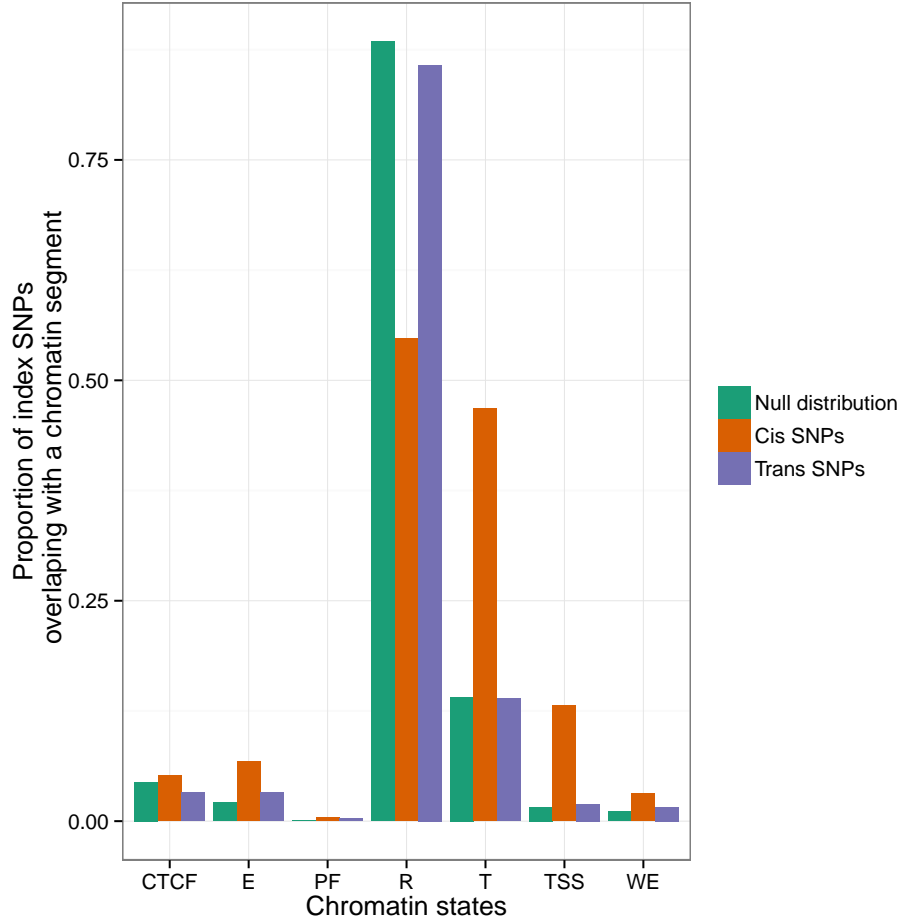


Figure S3: Location of SNPs relative to genomic features All SNPs within 1Mb and $r^2 > 0.8$ of each *cis*- and *trans*-SNP were taken to find which genomic features (x -axis) were covered by the SNPs that compose the 501 significant interactions. Green bars represent the proportion (y -axis) of the 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

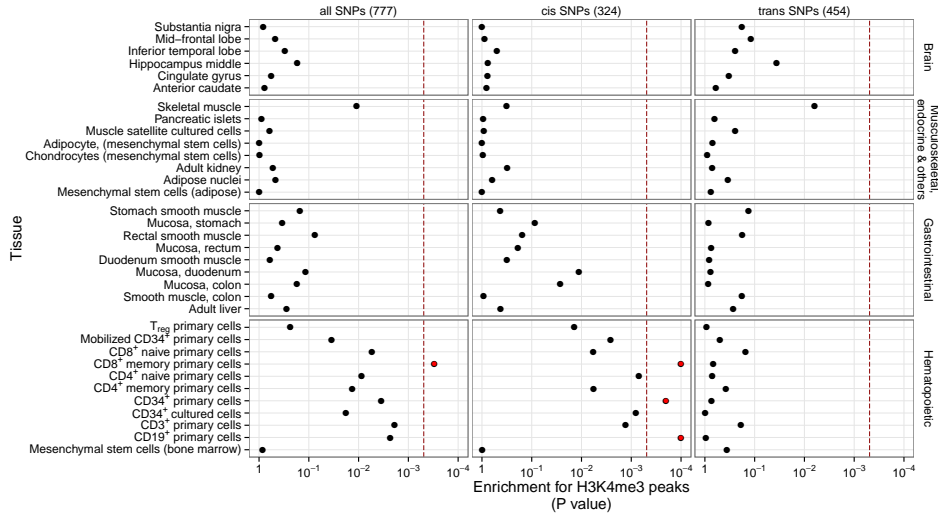


Figure S4: Tissue specific enrichment of SNPs in transcriptionally active regions The locations of transcriptional activity can be predicted by chromatin marks, assayed by H3K4me3.²⁶ Enrichment p -values are calculated using permutation analysis for 34 different cell types (y -axis) in four tissue types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

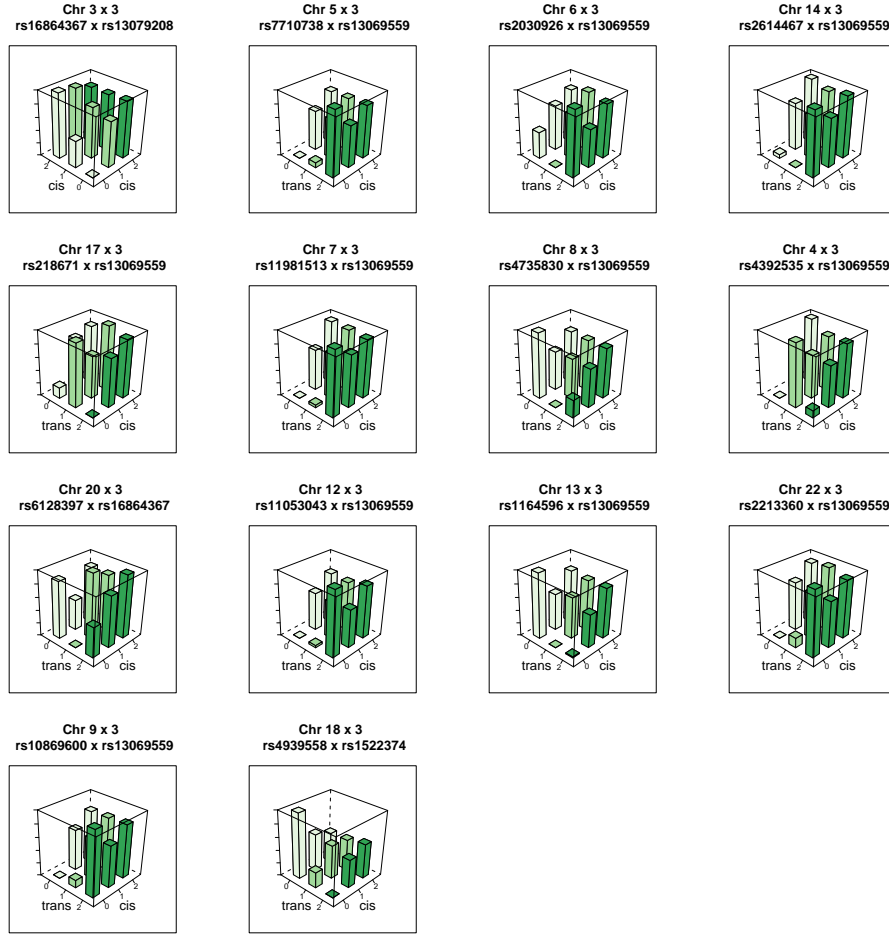


Figure S5: **Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions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

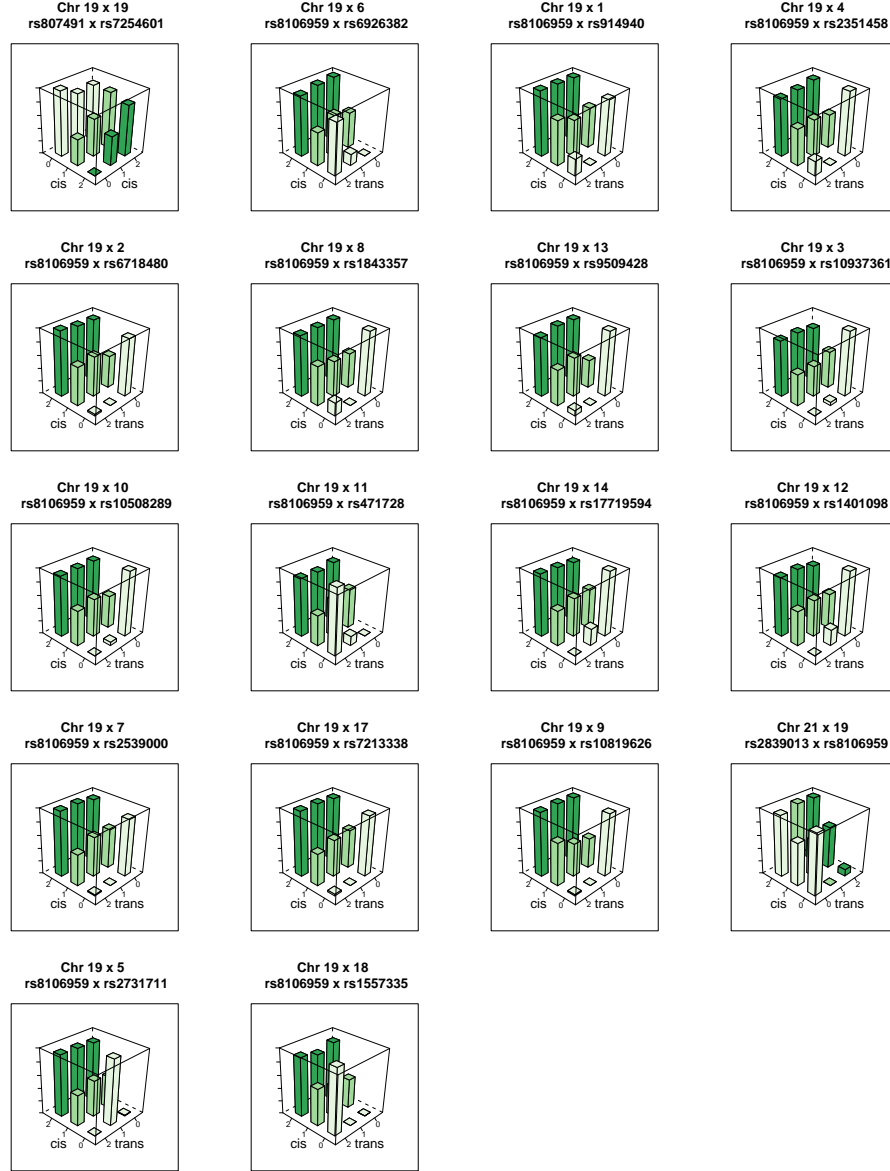


Figure S6: **Genotype-phenotype maps for 19 interactions influencing the expression of TMEM149** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of TMEM149, but in many of these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

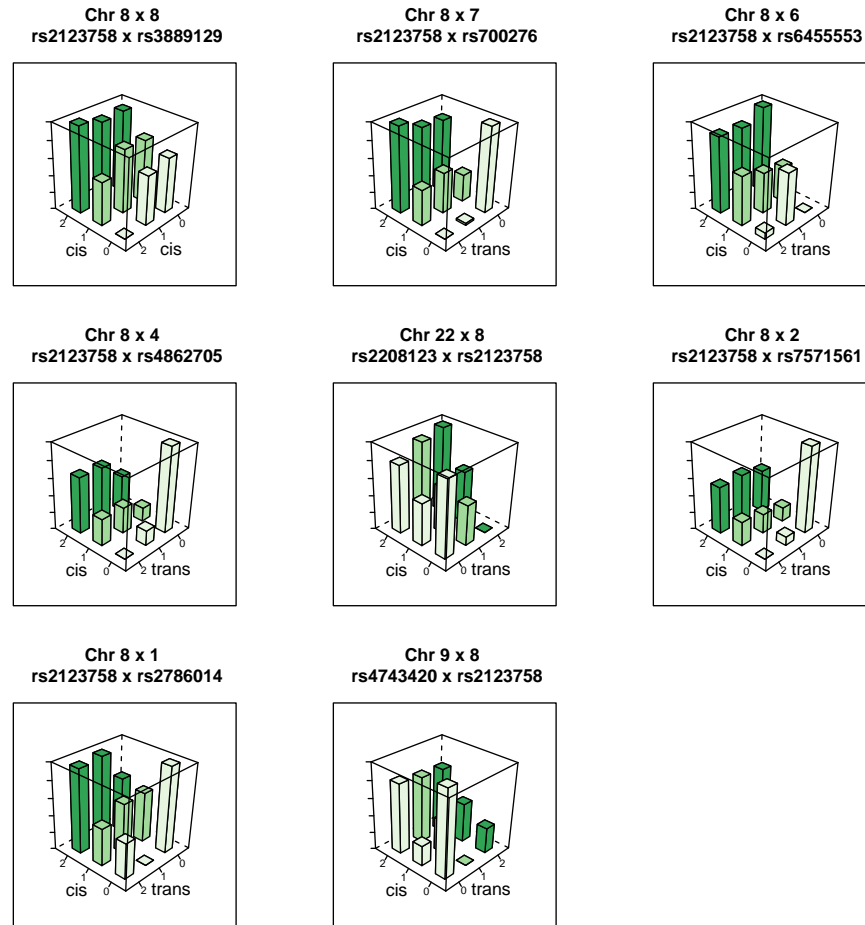


Figure S7: **Genotype-phenotype maps for 8 interactions influencing the expression of NAPRT1** Each bar represents the mean phenotypic value for individuals in that genotype class.

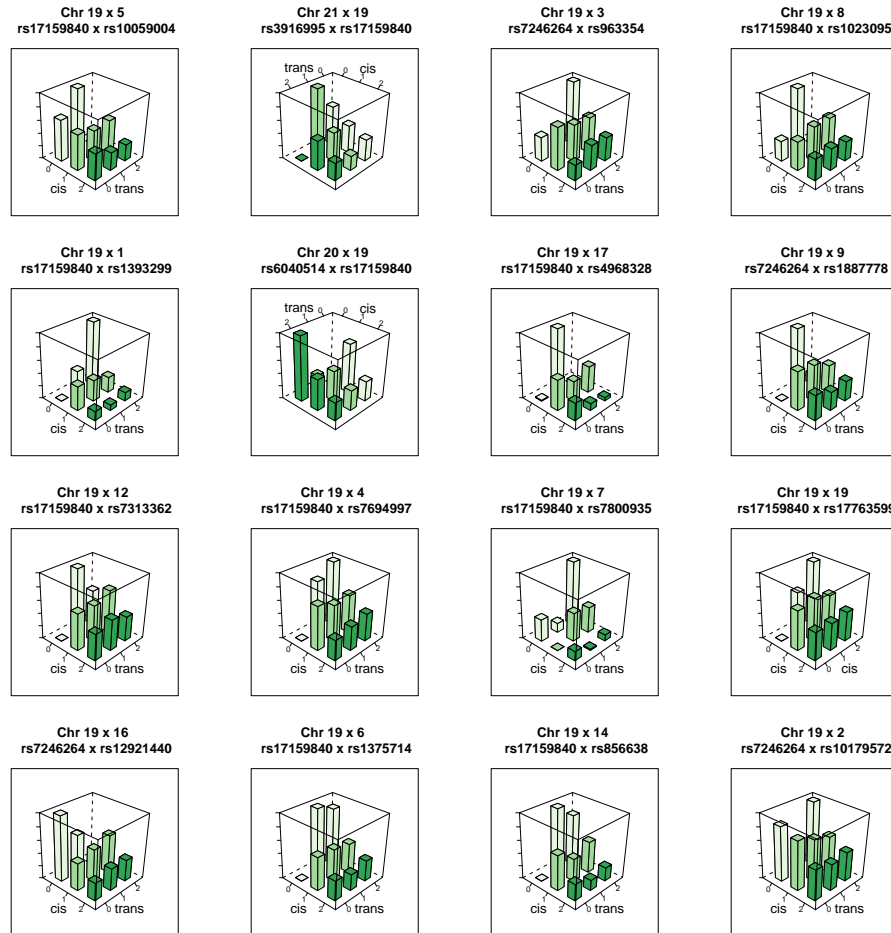


Figure S8: **Genotype-phenotype maps for 16 interactions influencing the expression of TRAPPC5** Each bar represents the mean phenotypic value for individuals in that genotype class.

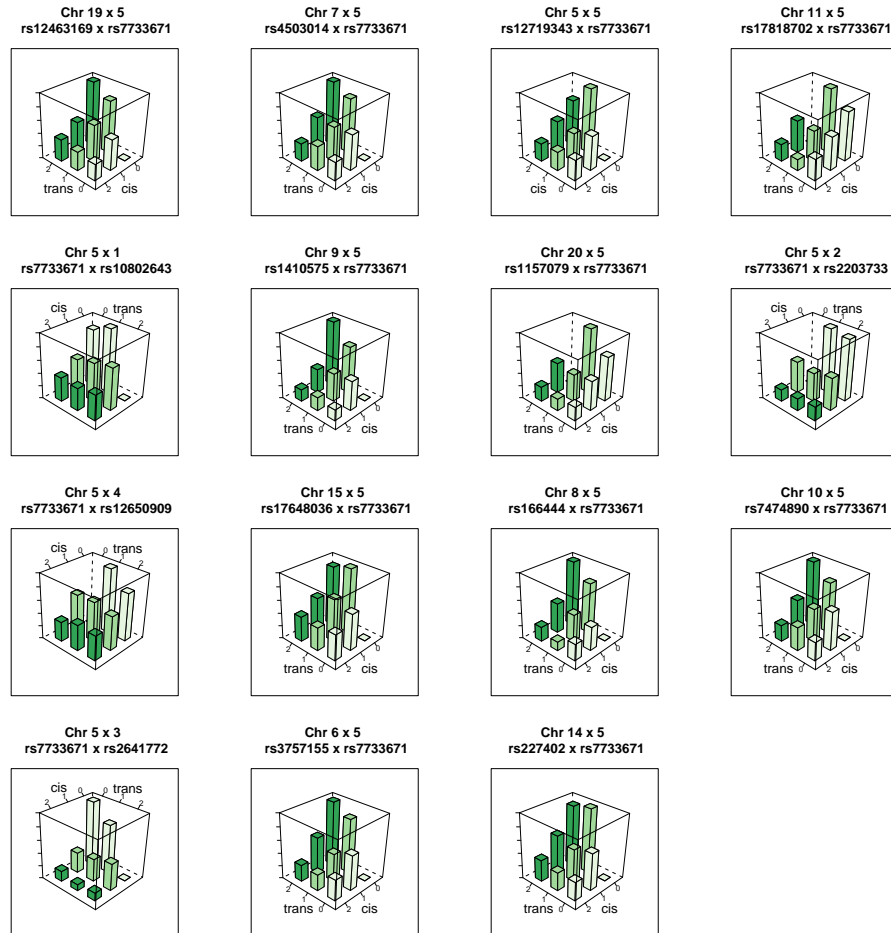


Figure S9: **Genotype-phenotype maps for 15 interactions influencing the expression of CAST** Each bar represents the mean phenotypic value for individuals in that genotype class.

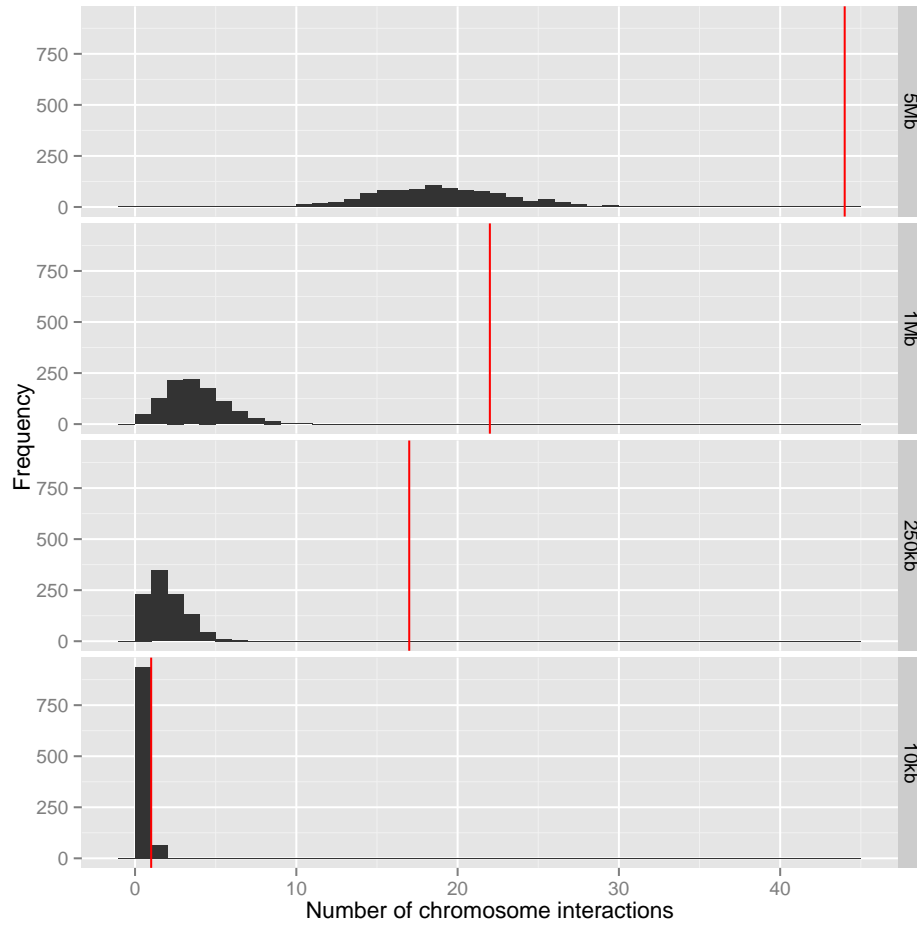


Figure S10: Number of overlaps between chromosome interactions and epistatic interactions Interacting chromosome regions may be a possible mechanism underlying epistatic interactions. The number of epistatic interactions within 20kb, 500kb, 2Mb and 10Mb of known chromosome interacting regions are shown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

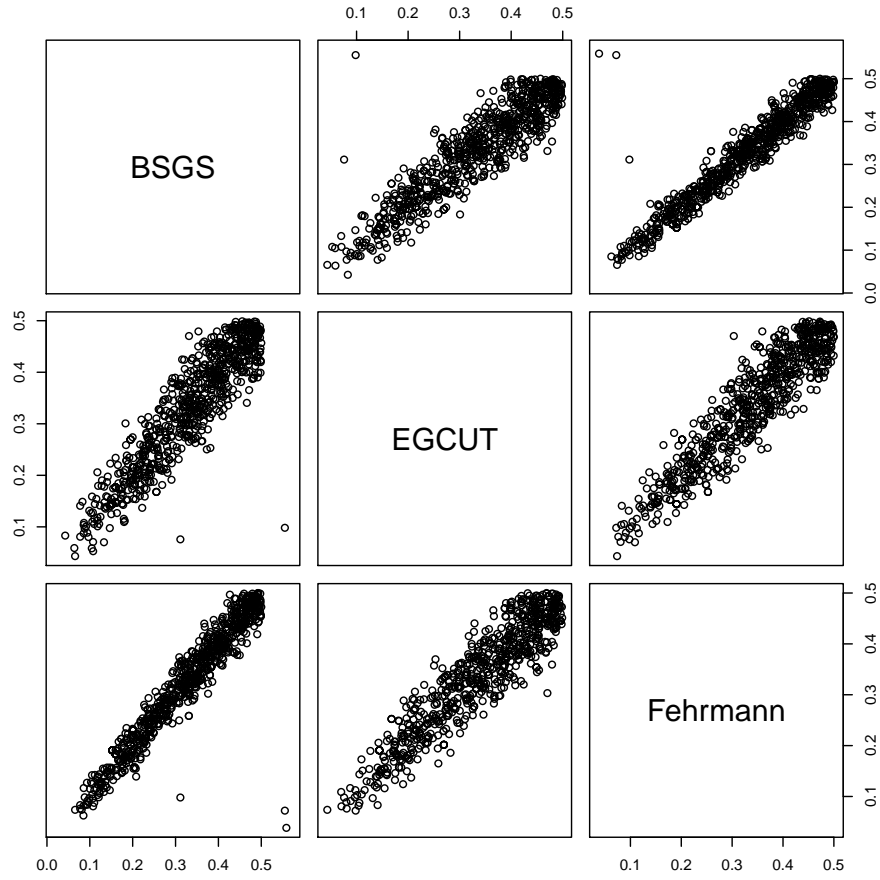


Figure S11: **Comparison of allele frequencies for 781 SNPs involved in genetic interactions across independent populations** Outliers were removed from the analysis as part of the filtering stage during replication.

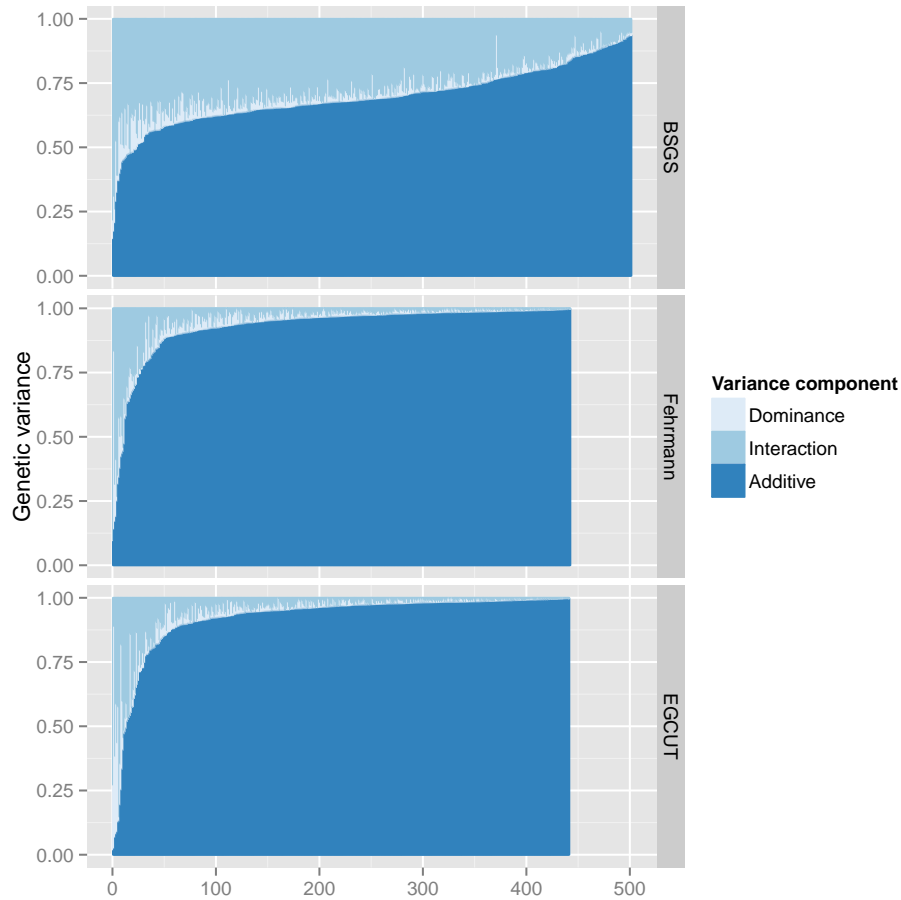


Figure S12: Comparison of variance distribution from different cohorts
 How does the estimated variance decomposition change in different cohorts? The cumulative proportion of the genetic variance that is additive, dominant, or epistatic for each putative interaction is shown on the y -axis. BSGS has 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

Gene ID ^a	Expression trait		SNP 1			SNP 2			Interaction statistic / $-\log_{10} p$ -values				Distance / Mb		
	Probe ID ^b	Chr.	rs ID	Chr.	Pos / Mb ^c	Association ^d	rs ID	Chr.	SNP 2	Association ^d	BSGS ^e	Fehrmann ^f		EGCUT ^g	Meta ^g
ABCA7	ILMN-1743205	19	rs3752237	19	1047161	ABCA7	rs596183	6	158100199		5.50	0.38	0.02	0.09	
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	ADCK1	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	0.517
AGAP6	ILMN-3239130	10	rs2611512	10	51515534	AGAP8	rs25477996	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	rs11773903	2	61388355	AHSA2	5.45	0.92	0.64	0.94	
AKTIP	ILMN-1665982	16	rs2896940	16	57721127	AKTIP	rs13332406	16	53489705	AKTIP	6.91	0.16	0.99	0.57	
AKTIP	ILMN-1665982	16	rs7189819	16	53536345	AKTIP	rs1362032	7	125543391		5.93	0.71	0.20	0.42	4.231
ADH3A2	ILMN-2401641	17	rs3760489	17	19581009	ADH3A2	rs1473017	4	179323762		6.18	0.27	0.30	0.23	
ANG	ILMN-1760727	14	rs9322855	14	21153299	ANG	rs11720112	3	161996349		6.26	0.33	1.37	1.01	
ANPEP	ILMN-1763837	15	rs9322855	15	90363995	ANPEP	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	
AP3B1	ILMN-1768867	5	rs6453374	5	77508159	AP3B1	rs6846031	4	178019148		6.31	0.47	0.17	0.26	
APPL2	ILMN-1765076	12	rs935251	12	105580918	APPL2	rs4684443	3	48187928		5.94	0.05			
ARL17B	ILMN-3231962	17	rs12947580	17	75768225		rs2769594	9	87918528	ARL17B	5.60	0.80	1.02	1.16	31.703
ARL17B	ILMN-3231962	17	rs2834541	21	35932619		rs8079215	17	44064851	ARL17B	5.96				
ARL17B	ILMN-3231962	17	rs8079215	17	44064851	ARL17B	rs1950646	14	94722497		6.65				
ARL17B	ILMN-3231962	17	rs8079215	17	44064851	ARL17B	rs2197777	12	125831219		7.04				
ARL17B	ILMN-3231962	17	rs8079215	17	44064851	ARL17B	rs2684789	15	99492045		5.98				
ATP13A1	ILMN-2134224	19	rs4284750	19	19810050		rs9834627	3	191203546		5.72				
BID	ILMN-1763386	22	rs8919	22	18213057	BID	rs9804943	12	129906275		5.72	12.18	3.25	14.23	0.071
BID	ILMN-1763386	22	rs181405	22	18233000		rs10888267	1	248059423		6.60	0.06	0.40	0.14	
C10ORF17	ILMN-1752988	11	rs2568061	11	8886260	C11ORF17	rs6553184	4	189150656		5.66	1.15	0.04	0.54	
C10ORF18	ILMN-2196550	13	rs2110603	16	6259852	C10ORF18	rs674754	13	46913416	C10ORF18	6.66	0.28	0.28	0.22	
C10ORF18	ILMN-2196550	13	rs674754	22	46913416	C10ORF18	rs6857876	4	153610164		3.87	0.38	0.50	0.43	
C10ORF173	ILMN-2393450	14	rs11089825	22	37575398		rs4983382	14	105189504	C10ORF173	6.02	0.60	0.84	0.85	
C10ORF173	ILMN-2393450	14	rs3935344	15	92276674		rs10754644	1	238724741	C10ORF173	5.98	0.31	0.28	0.24	
C10ORF173	ILMN-2393450	14	rs4983382	14	105189504	C10ORF173	rs2655991	14	77574438		7.15	0.42	0.34	0.35	
C10ORF4	ILMN-1804396	14	rs1293455	18	13819673		rs2655991	14	77574438		4.87				
C10ORF4	ILMN-1804396	14	rs2655991	14	77574438		rs10972462	9	35427324		4.32				
C10ORF4	ILMN-1804396	14	rs2655991	14	77574438		rs6445340	3	63371601		4.40				
C10ORF4	ILMN-1804396	14	rs2655991	14	77574438		rs9787151	1	63179138		4.05				
C10ORF4	ILMN-1804396	14	rs4793445	17	70416307		rs2655991	14	77574438		3.85				
C10ORF4	ILMN-1804396	14	rs6010061	22	51151724		rs2655991	14	77574438		4.61				
C10ORF4	ILMN-1804396	14	rs7245800	19	52083552		rs2655991	14	77574438		4.69				
C10ORF60	ILMN-1747347	17	rs9907897	17	63502633		rs7405659	17	77574438		6.79	0.53	0.05	0.19	
C10ORF60	ILMN-1747347	17	rs2334323	6	110577257		rs2257182	1	2082566	C10ORF60	5.90	0.01	0.50	0.13	
C10ORF86	ILMN-2097790	1	rs2279474	18	46384412		rs2460002	1	2119833	C10ORF86	5.65	0.03	0.03	0.37	
C10ORF86	ILMN-2097790	1	rs7188668	16	25711358		rs2460002	1	2119833	C10ORF86	5.59	0.29	0.50	0.37	
C21ORF57	ILMN-1795836	21	rs4819271	21	48052838		rs901964	12	48676038	ZNF641	4.91	6.08	0.08	0.28	
C21ORF57	ILMN-1795836	21	rs9978658	21	48027084		rs11701361	21	47644577	C5ORF4	9.42	17.67	16.36	21.67	0.263
C5ORF4	ILMN-1728742	5	rs1122762	18	45866512		rs286595	5	154348552	C5ORF4	5.55	0.72	0.04	0.27	
C5ORF59	ILMN-1653205	8	rs124529804	13	36577930		rs2896452	8	86102223	C5ORF59	5.49	0.29	0.02	0.07	
C5ORF59	ILMN-1653205	8	rs12454561	18	31272238		rs2896452	8	86102223	C5ORF59	5.45	0.31	0.02	0.07	
C5ORF59	ILMN-1653205	8	rs2896452	8	86102223		rs2896452	4	55242625		7.62	0.38	0.18	0.21	
C5ORF59	ILMN-1653205	8	rs7152284	14	52273663	C5ORF59	rs2896452	8	86102223	C5ORF59	5.67	2.18	0.07	1.33	

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Gene ID ^a	Expression trait	Chr.		SNP 1		SNP 2		Association ^d		Association ^d		Interaction statistic / $-\log_{10} p$ -values		Distance / Mb		
		rs ID	Chr.	Pos /Mb/c	Association ^d	rs ID	Chr.	Pos /Mb/c	Association ^d	BSGS ^e	Fehrmann ^f	EGCUT ^g	Meta ^h			
CORF59	ILMN.1653205	16	7188323							8	86102233	CSORF59	5.79	1.39	0.18	0.87
CORF72	rs105122902	9	27556780							1	242029101		6.36	0.96	0.01	0.37
CABD1	ILMN.1731064	10	4353908							1	227174210	CABC1	6.36	0.94	0.00	0.34
CARD9	rs14266763	9	139289825							1	82128660		5.81			
CARD9	ILMN.1712532	11	6026661							9	139266496	INPP5E	6.61	0.09	0.86	0.42
CARD9	rs1157079	20	6778978							5	96000269	CAST	7.07	0.23	0.96	0.62
CAST	ILMN.1712384	5	18140122							5	96000269	CAST	5.73	0.02	2.85	1.75
CAST	rs12463169	16	81840122							5	96000269	CAST	7.00			
CAST	rs12599264	16	17321669							5	96000269	CAST	6.58			
CAST	rs12719343	5	125369113							5	96000269	CAST	7.65	0.36	1.57	1.20
CAST	rs141010575	9	78255630							5	96000269	CAST	6.58	0.13	1.34	0.78
CAST	ILMN.1712384	5	18140122							5	96000269	CAST	7.01	0.27	0.52	0.37
CAST	rs166444	8	78392771							5	96000269	CAST	7.81	0.97	0.03	0.41
CAST	ILMN.1712384	5	1817648036							5	96000269	CAST	6.62	1.15	0.59	1.09
CAST	ILMN.1712384	5	1817818702							5	96000269	CAST	6.12	0.11	0.01	0.01
CAST	rs272402	14	70496867							5	96000269	CAST	6.87			
CAST	rs2822124	21	15166804							5	96000269	CAST	6.24	0.07	0.33	0.12
CAST	rs3757155	6	136458593							5	96000269	CAST	7.24	0.92	1.56	1.72
CAST	ILMN.1712384	5	181744890							5	96000269	CAST	5.88	0.49	0.12	0.23
CAST	rs4503014	7	31149140							5	96000269	CAST	6.74	0.23	0.49	0.10
CAST	ILMN.1712384	5	181744890							5	96000269	CAST	7.42	0.75	0.78	0.93
CAST	rs7733671	5	960003269							4	170192890		7.42	0.23	0.78	0.50
CAST	ILMN.1712384	5	181733671							2	224093101		6.07	0.22	0.87	0.54
CAST	rs7733671	5	960003269							3	195531841		6.93	0.19	0.26	0.15
CAST	ILMN.1712384	5	181733671							3	195531841		6.41	0.26	0.30	0.22
CAST	rs7733671	18	66175386							11	34447586	CAT	5.68	0.33	0.37	0.31
CODC8B8	ILMN.172208	11	17099980							11	64125142	CCDC8B8	5.62	0.13	0.18	0.14
CODC8B8	rs23523203	11	64097233							10	96989193	VAMP8	6.93	0.25	0.01	0.02
CODC8B8	rs694739	11	80280117							2	85816334	VAMP8	5.09	0.08	0.03	0.02
CODC8B8	ILMN.1784863	7	8218011834							1	2					

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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				Distance / Mb ^b				
		Chr.	rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c		Association ^d	BSGS ^e	Fehrmann ^f	EGCUT ^g
CPVL	ILMN-1682928	7	rs2835998	21	39202070		rs245884	7	29188475	CPVL	5.55	0.19	0.03	0.04
CRPT	ILMN-1513290	2	rs2131290	4	188859908		rs1531133	7	46843631	CRPT	5.47	0.28	0.10	0.12
CRUS1	ILMN-1737685	20	rs6139887	20	5986234	CRUS1	rs1473927	5	62406408		6.18	0.10	0.36	0.15
CS1B	ILMN-1761797	21	rs69979356	21	43230974		rs3761385	21	45196355		11.99	25.20	16.72	42.27
CTNNA1	ILMN-1804854	5	rs924943	18	69000505		rs176382	5	138226707	CTNNA1	5.74	0.02	0.41	0.11
CTSC	ILMN-1696347	11	rs2457684	11	88139983	CTSC	rs7079264	10	10679892		5.67	0.92	0.74	0.03
CTSC	ILMN-1696347	11	rs7532236	22	26250645		rs1728352	11	88087357	CTSC	5.84	0.49	0.73	0.73
CTSC	ILMN-2242463	11	rs7930237	21	88117962		rs1556895	11	88087357		7.16	18.76	15.06	33.53
CWFI9L1	ILMN-1651886	10	rs7108734	11	11450027		rs12784396	10	102027407	CWFI9L1	5.42	0.21	0.01	0.03
CYBRD1	ILMN-1712305	4	rs2592948	4	129994690		rs888427	2	172366120	CYBRD1	5.89	0.23	0.53	0.34
CYBRD1	ILMN-1712305	2	rs7852475	9	140698856		rs888427	2	172366120	CYBRD1	5.68	0.20	0.02	0.04
CYBRD1	ILMN-2087692	2	rs11257679	10	12318284		rs888427	2	172366120	CYBRD1	5.81	0.39	1.87	1.47
CYBRD1	ILMN-2087692	2	rs6137908	20	23344590		rs888427	2	172366120	CYBRD1	5.53	0.05	0.83	0.36
CYP27A1	ILMN-1704985	2	rs888427	2	172366120	CYBRD1	rs7591849	2	160112881	CYP27A1	5.85	0.87	0.10	0.44
CYP27A1	ILMN-1704985	2	rs6021982	20	36571928		rs933994	2	219650616	CYP27A1	5.42	0.29	0.86	0.60
DAB2	ILMN-2128428	5	rs7778910	17	110451383		rs835223	5	39581357	DAB2	5.44	0.48	0.41	0.44
DDKD	ILMN-1811648	17	rs9900173	17	43111688	DDT	rs1343244	9	824705988		9.12	0.00	0.58	0.14
DDKD	ILMN-1690982	22	rs9760102	22	24248761		rs275341	3	187475208		5.62	0.64	0.25	0.42
DDX58	ILMN-1797001	9	rs4857097	11	125962645	COQ10A	rs7042042	7	32451144		5.31	0.61	0.29	0.44
DEM1	ILMN-1783996	1	rs10120023	9	137810259		rs2519515	7	88204888		5.47	0.08	0.41	0.16
DEM1	ILMN-1733998	1	rs12363827	13	106703727		rs10120023	9	137810259	COQ10A	6.39	0.77	0.02	0.29
DHRS9	ILMN-1733998	2	rs1511956	12	89468283		rs7566044	2	169960422	DHRS9	6.00	0.06	1.17	0.58
DHRS9	ILMN-2384181	2	rs1528529	12	39468283		rs7566044	2	169960422	DHRS9	6.48	0.37	0.34	0.32
DHRS9	ILMN-2384181	2	rs2831914	21	29959453		rs2161037	2	169893419	DHRS9	5.51	0.88	0.04	0.37
DHRS9	ILMN-2384181	4	rs77661304	4	187776431		rs2161037	2	169893419	DHRS9	7.64	0.05	0.11	0.10
DIP2B	ILMN-1755589	12	rs11080134	17	29161503	LASS5	rs11169322	12	50610976	LASS5	4.65	0.32	0.05	0.10
DIP2B	ILMN-1755589	12	rs11669335	12	50636364		rs2872008	7	153134888		4.87	0.30	0.58	0.19
DIP2B	ILMN-1755589	12	rs3385855	19	41711815	LASS5	rs7134595	12	50730458	LASS5	5.31	0.38	0.22	0.19
DIP2B	ILMN-1755589	12	rs73134595	12	50730458	LASS5	rs1808634	8	61971140		4.40	0.37	0.09	0.02
DIP2B	ILMN-1755589	12	rs7312252	12	50744171	LASS5	rs4532958	10	115214154	LASS5	5.03	0.09	0.02	0.01
DIP2B	ILMN-1755589	12	rs871257	12	171994348		rs12427378	12	51074199	DNAJB6	5.92	0.48	0.23	1.45
DNAJB6	ILMN-1793770	7	rs2288842	15	157126093		rs3775539	7	157163614	LASS5	5.79	0.23	1.45	0.97
DPH3	ILMN-2349610	3	rs12232308	15	93400905	ECGF1	rs1566972	3	163020360	DPH3	6.17	1.58	0.27	1.12
ECGF1	ILMN-2109708	22	rs14323491	22	50971266		rs4891884	18	64004670	DPH3	4.81	0.15	1.18	0.70
ECGF1	ILMN-1671568	1	rs4324091	22	241911027		rs11206043	1	53402552	ECGF1	6.19	0.22	0.35	0.22
ECGF1	ILMN-1671568	1	rs5092637	22	17675900		rs11206043	1	53402552	ECGF1	5.58	0.64	0.16	0.35
EHDA4	ILMN-1720083	15	rs40043312	19	53244938		rs1048166	15	42192040	EHDA4	6.98	0.90	0.47	0.79
EIF2B2	ILMN-1719380	14	rs6567288	18	60218334		rs1754556	14	75503430	EIF2B2	5.56	0.23	0.11	0.10
EIF5A	ILMN-1704522	17	rs7216490	17	7221707	EIF5A	rs1269096	14	96693119	EIF5A	5.44	0.56	0.08	0.24
EIF5A	ILMN-1794522	17	rs7216490	17	7221707	EIF5A	rs1553474	2	49359676	EIF5A	5.55	0.28	0.59	0.41
EIF5A	ILMN-1794522	17	rs7216490	17	7221707	EIF5A	rs1553474	2	49359676	EIF5A	5.55	0.28	0.59	0.41
EIF5A	ILMN-1794522	17	rs7216490	17	7221707	EIF5A	rs4471434	11	126387391	EIF5A	5.52	0.05	1.12	0.53
EMR2	ILMN-2353633	19	rs2827076	21	23196249		rs9305048	19	14879034	EMR2	6.36	0.08	0.05	0.02
EMR2	ILMN-2353633	19	rs6132112	20	18761714		rs9305048	19	14879034	EMR2	6.51	0.36	0.04	0.11
EMR2	ILMN-2353633	19	rs9405048	19	14879034		rs3007765	13	102480759	EMR2	5.56	0.45	0.40	0.41
EMR2	ILMN-1709237	8	rs1107764	11	12790396	EMR2	rs13269963	13	102480759	EMR2	6.03	0.20	0.58	0.35
EPHX2	ILMN-1731001	8	rs10894861	11	13461176		rs12115088	8	578752	EPHX2	5.70	0.20	0.58	0.35
EPHX2	ILMN-1731001	8	rs5766218	22	45337329		rs12115088	8	578752	EPHX2	5.43	0.25	1.20	0.81
EPHX2	ILMN-1731001	8	rs726145	18	31187910		rs12115088	8	578752	EPHX2	6.11	0.20	0.11	0.09
EPHX2	ILMN-2104696	5	rs4735895	8	600729	ERICH1	rs1517297	4	189286760	ERICH1	5.63	0.67	1.03	1.06
EXOC3	ILMN-1789419	5	rs1578076	10	55228462		rs12188164	5	4928236	EXOC3	6.83	0.74	0.19	0.44
FAHD1	ILMN-2246661	16	rs1560104	16	12708208		rs344363	16	1972548	FAHD1	6.33	0.27	0.30	0.30
FCN1	ILMN-1668063	9	rs12580388	12	129591144		rs10120023	9	137810259	COQ10A	6.33	0.27	0.30	0.30

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Table S1 – continued from previous page

Gene ID ^a	Probe ID ^b	Expression trait		SNP 1			SNP 2			Interaction statistic ^f / -log ₁₀ p-values			Distance / Mb ^h		
		rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c	Association ^d	BSGS ^e	Fehrmann ^f	EGCUT ^g			
FE2Z	ILMN-1739586	2	rs2356400	19	44321776			rs13406184	2	36791226	FE2Z	5.78	0.14	0.33	0.16
FE2Z	ILMN-1739586	2	rs969010	4	159963132			rs11691600	2	36810133	FE2Z	6.59	0.14	0.28	0.14
FGD2	ILMN-2115005	6	rs4803848	19	46203030			rs31486	6	37001267	FGD2	5.69	0.12	0.25	0.11
FLJ20489	ILMN-2115005	12	rs9024634	10	133943931			rs831489	6	36999652	FLJ20489	5.49	1.20	0.11	0.66
FLJ20489	ILMN-1778144	12	rs17015703	12	117036766	FLJ20489		rs3782908	12	48169526	FLJ20489	5.81	0.06	0.70	0.29
FLJ20489	ILMN-1778144	12	rs472408	12	4569326			rs769951	12	16769951	FLJ20489	5.73	0.03	0.11	0.02
FLJ20489	ILMN-1778144	12	rs472408	12	4569326			rs82828	12	48169526	FLJ20489	5.73	0.03	0.11	0.02
FLJ20489	ILMN-1778144	12	rs934440	17	97033126			rs782908	12	48169526	FLJ20489	6.49	0.31	0.47	0.36
FLJ20489	ILMN-1778144	12	rs204135	16	50626195			rs3782908	12	48169526	FLJ20489	6.04	0.38	0.17	0.21
FLJ20489	ILMN-1763663	16	rs9325634	21	43818790			rs3782908	12	48169526	FLJ20489	6.04	0.38	0.17	0.21
FLJ43093	ILMN-212450	6	rs17112712	14	107276627			rs6906101	6	36667610	FLJ43093	5.48	0.14	0.95	0.53
FLJ43093	ILMN-212450	6	rs6906101	14	107276627	FLJ43093		rs13214069	6	32705248	FLJ43093	5.44	0.39	0.06	0.13
FN3KRP	ILMN-1652333	17	rs898095	17	80890638			rs9892064	17	808927903	FN3KRP	16.16	28.24	29.39	59.95
FUC1	ILMN-1752728	17	rs4971478	17	13406033			rs12744386	17	24168019	FUC1	6.41	0.01	0.30	0.06
FXD5	ILMN-2309848	19	rs1633921	19	35695200			rs788175	13	98338559	FXD5	3.70	0.09	0.41	0.17
FXD5	ILMN-2309848	19	rs17398183	20	55609148			rs2285515	19	35660450	FXD5	6.58	0.03	0.48	0.15
FXD5	ILMN-2309848	19	rs2285515	19	35660450	FXD5		rs13067700	3	95331048	FXD5	5.70	0.07	0.17	0.05
FXD5	ILMN-2309848	19	rs2285515	19	35660450	FXD5		rs17036504	2	47567329	FXD5	6.00	0.09	0.09	0.51
G3BP2	ILMN-231758	4	rs10230232	17	29390239			rs1553985	4	7654604	G3BP2	6.10	0.28	0.08	0.04
GAA	ILMN-2410783	17	rs11150847	17	78153130			rs12602462	17	78146016	GAA	13.91	19.98	12.99	32.60
GAA	ILMN-2410783	17	rs8068856	17	78100731	GAA		rs10902506	12	1332678089	GAA	5.65	0.11	0.39	0.17
GAPT	ILMN-1675191	5	rs10070522	5	57786110	GAPT		rs7605821	2	2335655228	GAPT	5.85	0.01	0.78	0.28
GAPT	ILMN-1675191	5	rs20838717	10	128038717			rs10070522	5	57786110	GAPT	5.72	0.26	0.11	0.11
GATS	ILMN-1699631	7	rs1147447	14	66460742			rs2950520	7	99827148	GATS	5.47	0.83	0.63	0.87
GATS	ILMN-1699631	7	rs2425256	20	35056572			rs2950520	7	99827148	GATS	6.22	0.38	0.35	0.33
GDPD3	ILMN-1774901	16	rs3809624	16	30102802	GDPD3		rs2197465	14	48572632	GDPD3	5.67	0.38	0.35	0.33
GDPD3	ILMN-1774901	16	rs7204270	16	30102802	GDPD3		rs1015111	4	128972357	GDPD3	5.86	0.55	0.09	0.24
GNLY	ILMN-1790692	2	rs145072	13	110899955			rs7577283	4	128972357	GNLY	5.78	0.02	0.45	0.13
GNLY	ILMN-1790692	2	rs1986426	16	26084476			rs7960552	12	111164237	GNLY	5.72	0.02	0.45	0.13
GNPN3	ILMN-3239426	12	rs1860563	16	6478898			rs2707210	12	6902002	GNPN3	5.49	0.36	0.46	0.39
GPR162	ILMN-1730816	12	rs2272500	12	79685913			rs2707210	12	6902002	GPR162	5.07	0.25	0.03	0.06
GPR162	ILMN-1730816	12	rs2707210	12	79685913			rs4740848	9	6554558	GPR162	5.47	0.25	0.06	0.07
GPR162	ILMN-1730816	12	rs2707210	12	6902002	GPR162		rs9827054	3	188880113	GPR162	6.21	0.96	0.06	0.44
GPR177	ILMN-1660549	1	rs11057383	12	124369421			rs12065581	1	68732819	GPR177	5.45	0.72	0.67	0.81
GPR177	ILMN-1660549	1	rs12527241	6	120468039			rs12065581	1	68732819	GPR177	5.76	0.17	0.40	0.22
GPR177	ILMN-1660549	1	rs12532999	9	127939793			rs12065581	1	68732819	GPR177	5.43	0.79	1.43	1.50
GPR177	ILMN-1660549	1	rs225613	16	11169683			rs12065581	1	68732819	GPR177	5.43	0.11	0.13	0.13
GPR177	ILMN-1660549	1	rs9575097	13	82986268			rs12065581	1	68732819	GPR177	6.04	0.95	0.21	0.60
GPR177	ILMN-2283325	1	rs6566669	18	70506011			rs12065581	1	68732819	GPR177	5.86	0.24	0.34	0.23
GPR177	ILMN-2283325	1	rs9290426	3	171399932			rs12065581	1	68732819	GPR177	6.50	0.01	0.24	0.04
GSDMB	ILMN-2347193	17	rs11557467	17	38028634	GSDMB		rs4965745	15	101508261	GSDMB	5.88	0.68	0.20	0.41
GSTM1	ILMN-2391861	1	rs12248673	10	53192833			rs11101992	1	110266754	GSTM1	6.11	0.27	1.14	0.79
GSTM1	ILMN-2391861	1	rs1547574	13	85345257			rs11101992	1	110266754	GSTM1	5.91	0.27	1.14	0.79
GSTM2	ILMN-2201580	1	rs6432807	13	96159560			rs3754446	1	110253241	GSTM2	6.77	0.36	0.27	0.19
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs4583333	2	77919015	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs4947007	15	58677017	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs9883949	21	19532546	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11	5271671	H1FO	6.36	0.66	0.52	0.65
H1FO	ILMN-1757467	22	rs139898	22	38399979			rs2855039	11						

Continued on next page

Table S1 – continued from previous page

Gene ID ^a	Expression trait ^b	Chr.	rs ID	Chr.	SNP 1	Pos/Mb ^c	Association ^d	rs ID	Chr.	SNP 2	Pos/Mb ^c	Association ^d	BSGS ^e	Fehrmann ^f	EGCUT ^g	Meta ^g	Distance / Mb ^h
HGB2	ILMN-2084825	11	rs12975066	19	35723501	35723501	HGB2	rs2855039	11	3271671	3271671	HGB2	5.77	0.08	0.13	0.05	
HGB2	ILMN-2084825	11	rs2855039	11	35723501	35723501	HGB2	rs2855039	11	3271671	3271671	HGB2	5.77	0.08	0.13	0.05	
HGB2	ILMN-2084825	11	rs2855039	11	35723501	35723501	HGB2	rs2855039	11	3271671	3271671	HGB2	5.77	0.08	0.13	0.05	
HDBA7	ILMN-2064825	11	rs2855039	11	35723501	35723501	HDBA7	rs2855039	11	35723501	35723501	HDBA7	5.77	0.08	0.13	0.05	
HDBA7	ILMN-2064825	11	rs2855039	11	35723501	35723501	HDBA7	rs2855039	11	35723501	35723501	HDBA7	5.77	0.08	0.13	0.05	
HDBA7	ILMN-2064825	11	rs2855039	11	35723501	35723501	HDBA7	rs2855039	11	35723501	35723501	HDBA7	5.77	0.08	0.13	0.05	
HEBP1	ILMN-1802567	12	rs2109029	16	6036851	6036851	HEBP1	rs2109029	16	6036851	6036851	HEBP1	5.75	0.00	0.46	0.10	
HEBP1	ILMN-1802567	12	rs2109029	16	6036851	6036851	HEBP1	rs2109029	16	6036851	6036851	HEBP1	5.75	0.00	0.46	0.10	
HEBP1	ILMN-1802567	12	rs2109029	16	6036851	6036851	HEBP1	rs2109029	16	6036851	6036851	HEBP1	5.75	0.00	0.46	0.10	
HEXDC	ILMN-1741180	17	rs1942719	18	71345613	71345613	HEXDC	rs1942719	18	71345613	71345613	HEXDC	5.81	0.15	0.59	0.32	
HEXDC	ILMN-1741180	17	rs1942719	18	71345613	71345613	HEXDC	rs1942719	18	71345613	71345613	HEXDC	5.81	0.15	0.59	0.32	
HEXDC	ILMN-1741180	17	rs1942719	18	71345613	71345613	HEXDC	rs1942719	18	71345613	71345613	HEXDC	5.81	0.15	0.59	0.32	
HLA-DRA	ILMN-2157441	6	rs4896635	14	75346732	75346732	HLA-DRA	rs4896635	14	75346732	75346732	HLA-DRA	5.81	1.61	0.34	1.22	
HLA-DRA	ILMN-2157441	6	rs4896635	14	75346732	75346732	HLA-DRA	rs4896635	14	75346732	75346732	HLA-DRA	5.81	1.61	0.34	1.22	
HLA-DRA	ILMN-2157441	6	rs4896635	14	75346732	75346732	HLA-DRA	rs4896635	14	75346732	75346732	HLA-DRA	5.81	1.61	0.34	1.22	
HMBX1	ILMN-1720059	8	rs12435486	14	98070849	98070849	HMBX1	rs12435486	14	98070849	98070849	HMBX1	5.94	0.90	0.16	0.52	
HMBX1	ILMN-1720059	8	rs12435486	14	98070849	98070849	HMBX1	rs12435486	14	98070849	98070849	HMBX1	5.94	0.90	0.16	0.52	
HMBX1	ILMN-1720059	8	rs12435486	14	98070849	98070849	HMBX1	rs12435486	14	98070849	98070849	HMBX1	5.94	0.90	0.16	0.52	
HMBX1	ILMN-1720059	8	rs2857803	21	42112794	42112794	HMBX1	rs2857803	21	42112794	42112794	HMBX1	6.54	1.00	0.47	0.86	
HMBX1	ILMN-1720059	8	rs2857803	21	42112794	42112794	HMBX1	rs2857803	21	42112794	42112794	HMBX1	6.54	1.00	0.47	0.86	
HMBX1	ILMN-1720059	8	rs2857803	21	42112794	42112794	HMBX1	rs2857803	21	42112794	42112794	HMBX1	6.54	1.00	0.47	0.86	
HMBX1	ILMN-1720059	8	rs47063451	12	127237464	127237464	HMBX1	rs47063451	12	127237464	127237464	HMBX1	6.62	0.05	1.11	1.34	
HMBX1	ILMN-1720059	8	rs47063451	12	127237464	127237464	HMBX1	rs47063451	12	127237464	127237464	HMBX1	6.62	0.05	1.11	1.34	
HMBX1	ILMN-1720059	8	rs47063451	12	127237464	127237464	HMBX1	rs47063451	12	127237464	127237464	HMBX1	6.62	0.05	1.11	1.34	
HMBX1	ILMN-1720059	8	rs5876339	8	28904086	28904086	HMBX1	rs5876339	8	28904086	28904086	HMBX1	6.80	0.39	3.13	2.52	
HMBX1	ILMN-1720059	8	rs5876339	8	28904086	28904086	HMBX1	rs5876339	8	28904086	28904086	HMBX1	6.80	0.39	3.13	2.52	
HMBX1	ILMN-1720059	8	rs5876339	8	28904086	28904086	HMBX1	rs5876339	8	28904086	28904086	HMBX1	6.80	0.39	3.13	2.52	
HMBX1	ILMN-1720059	8	rs8180944	8	28904086	28904086	HMBX1	rs8180944	8	28904086	28904086	HMBX1	6.88	3.38	0.63	4.44	
HMBX1	ILMN-1720059	8	rs8180944	8	28904086	28904086	HMBX1	rs8180944	8	28904086	28904086	HMBX1	6.88	3.38	0.63	4.44	
HMBX1	ILMN-1720059	8	rs8180944	8	28904086	28904086	HMBX1	rs8180944	8	28904086	28904086	HMBX1	6.88	3.38	0.63	4.44	
HMBX1	ILMN-2101920	5	rs6894268	13	110897444	110897444	HMBX1	rs6894268	13	110897444	110897444	HMBX1	6.12	0.34	0.66	0.52	
HMBX1	ILMN-2101920	5	rs6894268	13	110897444	110897444	HMBX1	rs6894268	13	110897444	110897444	HMBX1	6.12	0.34	0.66	0.52	
HMBX1	ILMN-2101920	5	rs6894268	13	110897444	110897444	HMBX1	rs6894268	13	110897444	110897444	HMBX1	6.12	0.34	0.66	0.52	
HMBX1	ILMN-3194087	1	rs505812	16	88882257	88882257	HMBX1	rs505812	16	88882257	88882257	HMBX1	5.51	0.66	0.67	10.37	
HMBX1	ILMN-3194087	1	rs505812	16	88882257	88882257	HMBX1	rs505812	16	88882257	88882257	HMBX1	5.51	0.66	0.67	10.37	
HMBX1	ILMN-3194087	1	rs505812	16	88882257	88882257	HMBX1	rs505812	16	88882257	88882257	HMBX1	5.51	0.66	0.67	10.37	
HMBX1	ILMN-3194087	1	rs6062359	12	121228953	121228953	HMBX1	rs6062359	12	121228953	121228953	HMBX1	6.61	0.61	0.61	0.61	
HMBX1	ILMN-3194087	1	rs6062359	12	121228953	121228953	HMBX1	rs6062359	12	121228953	121228953	HMBX1	6.61	0.61	0.61	0.61	
HMBX1	ILMN-3194087	1	rs6062359	12	121228953	121228953	HMBX1	rs6062359	12	121228953	121228953	HMBX1	6.61	0.61	0.61	0.61	
HMBX1	ILMN-3194087	1	rs7088538	10	101884937	101884937	HMBX1	rs7088538	10	101884937	101884937	HMBX1	6.48	0.40	0.50	0.29	
HMBX1	ILMN-3194087	1	rs7088538	10	101884937	101884937	HMBX1	rs7088538	10	101884937	101884937	HMBX1	6.48	0.40	0.50	0.29	
HMBX1	ILMN-3194087	1	rs7088538	10	101884937	101884937	HMBX1	rs7088538	10	101884937	101884937	HMBX1	6.48	0.40	0.50	0.29	
HMBX1	ILMN-1778010	16	rs1354999	16	3115628	3115628	HMBX1	rs1354999	16	3115628	3115628	HMBX1	5.53	0.19	0.23	0.44	
HMBX1	ILMN-1778010	16	rs1354999	16	3115628	3115628	HMBX1	rs1354999	16	3115628	3115628	HMBX1	5.53	0.19	0.23	0.44	
HMBX1	ILMN-1778010	16	rs1354999	16	3115628	3115628	HMBX1	rs1354999	16	3115628	3115628	HMBX1	5.53	0.19	0.23	0.44	
HMBX1	ILMN-2368530	16	rs705044	16	2603711	2603711	HMBX1	rs705044	16	2603711	2603711	HMBX1	5.53	0.19	0.23	0.44	
HMBX1	ILMN-2368530	16	rs705044	16	2603711	2603711	HMBX1	rs705044	16	2603711	2603711	HMBX1	5.53	0.19	0.23	0.44	
HMBX1	ILMN-2368530	16	rs705044	16	2603711	2603711	HMBX1	rs705044	16	2603711	2603711	HMBX1	5.53	0.19	0.23	0.44	
HMBX1	ILMN-1815727	7	rs778355	12	47970693	47970693	HMBX1	rs778355	12	47970693	47970693	HMBX1	5.64	0.65	0.33	0.33	
HMBX1	ILMN-1815727	7	rs778355	12	47970693	47970693	HMBX1	rs778355	12	47970693	47970693	HMBX1	5.64	0.65	0.33	0.33	
HMBX1	ILMN-1815727	7	rs778355	12	47970693	47970693	HMBX1	rs778355	12	47970693	47970693	HMBX1	5.64	0.65	0.33	0.33	
HMBX1	ILMN-1697536	21	rs2186344	21	55224635	55224635	HMBX1	rs2186344	21	55224635	55224635	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1697536	21	rs2186344	21	55224635	55224635	HMBX1	rs2186344	21	55224635	55224635	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1697536	21	rs2186344	21	55224635	55224635	HMBX1	rs2186344	21	55224635	55224635	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1691863	19	rs649216	19	84397119	84397119	HMBX1	rs649216	19	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1691863	19	rs649216	19	84397119	84397119	HMBX1	rs649216	19	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1691863	19	rs649216	19	84397119	84397119	HMBX1	rs649216	19	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1811104	3	rs4346053	13	84397119	84397119	HMBX1	rs4346053	13	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1811104	3	rs4346053	13	84397119	84397119	HMBX1	rs4346053	13	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1811104	3	rs4346053	13	84397119	84397119	HMBX1	rs4346053	13	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-236109	22	rs4329208	22	84397119	84397119	HMBX1	rs4329208	22	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-236109	22	rs4329208	22	84397119	84397119	HMBX1	rs4329208	22	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-236109	22	rs4329208	22	84397119	84397119	HMBX1	rs4329208	22	84397119	84397119	HMBX1	5.53	0.46	0.89	0.77	
HMBX1	ILMN-1689792	4	rs704087	4	132032868	132032868	HMBX1	rs704087	4	132032868	132032868	HMBX1	5.72	0.24	0.47	0.31	
HMBX1	ILMN-1689792	4	rs704087	4	132032868	132032868	HMBX1	rs704087	4	132032868	132032868	HMBX1	5.72	0.24	0.47	0.31	
HMBX1	ILMN-1689792	4	rs704087	4	132032868	132032868	HMBX1	rs704087	4	132032868	132032868	HMBX1	5.72	0.24	0.47	0.31	
HMBX1	ILMN-1700782	1	rs1														

Table S1 – continued from previous page

Gene ID ^a	Chr.	Expression trait		SNP 1		SNP 2		Interaction statistic ^f		EGCUT ^e / -log ₁₀ p-values		Distance / Mb ^b	
		rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c	Association ^d	BSGS ^e	Fehrmann ^f		
MBNL1	3	rs4392435	4	41513423		rs13069559	3	152187431	MBNL1	8.39	0.02	4.33	3.02
MBNL1	3	rs4735850	8	895841		rs15069559	3	152187431	MBNL1	6.74	0.32	4.21	3.38
MBNL1	3	rs4935958	18	46278091		rs1522374	3	15223530		7.72	0.03	0.27	0.07
MBNL1	3	rs6128397	20	57263132		rs10804367	3	152234166		7.22	1.34	1.15	1.73
MBNL1	3	rs710738	20	57263132		rs13069559	3	152187431	MBNL1	7.92	2.55	7.89	9.28
MBNL1	3	rs710738	20	57263132		rs10804367	3	152234166	MBP	7.40	0.03	0.23	0.07
MBP	18	rs30568	22	43210981		rs2051344	18	74715653	MBP	5.56	0.02	0.76	0.27
MBP	18	rs30568	22	43210981		rs1125539	3	155204939		5.79	0.02	0.76	0.27
MBP	18	rs2051344	18	74715653	MBP	rs1125539	3	155204939		6.03	0.15	0.50	0.26
MBP	18	rs2051344	18	74715653	MBP	rs2051344	18	74715653	MBP	5.82	0.03	0.47	0.14
MBP	18	rs4805021	19	33436367		rs4808076	19	74747424		5.40	7.06	3.13	1.71
MBP	18	rs8002433	18	74747424		rs966396	1	12050634	MBP	4.63	1.13	1.33	1.33
MBP	13	rs7989895	13	109401737		rs4846085	4	171860973	MBP	5.71	0.61	0.25	0.41
MBP	2	rs12718598	7	50428445		rs11725347	4	171860973	MBP	5.57	0.07	1.03	0.50
MBP	2	rs12718598	7	50428445		rs12718598	7	50428445	MBP	5.07	0.13	0.30	0.41
MBP	2	rs674608	16	82628245		rs12718598	7	50428445	MBP	5.07	0.11	1.02	0.05
MBP	2	rs674608	16	82628245		rs2660665	8	137526799	MBP	4.17	0.05	0.08	0.02
MBP	2	rs457871	20	26197931	MGC72104	rs2660665	8	137526799	MBP	5.45	0.57	0.27	0.40
MBP	2	rs457871	20	26197931	MGC72104	rs4147592	1	165600146	MBP	5.90	0.01	0.23	0.05
MBP	2	rs457871	20	26197931	MGC72104	rs11771552	7	154708716	MBP	5.64	0.97	1.08	1.35
MBP	2	rs1316716	12	118076069	MPZL2	rs1805	11	118076069	MPZL2	5.71	0.04	0.34	0.18
MBP	2	rs1316716	12	118076069	MPZL2	rs750495	5	1782046	MPZL2	6.89	0.34	0.18	0.19
MBP	2	rs17469061	16	84364332		rs2863095	10	102746503	MPZL2	5.71	0.26	0.14	0.22
MBP	2	rs17469061	16	84364332		rs3811188	14	42194916	MPZL2	6.56	0.14	0.64	0.70
MBP	2	rs1905857	14	26710271		rs722269	6	42158596	MPZL2	7.48	0.46	0.63	0.46
MBP	2	rs1905857	14	26710271		rs2395803	6	42158596	MPZL2	6.85	0.31	0.63	0.46
MBP	2	rs1905857	14	26710271		rs11698155	20	15063214	MPZL2	6.21	0.41	0.25	0.28
MBP	2	rs1905857	14	26710271		rs12431444	14	42068689	MPZL2	5.18	1.87	1.87	2.86
MBP	2	rs12431444	14	42068689	MPZL2	rs12431444	14	42068689	MPZL2	6.31	0.46	0.52	0.50
MBP	2	rs12431444	14	42068689	MPZL2	rs11160227	4	95514596	MPZL2	5.83	0.11	0.50	0.23
MBP	2	rs12431444	14	42068689	MPZL2	rs4973801	21	29363604	MPZL2	6.78	0.29	0.92	0.65
MBP	2	rs12431444	14	42068689	MPZL2	rs130120	21	29363604	MPZL2	5.56	0.13	0.46	0.23
MBP	2	rs12431444	14	42068689	MPZL2	rs1317149	11	4748685	MPZL2	6.78	0.29	0.92	0.65
MBP	2	rs12431444	14	42068689	MPZL2	rs124681	11	47529947	MPZL2	5.56	0.13	0.46	0.23
MBP	2	rs12431444	14	42068689	MPZL2	rs2737422	16	134485237	MPZL2	6.02	0.74	0.15	0.40
MBP	2	rs12431444	14	42068689	MPZL2	rs11694236	4	76870229	MPZL2	5.54	0.20	0.59	1.77
MBP	2	rs12431444	14	42068689	MPZL2	rs6826085	4	76870229	MPZL2	5.65	0.20	0.59	1.77
MBP	2	rs12431444	14	42068689	MPZL2	rs6826085	4	76870229	MPZL2	5.46	0.27	0.43	0.30
MBP	2	rs12431444	14	42068689	MPZL2	rs6826085	4	76870229	MPZL2	6.08	0.07	0.48	0.18
MBP	2	rs12431444	14	42068689	MPZL2	rs2786014	1	234897243	MPZL2	8.45	15.12	16.08	30.77
MBP	2	rs12431444	14	42068689	MPZL2	rs3889129	3	184613680	MPZL2	5.62	1.27	0.19	0.81
MBP	2	rs12431444	14	42068689	MPZL2	rs4862705	4	187445552	MPZL2	6.12	1.07	0.76	1.01
MBP	2	rs12431444	14	42068689	MPZL2	rs6455553	6	167811764	MPZL2	6.86	1.10	2.58	2.77
MBP	2	rs12431444	14	42068689	MPZL2	rs700276	7	146189057	MPZL2	6.03	0.13	0.47	0.23
MBP	2	rs12431444	14	42068689	MPZL2	rs1751561	2	213386267	MPZL2	6.60	0.29	0.88	0.63
MBP	2	rs12431444	14	42068689	MPZL2	rs1213758	8	144663661	MPZL2	5.50	0.12	0.17	0.08
MBP	2	rs12431444	14	42068689	MPZL2	rs2123758	8	144663661	MPZL2	5.58	0.67	1.10	0.40
MBP	2	rs12431444	14	42068689	MPZL2	rs930280	9	98391111	MPZL2	5.58	0.82	1.10	0.40
MBP	2	rs12431444	14	42068689	MPZL2	rs10852406	10	93976932	MPZL2	7.38	2.11	0.44	0.71
MBP	2	rs12431444	14	42068689	MPZL2	rs7077137	2	234721287	MPZL2	9.38	7.31	6.33	12.70
MBP	2	rs12431444	14	42068689	MPZL2	rs4773381	12	23228670	MPZL2	7.38	0.43	0.34	0.32
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	6.84	0.43	0.34	0.32
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42068689	MPZL2	rs12400878	3	183141003	MPZL2	5.90	0.24	0.04	0.06
MBP	2	rs12431444	14	42									

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Table S1 – continued from previous page

[illegible]

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Table S1 – continued from previous page

Gene ID ^a			Expression trait			SNP 1			SNP 2			Interaction statistic ^f			BGS ^g			-log ₁₀ p-values			Distance / Mb ^b		
Gene	ID ^a	Chr.	rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c	Association ^d	rs ID	Chr.	Pos/Mb ^c	F _{DR}	F _{DR} max	Meta ^g	EGCUT ^e	Meta ^g	EGCUT ^e	Meta ^g	Distance	Mb ^b	
RENE	ILMN_1802830	1	rs4982958	14	24987865		rs301819	1	8501786	RENE	rs301819	1	8501786	5.66	0.61	1.23	1.17						
RENE	ILMN_1802838	1	rs7697290	4	135248366		rs301819	1	8501786	RENE	rs301819	1	8501786	5.74	0.14	0.10	0.06						
RENE	ILMN_1802839	1	rs11085629	19	13174312		rs301819	1	8501786	RENE	rs301819	1	8501786	5.12	0.21	0.33	0.21						
RENE	ILMN_1802840	1	rs301819	3	12844086		rs301819	1	8501786	RENE	rs301819	1	8501786	5.71	0.08	0.60	0.26						
RENE	ILMN_1802841	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802842	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802843	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802844	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802845	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802846	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802847	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802848	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802849	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802850	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802851	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802852	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802853	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802854	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802855	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802856	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802857	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802858	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802859	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802860	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802861	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802862	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802863	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802864	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802865	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802866	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802867	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802868	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802869	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802870	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802871	1	rs301819	3	12844086	RNASE6	rs17495030	13	100601327		rs17495030	13	100601327	5.48	0.42	0.21	0.26						
RENE	ILMN_1802872	8	rs4143674	20	4741304	RPL8	rs2958482	8	145984615		rs2958482	8	145984615	5.48	0.42	0.21	0.26						
RENE	ILMN_1802873	8	rs4143674	20	4741304	RPL8	rs2958482	8	145984615		rs2958482	8	145984615	5.48	0.42	0.21	0.26						
RENE	ILMN_1802874	8	rs4143674	20	4741304	RPL8	rs2958482	8	145984615		rs2958482	8	145984615	5.48	0.42	0.21	0.26						
RENE	ILMN_1802875	8	rs4143674	20	4741304	RPL8	rs2958482	8	145984615		rs2958482	8	145984615	5.48	0.42	0.21	0.26						
RENE	ILMN_1802876	3	rs4889214	16	80948015	SEC13	rs4889214	16	80948015		rs4889214	16	80948015	5.48	0.42	0.21	0.26						
RENE	ILMN_1802877	3	rs4889214	16	80948015	SEC13	rs4889214	16	80948015		rs4889214	16	80948015	5.48	0.42	0.21	0.26						
RENE	ILMN_1802878	1	rs17085428	15	95388015	SEC13	rs17085428	15	95388015		rs17085428	15	95388015	5.48	0.42	0.21	0.26						
RENE	ILMN_1802879	1	rs17085428	15	95388015	SEC13	rs17085428	15	95388015		rs17085428	15	95388015	5.48	0.42	0.21	0.26						
RENE	ILMN_1802880	1	rs17085428	15	95388015	SEC13	rs17085428	15	95388015		rs17085428	15	95388015	5.48	0.42	0.21	0.26						
RENE	ILMN_1802881	1	rs17085428	15	95388015	SEC13	rs17085428	15	95388015		rs17085428	15	95388015	5.48	0.42	0.21	0.26						
RENE	ILMN_1802882	11	rs12147460	14	104412137	SES3	rs12147460	14	104412137		rs12147460	14	104412137	5.48	0.42	0.21	0.26						
RENE	ILMN_1802883	11	rs553391	15	46591793	SES3	rs553391	15	46591793		rs553391	15	46591793	5.48	0.42	0.21	0.26						
RENE	ILMN_1802884	11	rs553391	15	46591793	SES3	rs553391	15	46591793		rs553391	15	46591793	5.48	0.42	0.21	0.26						
RENE	ILMN_1802885	11	rs553391	15	46591793	SES3	rs553391	15	46591793		rs553391	15	46591793	5.48	0.42	0.21	0.26						
RENE	ILMN_1802886	11	rs553391	15	46591793	SES3	rs553391	15	46591793		rs553391	15	46591793	5.48	0.42	0.21	0.26						
RENE	ILMN_1802887	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802888	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802889	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802890	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802891	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802892	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802893	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802894	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE	ILMN_1802895	6	rs10838191	11	94906111	SES3	rs10838191	11	94906111		rs10838191	11	94906111	5.48	0.42	0.21	0.26						
RENE</																							

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Table S1 – continued from previous page

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Table S1 – continued from previous page

Expression trait		SNP 1				SNP 2				Interaction statistic / -log ₁₀ p-values					
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	Distance / Mb ^h
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	1.643
VASP	ILMN-1743646	19	rs1264226	19	40663167		rs2276470	19	45974668	VNN2	5.09	0.94	5.14	4.95	0.088
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-1804935	6	rs10278073	7	151662184		rs2267932	6	133067782	VNN3	6.44	0.16	0.74	0.41	
VNN3	ILMN-1804935	6	rs1443946	8	73006453		rs2267932	6	133067782	VNN3	5.74	0.23	0.48	0.31	
VNN3	ILMN-1804935	6	rs348462	9	73547169		rs2267932	6	133067782	VNN3	6.44	0.31	0.17	0.17	
VNN3	ILMN-1804935	6	rs7157055	14	83262064		rs2267932	6	133067782	VNN3	5.82	0.03	0.19	0.04	
VNN3	ILMN-2387680	6	rs2823165	21	5694253		rs2267932	6	133067782	VNN3	6.12	0.73	1.15	1.21	
VNN3	ILMN-2387680	6	rs9596457	13	51692548		rs2267932	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	1.17	0.26	
VSTM1	ILMN-1763455	19	rs9628570	22	30261219		rs10500316	19	54553697	VSTM1	5.88	0.81	1.38	1.47	
WDR48	ILMN-1762103	3	rs1388935	4	138927822		rs6778963	3	39091812	WDR48	5.88	0.09	0.33	0.09	
WDR48	ILMN-1762103	3	rs1887778	9	134635088	RAPGEF1	rs853349	3	39067925	WDR48	5.94	0.57	1.35	1.22	
WDR6	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		rs7715581	3	49194351	WDR6	4.86	1.64	1.43	2.25	
XAF1	ILMN-233053	17	rs1353031	21	9673170	XAF1	rs12591171	15	93119799		5.86	2.38	0.17	1.63	
ZFP90	ILMN-1684628	16	rs909446	17	37040648		rs1182968	16	68573945	ZFP90	5.79	0.09	0.36	0.15	
ZNF500	ILMN-1700238	16	rs4283723	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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