Detection and replication of epistasis influencing transcription in humans

Gibran Hemani[1,2,*], Konstantin Shakhbazov[1,2], Harm-Jan Westra[3], Anjali K Henders[4], Allan F. McRae[1,2], Andres Metspalu[5], Greg Gibson[6], Nick G Martin[4], Tonu Esko[5,7,8], Lude Franke[3], Grant W Montgomery[4], Peter M Visscher[1,2], and Joseph E Powell[1,2]

[1]University of Queensland Diamantina Institute, University of Queensland, Princess Alexandra Hospital, Brisbane, Queensland, Australia. [2]The University of Queensland, Queensland Brain Institute, Brisbane, QLD, Australia. [3]Department of Genetics, University Medical Center Groningen, University of Groningen, Hanzeplein 1, Groningen, the Netherlands. [4]Queensland Institute of Medical Research, Brisbane, Queensland, Australia. [5]Estonian Genome Center, University of Tartu, Tartu, 51010, Estonia. [6]School of Biology and Centre for Integrative Genomics, Georgia Institute of Technology, Atlanta, Georgia United States of America. [7]Divisions of Endocrinology, Children's Hospital, Boston, MA, 02115, US. [8]Medical and Population Genetics, Broad Institute, Cambridge, MA, 02142, US. [*]Corresponding author: g.hemani@uq.edu.au

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 traits[1] 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 techniques[10] 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 whole 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 interactions[13] ($p = 1.8 \times 10^{-10}$). 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 mutations[4] but also at the evolutionary scale in fitness adaptation[15] 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 re-

duced 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 testing[9] all make it more difficult to detect epistasis in comparison to additive effects. When genetic effect sizes are small, 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. 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, BSGS[22]) 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 whole 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, Fehrmann[12] 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, we observed that 316 of the remaining 404 discovery SNPs had replication interaction p-values exceeding the one-tailed 2.5% confidence interval under the null distribution of no 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 185 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 four 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 association[21] (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 ($p = 0.22$ 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 splicing[25]) 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 expresson 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 types[26] (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 lines[28] (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

4

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 perspective[31] 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 functional 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 portal to understanding molecular mechanisms and complex trait variation with greater clarity. 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 whole blood samples for 7,339

probes representing 6,158 RefSeq genes. Recent hardware and software[10] advances made it possible to perform the 1.03×10^{15} statistical tests to complete this analysis. We used permutation analysis[32] 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 sentinal 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 whole blood, the Fehrmann dataset[12] ($n = 1240$) and the Estonian Genome Centre University of the University of Tartu (EGCUT) dataset[11] ($n = 891$). 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

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
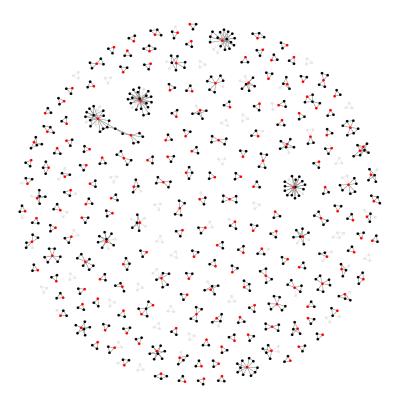
3 Figures

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.
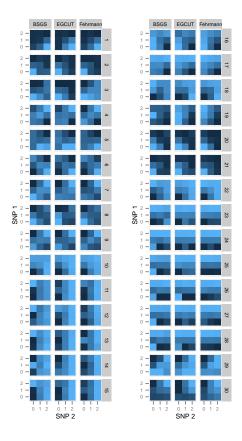
Figure 2: **Replication of GP maps in two independent populations** The GP maps for each epistatic interaction that is significant at the Bonferroni level in both replication datasets are shown. Each GP map consists of nine tiles where each tile represents the expression level for that two-locus genotype 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.
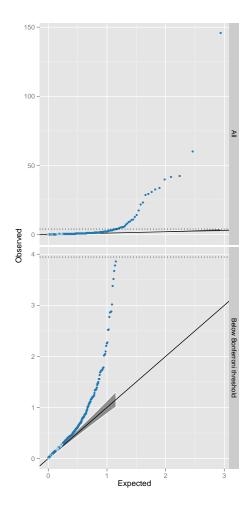
Figure 3: **Q-Q plots of interaction p-values from replication datasets**
The top panel shows all 434 discovery SNPs that were tested for interactions.
Observed p-values (y-axis, $-\log_{10}$ scale) are plotted against the expected p-values (x-axis, $-\log_{10}$ scale). The multiple testing correction 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.
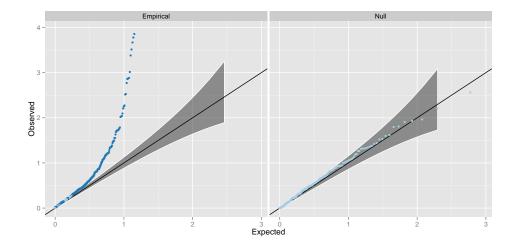
4   Supplementary Figures

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.
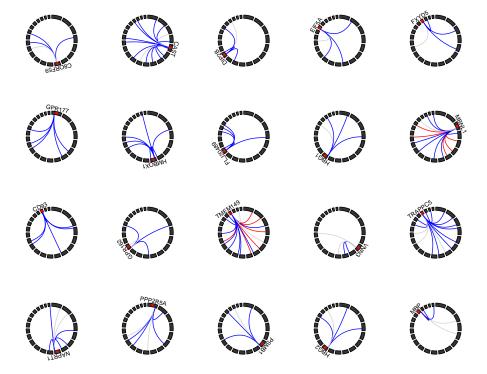
Figure S2: **Gene expression traits with four or more genetic interactions** Circle plots represent the genomic positions for SNPs (linking lines) and expression probes (red points). Chromosomes are represented by black blocks and ordered from 1 to 22 clockwise, starting from the top. Grey lines represent 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.
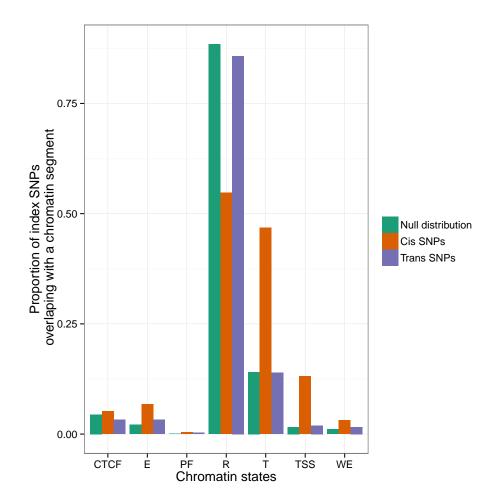
Figure S3: **Location of SNPs relative to genomic features** All SNPs within 1Mb and $r^2 > 0.8$ of each *cis-* and *trans*-SNP were taken to find which genomic features (*x*-axis) were covered by the SNPs that compose the 501 significant interactions. Green bars represent the proportion (*y*-axis) of 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
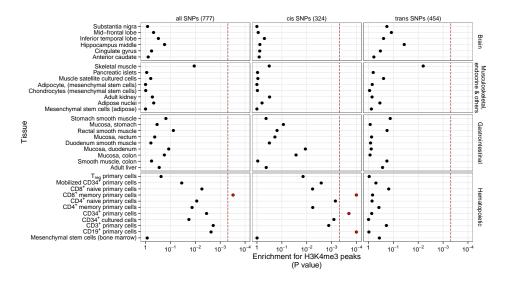
14

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.
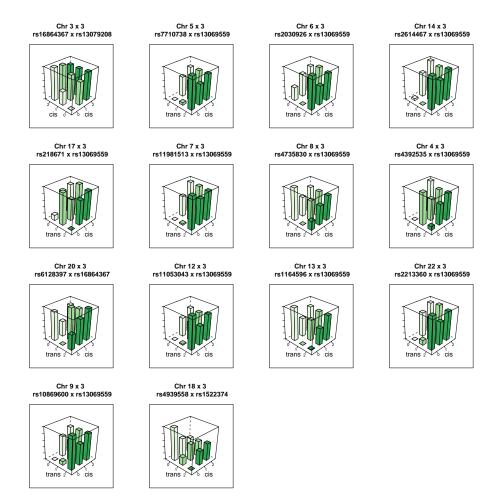
Figure S5: **Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions the *cis* effect is masked when the *trans* SNP is homozygous.
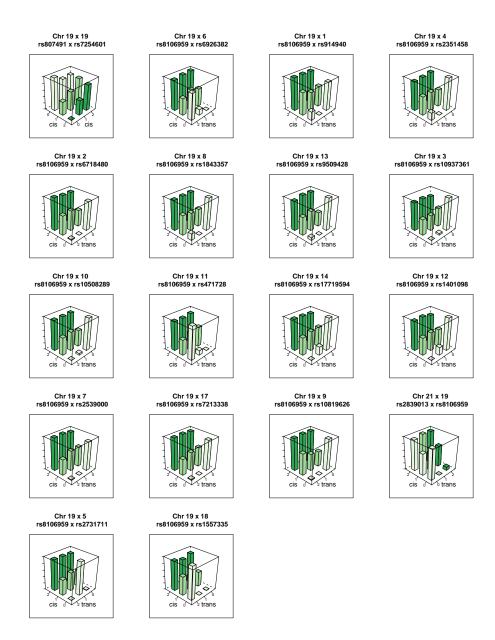
Figure S6: **Genotype-phenotype maps for 19 interactions influencing the expression of TMEM149** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of TMEM149, but in many of these interactions the *cis* effect is masked when the *trans* SNP is homozygous.
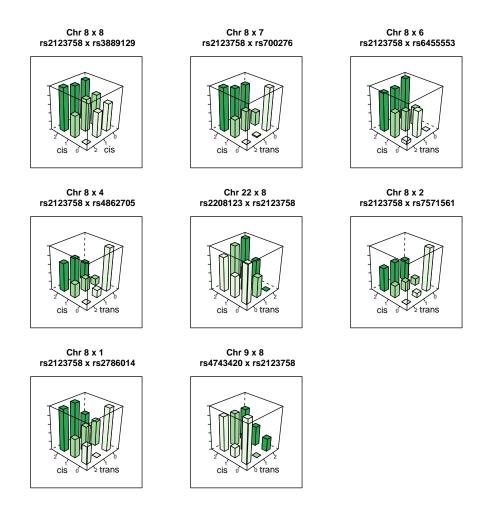
Chr 8 x 8
rs2123758 x rs3889129

Chr 8 x 7
rs2123758 x rs700276

Chr 8 x 6
rs2123758 x rs6455553

Chr 8 x 4
rs2123758 x rs4862705

Chr 22 x 8
rs2208123 x rs2123758

Chr 8 x 2
rs2123758 x rs7571561

Chr 8 x 1
rs2123758 x rs2786014

Chr 9 x 8
rs4743420 x rs2123758

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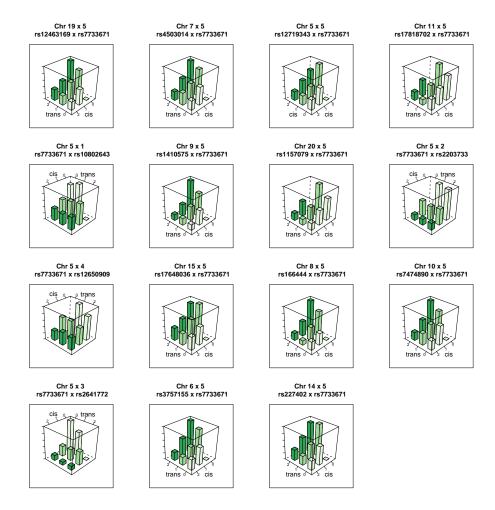
Figure S9: **Genotype-phenotype maps for 15 interactions influencing the expression of CAST** Each bar represents the mean phenotypic value for individuals in that genotype class.

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.
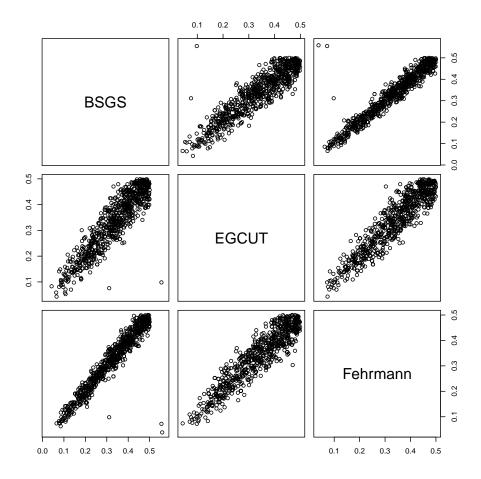
Figure S11: **Comparison of allele frequencies for 781 SNPs involved in genetic interactions across independent populations** Outliers were removed from the analysis as part of the filtering stage during replication.
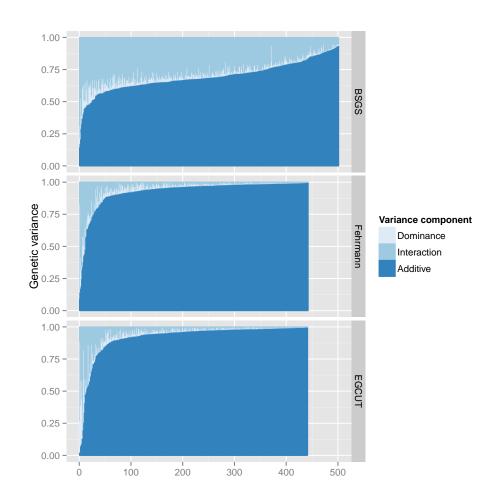
Figure S12: **Comparison of variance distribution from different cohorts**
How does the estimated variance decomposition change in different cohorts?
The cumulative proportion of the genetic variance that is additive, dominant,
or epistatic for each putative interaction is shown on the y-axis. BSGS has 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[f]	Meta[g]	
ABCA7	ILMN_1743205	19	rs3752237	19	1047161	ABCA7	rs596183	6	158100199		5.82	0.38	0.02	0.09	
ABCA7	ILMN_1743205	19	rs3752237	19	1047161	ABCA7	rs914737	9	139522101		5.50			0.95	
ABCC3	ILMN_1677814	17	rs9455	17	48771135	ABCC3	rs4732202	7	136057883		6.10	0.02	1.81	2.02	
ACAT1	ILMN_1800008	11	rs227064	11	108207393	ACAT1	rs4744894	9	72001517		6.59	1.04	1.78	2.05	
ADCK1	ILMN_1698777	14	rs12431896	14	78088813	ADCK1	rs4833241	4	122933691		6.58	0.36	0.83	0.87	
ADCK1	ILMN_1698777	14	rs8058066	16	88462550		rs12431896	14	78088813	ADCK1	6.69	2.04	21.21	1.14	
ADK	ILMN_2358626	10	rs2395095	10	76446305	ADK	rs10824092	10	75929517		6.22	18.33		39.82	0.517
AGAP6	ILMN_3239130	10	rs2611512	10	51515534	AGAP8	rs2547996	5	95174319		7.15				
AHSA2	ILMN_1798308	2	rs10881585	2	137112421	HLA-G	rs842647	2	61119471		5.45	1.83	1.93	2.88	
AHSA2	ILMN_1798308	2	rs2523971	2	29938258		rs1177303	2	61388355	AHSA2	6.91	0.92	0.64	0.94	4.231
AKTIP	ILMN_1665982	16	rs2896940	16	57721127	AKTIP	rs13332406	16	53489705	AKTIP	5.93	0.16	0.99	0.57	
AKTIP	ILMN_1665982	16	rs7189819	16	53536345	AKTIP	rs1362032	7	125543391		6.18	0.71	0.20	0.42	
AKTIP	ILMN_1665982	16	rs7189819	16	53536345		rs1473017	4	179323762		6.26	0.27	0.30	0.23	
ALDH3A2	ILMN_2401641	17	rs3760489	17	19581009	ALDH3A2	rs11720112	3	161996349		5.75	0.33	1.37	1.01	
ANG	ILMN_1760727	14	rs9322855	14	21153299	ANG	rs4866516	5	3032625		5.85	0.02	0.20	0.04	
ANPEP	ILMN_1763837	15	rs11073891	15	90363995	ANPEP	rs3823523	7	154511163		6.31	0.44	1.09	0.90	
ANPEP	ILMN_1763837	15	rs11073891	15	90363995	ANPEP	rs6846031	4	178019148		5.94	0.47	0.17	0.26	
AP3B1	ILMN_1768867	5	rs6453374	5	77508159	AP3B1	rs4684443	3	4818792		5.60	0.05			
APPL2	ILMN_1765076	12	rs9355251	12	105580918	APPL2	rs27769594	9	87918528		5.96	0.80	1.02	1.16	
ARL17B	ILMN_3231952	17	rs12947580	17	75768225	ARL17B	rs8079215	17	44064851	ARL17B	6.65				31.703
ARL17B	ILMN_3231952	17	rs2834541	21	35932619	ARL17B	rs8079215	17	44064851	ARL17B	7.64				
ARL17B	ILMN_3231952	17	rs8079215	17	44064851	ARL17B	rs1950646	14	94722497		6.26				
ARL17B	ILMN_3231952	17	rs8079215	17	44064851	ARL17B	rs2197777	12	125831219		5.98				
ARL17B	ILMN_3231952	17	rs8079215	17	44064851	ARL17B	rs2684789	15	99492045		5.72				
ATP13A1	ILMN_2134224	19	rs8079215	17	44064851		rs9834627	3	191203546		5.30				0.071
BID	ILMN_1763386	22	rs4284750	19	19810050	BID	rs8738770	19	19738554		5.84	12.18	3.25	14.23	
BID	ILMN_2372413	22	rs8919	22	18233057		rs9804943	12	129906275		6.60	0.06	0.40	0.14	
C11ORF17	ILMN_1752988	11	rs181405	22	18233000	C11ORF17	rs10888267	1	248059423		5.66	0.87	0.16	0.50	
C13ORF18	ILMN_2196550	13	rs2568061	11	8886260	C13ORF18	rs6553184	4	189150656	C13ORF18	6.66	1.15	0.04	0.54	
C13ORF18	ILMN_2196550	13	rs2110603	13	6259852		rs6857876	13	46913416		3.87	0.28	0.28	0.22	
C14ORF173	ILMN_2393450	14	rs674754	13	46913416	C14ORF173	rs4983382	4	153610164	C14ORF173	6.02	0.38	0.50	0.43	
C14ORF173	ILMN_2393450	14	rs11059825	22	37575398		rs4983382	14	105189504	C14ORF173	5.98	0.60	0.84	0.85	
C14ORF173	ILMN_2393450	14	rs3935344	15	92276674	C14ORF173	rs10754644	1	238724741		7.15	0.31	0.28	0.24	
C14ORF4	ILMN_1804396	14	rs4983382	14	105189504		rs2655991	14	77574438		4.87	0.42	0.34	0.35	
C14ORF4	ILMN_1804396	14	rs1293455	18	138190673		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	rs2655991	14	77574438		rs2655991	14	77574438		3.85				
C14ORF4	ILMN_1804396	14	rs4793445	17	70410630		rs2655991	14	77574438		4.61				
C14ORF4	ILMN_1804396	14	rs6010061	22	51151724		rs2655991	14	77574438		4.69				
C17ORF60	ILMN_1747347	17	rs7245800	19	52083552	C14ORF173	rs7405659	17	77574438	C17ORF60	6.79	0.53	0.05	0.19	
C1ORF86	ILMN_1726989	1	rs9907897	17	63502633		rs2257182	1	2082566	C1ORF86	5.90	0.01	0.50	0.13	
C1ORF86	ILMN_2097790	1	rs2334323	18	110577257		rs2460002	1	2119833	C1ORF86	5.65		0.03		
C1ORF86	ILMN_2097790	1	rs2279474	16	46384412		rs2460002	1	2119833	C1ORF86	5.59	0.29	0.50	0.37	
C21ORF57	ILMN_1795836	21	rs7188668	21	25711358		rs11701361	12	48676038	ZNF641	4.91	0.65	0.08	0.28	
C21ORF57	ILMN_1795836	21	rs4819271	21	48052838		rs901964	21	47764477		9.42	6.08	16.36	21.67	0.263
C5ORF4	ILMN_1728742	5	rs9978658	21	45866512		rs286595	5	154348552	C5ORF4	5.55	0.72	0.04	0.27	
C8ORF59	ILMN_1653205	8	rs1122762	18	45866512		rs2896452	8	86102223	C8ORF59	5.49	0.29	0.02	0.07	
C8ORF59	ILMN_1653205	8	rs12429804	13	36577930		rs2896452	8	86102223	C8ORF59	5.45	0.31			
C8ORF59	ILMN_1653205	8	rs12454561	18	31272238	C8ORF59	rs1004564	4	55242625		7.62	0.38	0.18	0.21	
C8ORF59	ILMN_1653205	8	rs7152284	14	52227366		rs2896452	8	86102223	C8ORF59	5.67	2.18	0.07	1.33	

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[f]	Meta[g]	Distance / Mb[h]
C8ORF59	ILMN_1653205	8	rs8051751	16	7188323		rs2896452	8	86102223	C8ORF59	5.79	1.39	0.18	0.87	
C9ORF72	ILMN_1741881	9	rs10122902	9	27556780	C9ORF72	rs2526698	1	242029101		6.36	0.96	0.01	0.37	
CABC1	ILMN_1731064	1	rs12765847	10	4353908		rs3738725	1	227174210	CABC1	6.36	0.94	0.00	0.34	
CARD9	ILMN_1712532	9	rs4266763	9	139289825	INPP5E	rs684040	1	82128660		5.81				
CARD9	ILMN_1712532	9	rs4573661	11	6026661		rs4077515	9	139266496	INPP5E	6.61	0.09	0.86	0.42	
CAST	ILMN_1717234	5	rs1157079	20	6778978		rs7733671	5	96000269	CAST	7.07	0.23	0.96	0.62	
CAST	ILMN_1717234	5	rs12463169	19	17321669		rs7733671	5	96000269	CAST	5.73	0.02	2.85	1.75	
CAST	ILMN_1717234	5	rs12599264	16	81840122		rs7733671	5	96000269	CAST	7.00	0.36	1.57	1.20	
CAST	ILMN_1717234	5	rs12719343	5	125369113		rs7733671	5	96000269	CAST	7.68	0.13	1.34	0.78	29.369
CAST	ILMN_1717234	5	rs1410575	9	78255630		rs7733671	5	96000269	CAST	6.55	0.27	0.52	0.37	
CAST	ILMN_1717234	5	rs164444	8	78392770		rs7733671	5	96000269	CAST	7.01	0.97	0.03	0.41	
CAST	ILMN_1717234	5	rs17648036	15	27311111		rs7733671	5	96000269	CAST	7.81	1.15	0.59	1.09	
CAST	ILMN_1717234	5	rs17818702	11	86107920		rs7733671	5	96000269	CAST	6.62	0.11	0.01	0.01	
CAST	ILMN_1717234	5	rs2277402	14	70496867		rs7733671	5	96000269	CAST	6.12	0.07	0.33	0.12	
CAST	ILMN_1717234	5	rs2822124	21	15166804		rs7733671	5	96000269	CAST	6.87	0.92	1.56	1.72	
CAST	ILMN_1717234	5	rs3757155	6	136458593		rs7733671	5	96000269	CAST	7.24	0.49	0.12	0.23	
CAST	ILMN_1717234	5	rs4503014	7	31149140		rs7733671	5	96000269	CAST	5.88	0.75	0.78	0.93	
CAST	ILMN_1717234	5	rs7474890	10	59590078		rs7733671	5	96000269	CAST	6.74	0.23	0.78	0.50	
CAST	ILMN_1717234	5	rs7733671	5	96000269	CAST	rs10802643	1	238120177		7.42	0.22	0.26	0.54	
CAST	ILMN_1717234	5	rs7733671	5	96000269	CAST	rs12650909	4	170192890		7.42	0.19	0.15	0.15	
CAST	ILMN_1717234	5	rs7733671	5	96000269	CAST	rs2203733	2	224093101		6.07	0.26	0.30	0.22	
CAST	ILMN_1717234	5	rs7733671	5	96000269	CAST	rs2641772	3	195531841		6.93	0.33	0.37	0.31	
CAT	ILMN_1651705	11	rs872311	18	66175386		rs11032695	11	34447586	CAT	6.41	0.26	0.30	0.22	
CCDC88B	ILMN_1772208	11	rs2353203	19	17099980		rs541207	11	64125142	CCDC88B	5.68	0.33	0.37	0.31	
CCDC88B	ILMN_1772208	11	rs6947339	11	64097233	CCDC88B	rs12711349	10	96998193		5.62	0.23	0.18	0.14	
CD36	ILMN_1784863	7	rs3211834	7	80280117		rs1254900	2	85816334	VAMP8	6.93	0.15	0.01	0.02	
CD55	ILMN_1800540	11	rs750801	11	76033374		rs6700168	1	207502534	CD55	5.09	0.08	0.03	0.02	
CD93	ILMN_1704730	20	rs1884655	20	230074375	CD93	rs10255470	7	157182040		6.06	1.74	0.24	1.20	
CD93	ILMN_1704730	20	rs1884655	20	230074375	CD93	rs4696726	4	7992632		5.71	0.13	0.80	0.42	
CD93	ILMN_1704730	20	rs1884655	20	230074375	CD93	rs7622580	3	196721395		5.56	0.04	0.27	0.08	
CD93	ILMN_1704730	20	rs1884655	20	230074375	CD93	rs838875	12	125145394		6.31	0.24	1.67	1.16	
CD93	ILMN_1704730	20	rs1884655	20	230074375	CD93	rs9576388	13	38434472		7.88	0.71	0.22	0.45	
CD93	ILMN_1704730	20	rs2868504	20	37771578	CD93	rs1884655	20	23074375	CD93	5.71	0.64	0.75	0.81	
CD93	ILMN_1704730	20	rs4813479	20	230076914	CD93	rs10925747	1	238899903		7.43				14.697
CD93	ILMN_1704730	20	rs4813479	20	230076914	CD93	rs2873420	8	136500554		7.02				
CD93	ILMN_1704730	20	rs4813479	20	230076914	CD93	rs4328531	18	74439542		6.13	0.08	0.03	0.02	
CDC16	ILMN_2339796	13	rs861544	14	104162263		rs4789981	17	77264482	CDC16	6.08	0.21	0.14	0.11	
CDK5R1	ILMN_1730928	17	rs9905940	17	46614102	HOXB2	rs7324744	13	115008038	CDK5R1	5.46	0.95	0.07	0.45	
CEACAM21	ILMN_1745949	19	rs200609	20	519566250	CEACAM21	rs11655031	17	30833162	CEACAM21	5.47	0.90	0.12	0.48	
CEACAM21	ILMN_1745949	19	rs4803481	19	42066556		rs4803481	19	42066556		6.15	2.16	0.16	1.44	15.781
CEP192	ILMN_1703754	18	rs6505780	18	13069782	CEP192	rs2421050	5	158943044		6.67	0.15	0.24	0.12	
CEP63	ILMN_1787808	3	rs3825569	3	101350298		rs13132719	4	180265266	ANAPC13	5.75	0.23	0.10	0.09	
CES1	ILMN_2359945	16	rs8192935	16	55861794	CES1	rs13079012	3	134247706		6.36	0.72	0.20	0.44	
CHPT1	ILMN_2202940	12	rs591967	13	38838122		rs772788	2	235248562	CHPT1	5.65	0.92	0.02	0.36	
CHPT1	ILMN_2202940	12	rs6539014	12	102277082		rs2695290	12	102087844		5.74	0.07	1.28	0.67	
CLEC12A	ILMN_1663142	12	rs429790	16	84471642		rs867578	11	81937002	CLEC12A	4.75	0.95	0.36	0.73	
CLEC12A	ILMN_2403228	12	rs7305054	12	10156646		rs7313235	12	10132283		5.55	0.07	0.27	0.02	
CLTB	ILMN_1674609	5	rs17129799	11	96929337		rs6863172	5	175595960	CLTB	7.54	0.07	0.07	0.02	
CNN2	ILMN_1770290	19	rs3752237	19	1047161	ABCA7	rs169130	16	63121080		5.55	0.07	0.07	0.02	
CNN2	ILMN_1770290	19	rs3752237	19	1047161	ABCA7	rs7336017	13	67713633		7.56	1.92	0.28	1.39	
CPSF1	ILMN_1654545	8	rs4333645	8	145569535		rs1455268	4	61738094		6.33	0.10	0.01	0.01	
CPVL	ILMN_1082928	7	rs12596791	16	26115562		rs245884	7	29188475	CPVL	5.74	0.06	0.57	0.23	

26

Gene ID[a]	Probe ID[b]	Chr.	SNP 1 rs ID	SNP 1 Pos/Mb[c]	SNP 1 Chr.	SNP 1 Association[d]	SNP 2 rs ID	SNP 2 Pos/Mb[c]	SNP 2 Chr.	SNP 2 Association[d]	BSGS[e]	Fehrmann[f]	EGCUT[f]	Meta[g]	Distance / Mb[h]
CPVL	ILMN_1682928	7	rs2835998	39202070	21		rs245884	29188475	7	CPVL	5.55	0.19	0.03	0.04	
CRIPT	ILMN_1813256	2	rs2131290	188859908	4		rs1531133	46843631	2	CRIPT	5.47	0.28	0.10	0.12	
CRLS1	ILMN_1737685	20	rs6139887	5986234	20	CRLS1	rs1473927	62406408	5		6.18	0.10	0.36	0.15	0.033
CSTB	ILMN_1761797	21	rs9979356	45230974	21		rs3761385	45198355	21		11.99	25.20	16.72	42.27	
CTNNA1	ILMN_1804854	5	rs924943	69500505	18	CTNNA1	rs176382	135226767	5	CTNNA1	5.74	0.02	0.41	0.11	
CTSC	ILMN_1696347	11	rs2457684	88139983	11	CTSC	rs7079264	108679892	10		5.67	0.92	0.74	1.03	
CTSC	ILMN_1696347	11	rs5752236	26250645	22		rs7128352	88087357	11	CTSC	5.84	0.49	0.80	0.73	
CTSC	ILMN_2242463	11	rs7930237	88117962	11		rs556895	88077479	11	CTSC	7.16	18.76	15.06	33.53	0.040
CWF19L1	ILMN_1651886	10	rs7108734	11456027	11		rs12784396	102027407	10	CWF19L1	5.42	0.21	0.01	0.03	
CYBRD1	ILMN_1712305	2	rs2592948	129994690	4		rs888427	172368120	2	CYBRD1	5.89	0.23	0.53	0.34	
CYBRD1	ILMN_1712305	2	rs7852475	140698856	9		rs888427	172368120	2	CYBRD1	5.68	0.20	0.02	0.04	
CYBRD1	ILMN_2087692	2	rs11257679	12318284	10		rs888427	172368120	2	CYBRD1	5.81	0.39	1.87	1.47	
CYBRD1	ILMN_2087692	2	rs6137908	23344590	20		rs888427	172368120	2	CYBRD1	5.53	0.05	0.83	0.36	
CYBRD1	ILMN_2087692	2	rs888427	172368120	2	CYBRD1	rs7591849	160112881	2		5.85	0.87	0.10	0.44	12.255
CYP27A1	ILMN_1704985	2	rs6021982	36571928	20		rs933994	219650616	2	CYP27A1	5.42	0.29	0.86	0.60	
DAB2	ILMN_2128428	5	rs7778910	110451383	7		rs835223	39381357	5	DAB2	5.44	0.48	0.41	0.44	
DCAKD	ILMN_1811648	17	rs9900173	43111688	17		rs1343244	82076988	6		9.12	0.00	0.58	0.14	
DDT	ILMN_1690982	22	rs5760102	24248761	22	DDT	rs2378341	187475208	3		5.62	0.64	0.25	0.42	
DDX58	ILMN_1797001	9	rs4937097	125962645	11		rs7042042	32451144	9		5.31	0.61	0.29	0.44	
DEM1	ILMN_1783996	1	rs10120023	137810259	9	COQ10A	rs2519515	88204888	7		5.47	0.08	0.41	0.16	
DEM1	ILMN_1783996	1	rs12363827	106703727	11		rs10120023	137810259	9	COQ10A	6.39	0.77	0.02	0.29	
DHRS9	ILMN_1733998	2	rs1519956	89468283	12		rs7566044	169960422	2	DHRS9	6.00	0.06	1.17	0.58	
DHRS9	ILMN_1733998	2	rs1528529	147132505	7		rs7566044	169960422	2	DHRS9	6.48	0.37	0.34	0.32	
DHRS9	ILMN_2384181	2	rs2831914	29959453	21		rs2161037	169893419	2	DHRS9	5.51	0.88	0.04	0.37	
DHRS9	ILMN_2384181	2	rs7661304	187776431	4		rs2161037	169893419	2	DHRS9	7.64	0.05	0.11	0.03	
DIP2B	ILMN_1755589	12	rs11080134	29161503	17		rs11169322	50610976	12	LASS5	4.65	0.32	0.05	0.10	
DIP2B	ILMN_1755589	12	rs11169335	50636364	12		rs2872008	153134888	7		4.87	0.30	0.58	0.19	
DIP2B	ILMN_1755589	12	rs3385585	41711815	12	LASS5	rs7134595	50730458	12	LASS5	5.31	0.37	0.22	0.01	
DIP2B	ILMN_1755589	12	rs7134595	50730458	12		rs1808634	61971140	8		4.40	0.09	0.02	0.11	
DIP2B	ILMN_1755589	12	rs7312252	50744171	12	LASS5	rs4532958	115214154	10		5.03	0.48	0.00	0.97	
DIP2B	ILMN_1755589	12	rs8711257	117994348	12		rs12427378	51074199	12	LASS5	5.92	0.23	1.45	1.12	66.920
DNAJB6	ILMN_1793770	7	rs2286842	157216093	7		rs3779589	157163614	7	DNAJB6	5.79	0.23	0.27	0.70	0.052
DPH3	ILMN_2349610	3	rs12232308	93409054	15		rs1566972	16320360	3	DPH3	6.17	1.58	1.18	1.12	
ECGF1	ILMN_2109708	22	rs1405222	50971266	22	ECGF1	rs4891884	64004670	18		4.81	0.15	0.35	0.70	
ECHDC2	ILMN_1671568	1	rs4234091	241911027	2		rs11206043	53402552	1	ECHDC2	6.19	0.22	0.16	0.22	
ECHDC2	ILMN_1671568	1	rs5992637	17675900	22		rs11206043	53402552	1	ECHDC2	5.58	0.64	0.35	0.35	
EHD4	ILMN_1720083	15	rs10403312	53244938	19		rs1048166	42192040	15	EHD4	6.98	0.90	0.47	0.79	
EIF2B2	ILMN_1713380	14	rs6567288	60218334	18		rs175450	75590340	14	EIF2B2	5.56	0.23	0.11	0.10	
EIF5A	ILMN_1794522	17	rs7216490	7221707	17	EIF5A	rs1269096	96003119	14		5.44	0.56	0.08	0.24	
EIF5A	ILMN_1794522	17	rs7216490	7221707	17	EIF5A	rs1553474	49359676	2		5.55	0.28	0.59	0.41	
EIF5A	ILMN_1794522	17	rs7216490	7221707	17	EIF5A	rs2197210	129624067	8		6.36	0.08	0.05	0.02	
EIF5A	ILMN_1794522	17	rs7216490	7221707	17	EIF5A	rs4471434	126387391	11		5.52	0.05	1.12	0.53	
EMR2	ILMN_2827076	19	rs61132112	23196249	21	EMR2	rs9305048	14879034	19	EMR2	6.51	0.36	0.40	0.11	
EMR2	ILMN_2353633	19	rs9305048	18761714	20		rs9305048	14879034	19	EMR2	5.56	0.45	0.58	0.41	
EMR2	ILMN_2353633	19	rs9305048	14879034	19		rs30077765	102480759	13		6.03	0.20	1.20	0.35	
EPHX2	ILMN_1709237	8	rs1107764	127909396	11		rs13269963	27400604	8	EPHX2	5.70	0.20	0.58	0.35	
ERICH1	ILMN_1731001	8	rs10894861	134611176	11	ERICH1	rs12115088	578742	8	ERICH1	5.43	0.25	1.20	0.81	
ERICH1	ILMN_1731001	8	rs5766218	45337329	22		rs4735900	607161	8	ERICH1	6.11	0.20	0.09	0.09	
ERICH1	ILMN_1731001	8	rs726145	31187910	18		rs12115088	578742	8	ERICH1	5.65	0.29	0.04	0.08	
ERICH1	ILMN_1731001	8	rs4735895	600729	8		rs1517297	182786760	4		5.63	0.67	1.03	1.06	
EXOC3	ILMN_1789419	5	rs1870076	55228462	10		rs12188164	428236	5	EXOC3	6.83	0.74	0.19	0.44	
FAHD1	ILMN_2246661	16	rs1560104	12708208	16		rs344363	1972548	16	FAHD1	5.61	0.19	1.38	0.44	10.736
FCN1	ILMN_1668063	9	rs12580388	129591144	12		rs10120023	137810259	9	COQ10A	6.33	0.27	0.30	0.23	

27

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[f]	Meta[g]	
FEZ2	ILMN_1739586	2	rs2356400	19	44321776		rs13406184	2	36791226	FEZ2	5.78	0.14	0.33	0.16	
FEZ2	ILMN_1739586	2	rs969010	4	159963132		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	6	rs902634	10	133943951		rs831489	6	36999682	FGD2	5.49	1.20	0.11	0.66	
FLJ20489	ILMN_1778144	12	rs17615703	12	117036766	FLJ20489	rs3782908	12	48169526	FLJ20489	5.81	0.06	0.70	0.29	68.867
FLJ20489	ILMN_1778144	12	rs3782908	12	48169526		rs897511	4	167695661	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	97033129		rs3782908	12	48169526	FLJ20489	6.49	0.31	0.47	0.36	
FLJ20489	ILMN_1778144	12	rs7204135	16	50626195		rs3782908	12	48169526	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	rs17112712	14	107276627		rs6906101	6	36667610	FLJ20718	5.48	0.39	0.06	0.13	
FLJ43093	ILMN_2123450	6	rs6906101	6	36667610	FLJ43093	rs13214069	6	32705248	FLJ43093	5.44	0.00	0.64	0.18	
FN3KRP	ILMN_1652333	17	rs890095	17	80890638		rs9892064	17	80827903		16.16	28.24	29.39	59.95	3.962
FUCA1	ILMN_1752728	1	rs4971478	2	1346063		rs12744386	1	24168019	FUCA1	6.41	0.01	0.30	0.06	0.063
FXYD5	ILMN_2309848	19	rs1633921	19	35695200		rs788178	13	98328559		3.70	0.09	0.41	0.17	
FXYD5	ILMN_2309848	19	rs17398183	20	55609148		rs2285515	19	35660450	FXYD5	6.58	0.03	0.48	0.15	
FXYD5	ILMN_2309848	19	rs2285515	19	35660450	FXYD5	rs11739594	5	141709563		5.70	0.07	0.17	0.05	
FXYD5	ILMN_2309848	19	rs2285515	19	35660450	FXYD5	rs13067700	3	95331048		6.00	0.09	0.51	0.22	
G3BP2	ILMN_2381758	4	rs10230232	17	29390239		rs17036504	4	76554604		6.10	0.28	0.37	0.14	
GAA	ILMN_2410783	17	rs11115847	17	78153130	GAA	rs10902506	12	132678089		5.19	0.08	0.39	0.17	
GAA	ILMN_2410783	17	rs8068856	17	78100731	GAPT	rs12602462	17	78146016		13.91	19.98	12.99	32.60	0.007
GAPT	ILMN_1675191	5	rs10070522	10	57786110		rs7605821	2	235695228	GAPT	5.65	0.11	0.78	0.28	
GAPT	ILMN_1675191	5	rs7082031	10	128038717		rs10070522	5	57786110		5.85	0.01	0.11	0.11	
GATS	ILMN_1699631	7	rs1147447	14	66460742		rs2950520	7	99827148	GATS	5.72	0.26	0.63	0.11	
GATS	ILMN_1699631	7	rs2425256	20	35056572		rs2950520	7	99827148	GATS	5.47	0.83	0.87	0.87	
GDPD3	ILMN_1774901	16	rs3809624	16	30102802	GDPD3	rs2197465	14	48572632		6.22	0.38	0.35	0.33	
GDPD3	ILMN_1774901	16	rs7204270	16	30156963	GDPD3	rs1015111	4	128972357		6.57	0.55	0.09	0.24	
GNLY	ILMN_1790692	2	rs4145072	13	110899955		rs7577293	2	85935282	GNLY	5.86	0.02	0.45	0.13	
GPN3	ILMN_3339426	12	rs7198646	16	26084476		rs7960552	12	111164237	GPN3	5.78	0.36	0.02	0.39	
GPR162	ILMN_1730816	12	rs1860563	16	6478898		rs2707210	12	6902002	GPR162	5.72	0.25	0.46	0.06	
GPR162	ILMN_1730816	12	rs2272500	12	79685913		rs2707210	12	6902002	GPR162	5.49	0.25	0.03	0.07	72.784
GPR162	ILMN_1730816	12	rs2707210	12	6902002	GPR162	rs4740848	9	6554558		5.07	0.96	0.06	0.44	
GPR162	ILMN_1730816	12	rs2707210	12	6902002	GPR162	rs9827054	3	188880113		5.47	0.17	0.44	0.07	
GPR177	ILMN_1660549	1	rs11057383	12	124369421		rs12065581	1	68732819	GPR177	6.21	0.72	0.67	0.81	
GPR177	ILMN_1660549	1	rs12527241	6	120468039		rs12065581	1	68732819	GPR177	5.45	0.17	0.40	0.22	
GPR177	ILMN_1660549	1	rs12532999	7	127939793		rs12065581	1	68732819	GPR177	5.76	0.79	1.43	1.50	
GPR177	ILMN_1660549	1	rs7256613	16	11169683		rs12065581	1	68732819	GPR177	6.50	0.31	0.11	0.13	
GPR177	ILMN_1660549	1	rs9575097	13	82986268		rs12065581	1	68732819	GPR177	5.43	0.95	0.21	0.60	
GPR177	ILMN_2283325	1	rs6566669	18	70506011		rs12065581	1	68732819	GPR177	6.04	0.24	0.34	0.23	
GPR177	ILMN_2283325	1	rs9290426	3	171399321		rs12065581	1	68732819	GPR177	5.86	0.01	0.24	0.04	
GSDMB	ILMN_2347193	17	rs11557467	17	38028634	GSDMB	rs4965745	15	101508261		6.50	0.68	0.20	0.41	
GSTM1	ILMN_2391861	1	rs12248673	10	53192833		rs11101992	1	110266754	GSTM1	5.88	0.27	0.19	0.16	
GSTM1	ILMN_2391861	1	rs1547574	13	85344527		rs11101992	1	110266754	GSTM1	6.11	0.27	0.16	0.79	
GSTM2	ILMN_2201580	1	rs6492807	13	96159560		rs3754446	1	110253241	GSTM1	5.91	0.52	1.14	0.65	
H1F0	ILMN_1757467	22	rs1639898	22	38399979		rs4853333	2	77919015		6.77	0.27	0.66	0.23	
H1F0	ILMN_1757467	22	rs1639898	22	38399979		rs6497007	15	85877017		6.36	0.25	0.31	0.32	
H1F0	ILMN_1757467	22	rs11078523	22	38399979		rs9983949	21	19532546		6.52	0.00	0.48	0.19	
HBG1	ILMN_1796678	11	rs12975066	19	35723501		rs2855039	11	5271671	HBG2	5.70	0.15	0.66	0.12	
HBG1	ILMN_1796678	11	rs2855039	11	5271671	HBG2	rs2855039	11	5271671	HBG2	5.47	0.08	0.24	0.21	
HBG1	ILMN_1796678	11	rs2855039	11	5271671	HBG2	rs12042181	11	213088494	LQK1	5.98	0.01	0.52	0.11	
HBG1	ILMN_1796678	11	rs12503379	4	141533832		rs12503379	4	141533832		6.78	0.01	0.46	0.10	
HBG2	ILMN_2084825	11	rs11078523	17	45233167		rs16912979	11	53309695	HBG2	6.42	0.01	0.41		

28

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[f]	Meta[g]	
HBG2	ILMN_2084825	11	rs12975066	11	35723501	HBG2	rs2855039	11	5271671	HBG2	5.77	0.08	0.13	0.05	
HBG2	ILMN_2084825	11	rs2855039	11	5271671	HBG2	rs12042181	1	213088494	LQK1	6.84	0.06	0.54	0.21	
HBG2	ILMN_2084825	11	rs2855039	11	5271671	HBG2	rs12503379	4	141533832		5.98	0.00	0.46	0.10	
HDAC7	ILMN_3266186	12	rs21009029	16	6036851		rs4760636	12	48173352	HDAC7	5.75				103.850
HEBP1	ILMN_1802557	12	rs3782567	12	13145613	HEBP1	rs17686635	8	135220622		5.98	0.15	0.59	0.32	
HEXDC	ILMN_1741180	17	rs1942719	18	71237270		rs7213057	17	80378939	HEXDC	5.81	1.61	0.34	1.22	
HLA-DRA	ILMN_2157441	6	rs4899635	14	77532672		rs7192	6	32411646	HLA-DRB6	5.94	0.90	0.16	0.52	
HLA-F	ILMN_1762861	6	rs11660982	6	75467313		rs2523404	6	29695713	HLA-H	5.69	1.00	0.47	0.86	
HMBOX1	ILMN_1720059	8	rs12435486	14	98670849		rs7837237	8	28876221	HMBOX1	6.54	0.92	1.11	1.34	
HMBOX1	ILMN_1720059	8	rs2837803	8	42112794		rs4732890	8	28751381	HMBOX1	6.62	0.05	1.01	0.46	
HMBOX1	ILMN_1720059	8	rs4765451	12	127237464		rs8180944	8	28904086	HMBOX1	5.80	0.39	3.13	2.52	
HMBOX1	ILMN_1720059	8	rs587639	8	132725731		rs7837237	8	28876221	HMBOX1	6.58	0.55	0.34	0.44	
HMBOX1	ILMN_1720059	8	rs8180944	8	28904086	HMBOX1	rs4553956	3	189533772		6.88	3.38	0.03	2.20	
HMBOX1	ILMN_1720059	8	rs8180944	8	28904086	HMBOX1	rs7810884	7	158276926		6.12	0.34	0.66	0.52	
HMBOX1	ILMN_1720059	8	rs9521666	13	110897444		rs8180944	8	28904086	HMBOX1	5.45	0.67	0.26	0.45	
HNRPH1	ILMN_2101920	5	rs6894268	5	179032488		rs4700810	5	178991794	HMBOX1	15.38	8.55	3.01	10.37	0.041
HSPC157	ILMN_3194087	1	rs5558112	16	88882257		rs4654783	1	22439520	HSPC157	5.51	0.19	0.50	0.29	
HSPC157	ILMN_3194087	1	rs6063164	20	46486900		rs4654783	1	22439520	HSPC157	6.51	0.69	0.23	0.44	
HSPC157	ILMN_3194087	1	rs662739	12	121229893		rs4654783	1	22439520	HSPC157	6.61	1.46	0.84	1.55	
HSPC157	ILMN_3194087	1	rs7088558	10	101884937	CWF19L1	rs4654783	1	22439520	HSPC157	6.48	0.02	0.26	0.05	
IL32	ILMN_1778010	16	rs1554999	16	3115628	IL32	rs4759890	12	131757163		6.90	0.65	0.13	0.33	
IL32	ILMN_2368530	16	rs765044	19	2560423		rs1554999	16	3115628	IL32	5.53	0.69	0.89	0.44	
INPP5E	ILMN_1811301	9	rs8044524	16	81603771		rs1127152	9	139335599	INPP5E	5.58	1.46	0.80	0.37	
JAZF1	ILMN_1675756	7	rs7573355	12	47970693		rs849341	7	5570771		8.16	0.02	0.08	0.28	
KCNJ15	ILMN_1691803	19	rs2186344	21	39606769	KCNJ15	rs424299	7	28288174		5.64	0.46	0.04	0.09	
KIR2DS5	ILMN_1811104	3	rs649216	19	55324635	KIR2DL1	rs6419960	4	189055298		4.74	0.08	0.80	0.31	
KTELC1	ILMN_1811104	3	rs4349034	13	84597119		rs727905	3	119119433	KTELC1	5.53	0.64	0.08	0.28	
KTELC1	ILMN_1811104	3	rs6815953	4	183109012		rs6414283	3	119195913	KTELC1	5.45	0.33	0.08	0.09	
L3MBTL2	ILMN_2336109	22	rs4822006	22	41519362	L3MBTL2	rs1294338	1	233438952		5.88	0.24	0.04	0.09	
LAP3	ILMN_1683792	4	rs7042087	9	132602868		rs7658240	4	175589050	LAP3	5.72	0.47	0.47	0.31	
LAX1	ILMN_1769782	1	rs1891432	1	203877662		rs10900520	1	203780591		19.16	18.60	11.22	29.24	0.097
LDLRAP1	ILMN_1809040	1	rs1552032	15	59971635		rs6687605	1	25889632		6.00	0.35	0.40	0.34	
LGALS9	ILMN_2412214	17	rs12450521	17	26083392		rs11749727	5	179608360	LDLRAP1	5.16	0.23	0.13	0.05	
LILRA5	ILMN_2357419	19	rs3859532	19	54827248	LILRA5	rs714789	18	71561497		6.13	0.11	0.13	0.15	
LINS1	ILMN_2338197	15	rs11247226	15	101120963	LINS1	rs1278387	10	127804531		5.89	0.13	0.35	0.07	
LRRC25	ILMN_2150196	19	rs6009951	22	51151350		rs8101804	19	18496107	LRRC25	5.68	0.49	0.15	0.03	
LY86	ILMN_1807825	6	rs9777785	6	6588881	LY86	rs1543675	1	78946879		5.61	0.13	0.03	0.16	
LYZ	ILMN_1815205	12	rs2168029	12	69734641	LYZ	rs11981725	7	154137150		5.95	0.15	0.03	0.49	
LYZ	ILMN_2162972	12	rs1778520	18	77276964		rs2168029	12	69734641	LYZ	5.71	0.49	0.36	0.59	
LYZ	ILMN_2162972	12	rs2168029	12	69734641	LYZ	rs2253135	9	130319560		5.62	0.61	0.88	0.49	
MAD1L1	ILMN_2358069	7	rs7983718	13	103203146	MAD1L1	rs1096699	6	43528441	MAD2L1BP	5.93	0.25	1.11	0.59	
MAD2L1BP	ILMN_1694711	6	rs974607	21	29435869		rs6060034	20	33351864	MAP1LC3A	5.78	0.63	0.11	1.09	
MAP1LC3A	ILMN_1776188	20	rs10869600	9	78225815		rs13069559	3	152187431	MBNL1	7.96	0.79	0.27	0.54	
MBNL1	ILMN_2313158	3	rs11053043	12	9932070		rs13069559	3	152187431	MBNL1	6.70	0.08	2.21	1.37	
MBNL1	ILMN_2313158	3	rs11164596	13	97100681		rs13069559	3	152187431	MBNL1	7.38	1.43	0.63	1.34	
MBNL1	ILMN_2313158	3	rs11981513	7	94648239		rs13069559	3	152187431	MBNL1	7.71	0.43	5.36	4.58	
MBNL1	ILMN_2313158	3	rs16864367	3	152234166		rs13079208	3	152116652	MBNL1	13.49	16.25	24.74	41.56	0.118
MBNL1	ILMN_2313158	3	rs2030926	6	114067127		rs13069559	3	152187431	MBNL1	7.10	0.91	5.80	5.53	
MBNL1	ILMN_2313158	3	rs2186671	17	6604708		rs13069559	3	152187431	MBNL1	7.63	0.62	5.82	5.23	
MBNL1	ILMN_2313158	3	rs2213360	22	34291750		rs13069559	3	152187431	MBNL1	6.05	0.52	0.72	0.70	
MBNL1	ILMN_2313158	3	rs2305802	19	16038535		rs13069559	3	152187431	MBNL1	6.94	1.67	2.22	5.30	
MBNL1	ILMN_2313158	3	rs2614467	14	99770138		rs13069559	3	152187431	MBNL1	5.74	4.13			

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	Pos/Mb[c]	Chr.	Association[d]	rs ID	Pos/Mb[c]	Chr.	Association[d]	BSGS[e]	Fehrmann[f]	EGCUT[f]	Meta[g]	
MBNL1	ILMN_2313158	3	rs4392535	41513423	4		rs13069559	152187431	3	MBNL1	8.39	0.02	4.33	3.02	
MBNL1	ILMN_2313158	3	rs4735830	895841	8		rs13069559	152187431	3	MBNL1	6.74	0.32	4.21	3.38	
MBNL1	ILMN_2313158	3	rs4939558	46278591	18		rs1522374	152235530	3		7.72	0.03	0.27	0.07	
MBNL1	ILMN_2313158	3	rs6128397	57253132	20		rs16864367	152234166	3		7.22	1.34	1.15	1.73	
MBNL1	ILMN_2313158	3	rs7710738	22101322	5		rs13069559	152187431	3	MBNL1	7.92	2.55	7.89	9.28	
MBP	ILMN_2331544	18	rs6079849	154626611	20		rs2051344	74715653	18	MBP	6.26	0.10	0.03	0.02	
MBP	ILMN_2398939	18	rs1395568	42210985	22		rs2051344	74715653	18	MBP	5.56	0.03	0.23	0.05	
MBP	ILMN_2398939	18	rs2051344	74715653	18	MBP	rs1125539	155204939	3		5.79	0.02	0.76	0.27	
MBP	ILMN_2398939	18	rs2051344	74715653	18	MBP	rs2619046	55097534	5		6.03	0.15	0.50	0.26	
MBP	ILMN_2398939	18	rs4805021	33436367	19		rs2051344	74715653	18	MBP	5.82	0.03	0.47	0.14	
MBP	ILMN_2398939	18	rs8092433	74747424	18		rs4890876	74732087	18	MBP	5.40	7.06	21.91	28.73	0.015
MEGF9	ILMN_2290118	9	rs13039689	51922071	20		rs966396	123453281	9	MEGF9	4.63	1.13	1.33	1.71	
MFN2	ILMN_1651385	1	rs7989895	109401737	13		rs4846085	12050634	1	MFN2	5.76	0.61	0.25	0.41	
MGC13057	ILMN_1787526	2	rs12718598	50428445	7	MGC13057	rs11725347	171860973	4		5.81	0.13	0.30	0.14	
MGC13057	ILMN_1787526	2	rs674608	69070772	18		rs12718598	50428445	7	MGC13057	5.57	0.07	1.03	0.50	
MGC13057	ILMN_1787526	2	rs8058318	82628245	16		rs12718598	50428445	7	MGC13057	7.05	0.11	0.12	0.05	
MGC72104	ILMN_1688318	20	rs845787	26197931	20	MGC72104	rs2660665	137526799	8		4.17	0.05	0.08	0.02	
MGST3	ILMN_1751956	1	rs740441	55779644	17		rs4147592	165600146	1	MGST3	5.45	0.57	0.27	0.40	
MPZL2	ILMN_1752932	11	rs1805	118076069	11	MPZL2	rs11771552	154708716	7		5.90	0.01	0.23	0.04	
MPZL2	ILMN_1752932	11	rs7316716	19953193	12		rs1805	118076069	11	MPZL2	5.64	0.97	1.08	1.35	
MRPL36	ILMN_1800197	5	rs17469061	74690061	5		rs750495	1782046	5	MRPL36	6.89	0.34	0.18	0.19	
MRPL43	ILMN_2258774	10	rs6564769	80641040	16		rs2863095	102746503	10	MRPL43	5.71	0.26	0.44	0.22	
MRPL52	ILMN_1713966	14	rs1950857	26710271	14		rs3811188	42194916	14	MRPL52	6.56	0.14	0.70	0.64	
MRPS10	ILMN_1663664	6	rs10955512	102200230	8		rs722269	42158596	6	MRPS10	7.48	0.46	0.63	0.46	
MRPS10	ILMN_1663664	6	rs11698155	150632214	20		rs2395803	42164401	6	MRPS10	6.85	0.31	0.25	0.28	
MRPS10	ILMN_1663664	6	rs1420537	52453567	6		rs12431444	42068689	14	MRPS10	6.21	0.41	1.87	2.86	
MTMR15	ILMN_2152178	15	rs7178375	312215935	15	MTMR10	rs11160227	95114596	14		5.18	1.87	0.52	0.50	
MX1	ILMN_1662358	21	rs459498	42795027	21		rs49738501	26706382	3		6.31	0.46	0.50	0.23	
MX1	ILMN_1662358	21	rs459498	42795027	21		rs8130120	29363604	21		5.83	0.11	0.92	0.65	13.431
MX1	ILMN_1662358	21	rs459498	42795027	21		rs1317149	47486885	11		6.78	0.29	0.46	0.23	
MYBPC3	ILMN_1781184	11	rs101334030	61593110	14		rs7124681	47529947	11	MYBPC3	5.56	0.13	0.08	0.02	
MYBPC3	ILMN_1781184	11	rs7322768	109550561	13		rs2737422	134485237	11	MYBPC3	5.70	0.04	0.15	0.40	
MYOM1	ILMN_1680344	18	rs4798075	3247256	18	MYOM1	rs11649236	48632478	8		6.02	0.74	0.59	1.77	
N4BP1	ILMN_2201966	16	rs12444224	87580855	16		rs6826085	48632478	16	N4BP1	5.54	2.00	0.03	0.04	38.948
NAAA	ILMN_1668605	4	rs2707575	147638723	7		rs6826085	76870229	4	NAAA	5.65	0.20	0.43	0.30	
NAAA	ILMN_2391512	4	rs2071856	377770630	22		rs6826085	76870229	4	NAAA	5.46	0.27	0.48	0.18	
NAPRT1	ILMN_1710752	8	rs2123758	144663661	8	NAPRT1	rs2786014	234897243	1		6.08	0.07	0.48	0.18	
NAPRT1	ILMN_1710752	8	rs2123758	144663661	8	NAPRT1	rs3889129	144613680	8		8.45	15.12	16.08	30.77	0.050
NAPRT1	ILMN_1710752	8	rs2123758	144663661	8	NAPRT1	rs4862705	187445552	4		5.62	1.27	0.19	0.81	
NAPRT1	ILMN_1710752	8	rs2123758	144663661	8	NAPRT1	rs6455553	167811764	6		6.12	0.87	0.76	1.01	
NAPRT1	ILMN_1710752	8	rs2123758	144663661	8	NAPRT1	rs700276	146189057	6		6.86	1.10	2.58	2.77	
NAPRT1	ILMN_1710752	8	rs2208123	48214812	22		rs2123758	144663661	8	NAPRT1	6.03	0.13	0.47	0.23	
NAPRT1	ILMN_1710752	8	rs4743420	103488089	9		rs2123758	144663661	8	NAPRT1	5.50	0.29	0.88	0.63	
NAPSA	ILMN_1784040	19	rs1405655	50882619	19	NAPSB	rs9302800	98391111	9		5.58	0.12	0.17	0.08	
NAPSB	ILMN_2109416	19	rs1405655	50882619	19	NAPSB	rs10882406	95976932	10		5.58	0.82	0.10	0.40	
NAPSB	ILMN_2109416	19	rs1405655	50882619	19	NAPSB	rs7577137	234721287	2		5.58	0.67	0.44	1.12	
NCL	ILMN_2121437	2	rs7563453	232301670	2		rs4973397	232291471	2		7.31	2.11	6.33	1.71	0.010
NDUFA12	ILMN_1737738	12	rs27746971	37101890	22		rs11107847	95386791	12	NDUFA12	3.88	7.51	0.18	12.70	
NMT2	ILMN_1656378	10	rs10906857	15239498	10	NMT2	rs12490878	183114008	3		6.84	0.39	0.34	0.22	
NOD2	ILMN_1762594	16	rs29676636	7067773	19		rs9302752	50719103	16	NOD2	5.90	0.42	0.04	0.35	
NRBF2	ILMN_3237385	10	rs11063498	52090048	12		rs7923609	65133822	10	NRBF2	5.45	0.24	0.34	0.06	
NRBF2	ILMN_3237385	10	rs2375269	69876894	11		rs7923609	65133822	10	NRBF2	5.53	0.42	0.04	0.35	

30

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	Pos/Mb[c]	Association[d]	Chr.	rs ID	Pos/Mb[c]	Association[d]	BSGS[e]	Fehrmann[f]	EGCUT[f]	Meta[g]	
NRBF2	ILMN_3237385	20	rs6025645	56157341		10	rs7923609	65133822	NRBF2	5.45			0.17	
NRBF2	ILMN_3237385	10	rs6517815	19819016		10	rs7923609	65133822	NRBF2	6.11			0.15	
NRD1	ILMN_1800897	2	rs4852124	240080022		1	rs6588415	52334047		6.13	0.47	0.05	0.17	
NUDT18	ILMN_1787885	8	rs5017351	254534482		8	rs1005901	21964378	NUDT18	5.44	0.03	0.46	0.15	
OAS1	ILMN_1658247	12	rs11613438	113480510		6	rs1047944	163997467		8.59	1.27	1.55	2.03	0.039
OAS1	ILMN_1658247	12	rs13311	113448652		12	rs2072133	113409260		4.13	4.12	0.81	3.86	
OAS1	ILMN_1675640	12	rs2892233	49160255		12	rs3741981		OAS1	4.38	0.87	0.46	0.76	
OPTN	ILMN_2381899	10	rs7192613	74286646		10	rs17512962	13169066	OPTN	5.64	0.42	0.06	0.14	
OSBPL5	ILMN_2307032	11	rs2829679	26662543		11	rs998639	3149249	OSBPL5	5.00	0.36	0.00	0.07	
OSTF1	ILMN_1742456	9	rs17780195	70624189	OSTF1	9	rs2273770	77755469	OSTF1	5.42	0.16	0.87	0.49	
OSTF1	ILMN_1742456	9	rs2273770	77755469		5	rs7718088	179590952		5.42	1.20	0.08	0.62	
OVGP1	ILMN_1734542	1	rs10802822	240132968		1	rs1264898	111992823	OVGP1	5.43	0.13	1.48	0.88	128.140
OVGP1	ILMN_1734542	1	rs347331	140148107		1	rs1264894	111969719	OVGP1	6.04	0.25	1.21	0.82	
PAM	ILMN_2313901	5	rs28092	102149795	PAM	1	rs784600	40139553	HPCAL4	5.59	0.66	0.44	0.59	
PCYOX1L	ILMN_1815951	5	rs2438490	148726162	PCYOX1L	3	rs2731939	213395989		6.20	0.19	0.26	0.16	
PEX5	ILMN_1660232	12	rs10444467	128052636		12	rs4329748	7364442	PEX5	5.85	0.09	0.71	0.32	120.688
PEX5	ILMN_1660232	15	rs7495797	27246462		12	rs4329748	7364442	PEX5	5.74	0.34	0.09	0.13	
PFAAP5	ILMN_1797893	22	rs131969	49151303		13	rs7328733	33126737	PFAAP5	5.64	0.87	0.36	0.67	
PGLYRP1	ILMN_1704870	19	rs12982353	46529456	PGLYRP1	14	rs1263806	21982957		6.51	0.03	0.65	0.24	
PHCA	ILMN_1812552	11	rs493642	123097386		11	rs10736812	76708086	PHCA	5.51	0.36	0.90	0.70	46.389
PIK3IP1	ILMN_1719986	22	rs4141404	31675185	PIK3IP1	1	rs2065841	61728597		5.60	0.20	0.01	0.03	
PISD	ILMN_1793934	22	rs470072	32263131	PISD	14	rs10498313	30398876		5.23	0.02	0.87	0.33	
PISD	ILMN_1793934	22	rs6518752	31999127	PISD	1	rs954627	18236681		7.11	0.00	1.19	0.48	1.137
PISD	ILMN_1793934	22	rs715572	33234931		22	rs6518754	32097775	PISD	4.12	0.05	0.42	0.15	
PNKD	ILMN_1774604	5	rs6869411	158781604		2	rs4672884	219182481	PNKD	6.35	0.16	0.04	0.04	
PNPLA7	ILMN_1662587	16	rs11639998	4527109		9	rs928046	140487108	PNPLA7	4.44	0.29	0.78	0.56	
PPFIBP2	ILMN_1675656	20	rs911019	49668255		11	rs4758001	7559930	PPFIBP2	5.15	0.31	0.33	0.26	
PPP2R3C	ILMN_1662617	15	rs12914603	58350896		14	rs11156875	35619816	PPP2R3C	5.81	0.12	0.42	0.19	
PPP2R5A	ILMN_1738784	1	rs10930170	166399467		1	rs12120009	212447167	PPP2R5A	5.63	0.72	0.48	0.66	
PPP2R5A	ILMN_1738784	12	rs12423255	123595064		1	rs12120009	212447167	PPP2R5A	5.72	0.08	0.95	0.46	
PPP2R5A	ILMN_1738784	13	rs1889083	66222691		1	rs12120009	212447167	PPP2R5A	5.61	0.36	0.13	0.17	
PPP2R5A	ILMN_1738784	11	rs682334	107417238		1	rs12120009	212447167	PPP2R5A	5.65	1.69	0.28	1.21	
PPP2R5A	ILMN_1738784	1	rs7757871	135030045		1	rs12120009	212447167	PPP2R5A	5.95	0.37	0.06	0.12	
PPP2R5A	ILMN_1738784	9	rs7871178	271148475		1	rs12120009	212447167	PPP2R5A	5.72	0.16	0.30	0.16	
PRDX5	ILMN_1711606	14	rs8019823	95040482		11	rs11600990	64082807	PRDX5	6.43	0.81	0.14	0.16	11.228
PRKCB1	ILMN_1713603	16	rs2188355	23867776		16	rs10492793	12639800		7.34	0.53	0.11	0.44	
PRMT2	ILMN_1675038	21	rs1029231	47931653	C21ORF57	18	rs958127	314973346	C21ORF57	5.60	0.19	0.03	0.25	
PRMT2	ILMN_1675038	21	rs2839372	48063862		21	rs11701058	47776382	C21ORF57	4.81	0.69	4.47	4.06	0.287
PSMB1	ILMN_1789176	11	rs3862607	121774705		6	rs13307114	170877444	PSMB1	5.79		0.44	0.04	
PSMB1	ILMN_1789176	18	rs4890648	43983954		6	rs6928843	170890384	PSMB1	5.14	0.00	0.26	0.27	
PSMB1	ILMN_1789176	20	rs6000930	30347832	PSMB1	6	rs9295415	170823379	PSMB1	5.44	0.44	0.21	1.78	
PSMB1	ILMN_1789176	6	rs6928843	170890384	PSMB1	6	rs2769689	225797957		4.58	1.95	0.32	0.86	
PWP1	ILMN_1743049	12	rs2353567	95478823		6	rs13207114	170877444	PSMB1	5.42	1.18	0.48	0.15	
PWP1	ILMN_1743049	17	rs4969205	76598123		11	rs110362212	5221825	PTDSS1	5.00	0.03	0.08	0.38	
QDPR	ILMN_1672443	11	rs631562	126852438		11	rs110362212	5221825	PTDSS1	5.90	0.80	0.40	0.11	
RAB3IP	ILMN_1803197	6	rs4946705	106348246		11	rs10020773	175266682	PTDSS1	5.70	0.02	1.25	1.55	
RABAC1	ILMN_2207363	22	rs241730	33375704	RABAC1	4	rs10020773	175266682	QDPR	5.75	1.03	0.08	0.09	
RBL2	ILMN_1756999	19	rs1075728	42462788	AKTIP	12	rs7305307	70235726		6.55	0.25	0.84	0.59	
RCN1	ILMN_1800276	16	rs9931702	53526551		11	rs7951628	120161117		6.42	0.28	0.31	0.08	
RCN1	ILMN_1800276	12	rs10879131	41147155	RCN1	15	rs1863464	26938488		6.38	0.03	0.37	0.47	
RCN1	ILMN_1800276	11	rs4922579	32136436	RCN1	11	rs4922579	32136436	RCN1	5.23	0.58	0.09	0.17	
RCN1	ILMN_1800276	11	rs4922579	32136436	RCN1	8	rs11166957	141177468		4.32	0.41		0.17	
RCN1	ILMN_1800276	11	rs4922579	32136436	RCN1	1	rs1341899	102740645		5.40	0.04	0.26	0.07	

Table S1 – continued from previous page

Expression trait			SNP 1				SNP 2				Interaction statistic / −log₁₀ p-values				Distance / Mb[h]
Gene ID[a]	Probe ID[b]	Chr.	rs ID	Pos/Mb[c]	Association[d]	Chr.	rs ID	Pos/Mb[c]	Association[d]	Chr.	BSGS[e]	Fehrmann[f]	EGCUT[f]	Meta[g]	
RERE	ILMN_1802380	1	rs4982958	24987865		14	rs301819	8501786	RERE	1	5.66	0.61	1.23	1.17	
RERE	ILMN_1802380	1	rs7697290	135248366		4	rs301819	8501786	RERE	1	5.74	0.14	0.10	0.06	
RERE	ILMN_2327795	1	rs11085829	13174312		19	rs301819	8501786	RERE	1	5.12	0.21	0.33	0.21	
RERE	ILMN_2327795	1	rs3852011	112844086		3	rs301819	8501786	RERE	1	5.71	0.08	0.60	0.26	
RNASE6	ILMN_1780533	14	rs11628398	21182800	RNASE6	14	rs7324365	100601327	RNASE6	13	5.48	0.42	0.21	0.26	
RNASE6	ILMN_1780533	14	rs6603134	81106521		19	rs11628398	21182800	RNASE6	14	5.11	0.09	0.22	0.08	
RNF167	ILMN_1794726	17	rs2382230	4875566		17	rs4884857	54668512		13	4.37				
RNF167	ILMN_1794726	17	rs400688	4839930	RNF167	17	rs11706900	36348968		3	5.59	0.71	0.46	0.64	
RNPEP	ILMN_1738347	1	rs1107121	46127549		21	rs2819365	201983242		1	6.27	0.11	0.30	0.13	
RNPEP	ILMN_1738347	1	rs8071611	67153386		17	rs2819365	201983242		1	4.32	1.48	0.52	1.28	
RPL13	ILMN_2413278	16	rs352935	89648580		16	rs2965817	89513234		16	4.98	3.79	14.41	17.24	0.135
RPL23AP7	ILMN_2222750	2	rs1401202	80320056		16	rs4849261	114450028	RPL23AP7	2	5.55	0.13	0.73	0.38	
RPL36AL	ILMN_2189933	14	rs3007033	50103816	RPL36AL	14	rs17495030	138038093		9	5.46	0.09	0.06	0.02	
RPL36AL	ILMN_2189936	14	rs4900928	50020817	RPL36AL	14	rs1502991	66137260		6	5.86	0.32	0.20	0.19	
RPL8	ILMN_1764721	8	rs2958482	145984615	RPL8	8	rs1619856	234585790		1	4.59	0.10	0.37	0.15	
RPL8	ILMN_1764721	8	rs4143674	4741304		20	rs2958482	145984615	RPL8	8	4.33	0.13	0.45	0.22	
SEC13	ILMN_3297880	3	rs4889214	80913946		16	rs696221	10342876	SEC13	3	6.48	0.22	1.73	1.17	
SEMA4A	ILMN_1702787	1	rs17085428	95388015		5	rs7695	156147326	SEMA4A	1	5.70	0.02	0.51	0.15	
SESN3	ILMN_1694027	11	rs12147460	104412137		14	rs684856	94906111	SESN3	11	5.50	0.31	0.06	0.10	
SESN3	ILMN_1694027	11	rs355391	46591793		15	rs684856	94906111	SESN3	11	5.67	0.31	0.51	0.31	
SESN3	ILMN_1694027	11	rs684856	94906111	SESN3	11	rs7004947	134606425		8	5.60	0.21	0.12	0.35	
SH3BGRL2	ILMN_1762764	6	rs10838191	43936658		11	rs1354034	56849749	PPBP	3	5.52	0.70	0.51	0.30	
SH3BGRL2	ILMN_1762764	6	rs2545385	66383979		5	rs1354034	56849749	PPBP	3	5.97	0.20	0.71	0.53	
SH3BGRL2	ILMN_1762764	6	rs6845304	88280502		4	rs1354034	56849749	PPBP	3	5.23	0.32	0.18	0.13	
SH3GLB2	ILMN_2158336	9	rs1034120	18196922		21	rs17455517	131785369	SH3GLB2	9	7.40	0.22	0.18	0.17	
SIRPG	ILMN_1771801	20	rs1535883	1612819	SIRPG	20	rs6842739	60489510		4	5.74	0.29	0.24	0.09	
SLC22A18	ILMN_2382505	11	rs11673260	52181798		19	rs367035	2923826	SLC22A18	11	5.70	0.09	0.10	0.06	
SLC22A18	ILMN_2382505	11	rs367035	2923826	SLC22A18	11	rs3110874	153224179		7	6.15	0.15	0.13	0.19	
SLC22A18	ILMN_2382505	11	rs367035	2923826	SLC22A18	11	rs3772054	241678528		2	5.88	0.39	0.82	1.24	
SLC41A3	ILMN_2356111	3	rs1912136	24616743		11	rs6771703	125801067	SLC41A3	3	5.95	1.10	0.07	0.40	
SLC45A4	ILMN_1745778	8	rs6985508	142337734		11	rs7701916	174598073		5	5.52	0.86	0.58	0.26	
SLC46A3	ILMN_1658639	13	rs949805	55602091		17	rs79811190	29259349	SLC46A3	13	6.52	0.09	0.09	0.06	
SMG7	ILMN_1706553	1	rs8035259	97403923		15	rs109113353	183489203	SMG7	1	5.68	0.17	0.62	0.52	
SMOX	ILMN_1775380	20	rs8118315	4161500	SMOX	20	rs11677815	65800982		4	6.11	0.39	0.09	0.17	
SNHG8	ILMN_3309349	4	rs1105621	130050233		9	rs705837	119225940		4	6.60	0.15	0.13	0.09	
SNORD14A	ILMN_1799381	11	rs1520429	46259108		15	rs214097	17291499	SNORD14A	11	7.31	0.29	1.03	0.72	
SNORD14A	ILMN_1799381	11	rs2634462	17339127		11	rs6486334	17015557	SNORD14A	11	6.08	13.11	10.96	23.22	0.324
SNORD89	ILMN_3238662	2	rs104455863	115929241		2	rs750783	101889306	SNORD89	2	5.96				14.040
SNORD89	ILMN_3238662	2	rs11605822	122986326		11	rs750783	101889306	SNORD89	2	6.33				
SNORD89	ILMN_3238662	2	rs2135064	267778066		5	rs750783	101889306	SNORD89	2	6.45				
SNUPN	ILMN_1733932	15	rs8134646	46376528	SNUPN	21	rs7185362	81888905		16	5.59	0.13	1.41	0.83	
SNUPN	ILMN_2364535	15	rs8134646	46376528	SNUPN	21	rs1472075	193706323		3	5.44	0.34	0.00	0.06	
SPATA5L1	ILMN_1131620	15	rs1131620	41117869		19	rs4774580	45652086	SPATA5L1	15	5.65	0.67	0.12	0.33	
STARD10	ILMN_1717052	11	rs2221406	90174526		13	rs1000620	72509713	STARD10	11	5.88	0.57	0.17	0.31	
STYXL1	ILMN_2210729	7	rs4073164	109477517		14	rs176685	75616105	STYXL1	11	5.51	0.46	0.24	0.30	
SULF2	ILMN_2345142	20	rs117000063	46153148	SULF2	20	rs939294	180439236		4	7.05	0.01	0.05	0.00	
SULT1A4	ILMN_2336133	16	rs1463965	74332954		18	rs3785354	28550667	TUFM	16	5.83	0.26	0.16	0.14	
SULT1A4	ILMN_2336133	16	rs2836657	40119768		21	rs3785354	28550667	TUFM	16	6.14	0.28	0.31	0.24	
SURF6	ILMN_1778032	9	rs6099626	56013994		20	rs3118663	136281753	SURF6	9	5.47	0.26	0.16	0.14	
SYTL2	ILMN_2336609	11	rs1375719	103410782		13	rs485485	84495269	SYTL2	11	5.55	0.28	0.31	0.24	
THBS3	ILMN_1804663	1	rs1939875	95422867		11	rs4072037	155162067	THBS3	1	5.65	0.03	0.15	0.03	
THBS3	ILMN_1804663	1	rs8014956	20687978		14	rs2049805	155194980	THBS3	1	5.22	0.31	0.76	0.55	
TIPRL	ILMN_1781457	1	rs2823245	16745523		21	rs1320993	168154599	TIPRL	1	5.22	0.07	0.40	0.15	

32

Table S1 – continued from previous page

Gene ID[a]	Probe ID[b]	Chr.	rs ID	Pos/Mb[c]	Association[d]	rs ID	Chr.	Pos/Mb[c]	Association[d]	BSGS[e]	Fehrmann[f]	EGCUT[f]	Meta[g]	Distance / Mb[h]
				SNP 1				SNP 2			Interaction statistic / −log₁₀ p-values			
TMED4	ILMN_1804148	7	rs1940400	132389627		rs17725246	7	44581986	TMED4	5.70	0.06	1.34	0.70	
TMEM149	ILMN_1786426	19	rs2839013	47248981		rs8106959	19	36219525	TMEM149	8.11	0.16	0.48	0.26	
TMEM149	ILMN_1786426	19	rs57762235	27925288		rs8106959	19	36219525	TMEM149	6.79				
TMEM149	ILMN_1786426	19	rs6090518	45207005		rs8106959	19	36219525	TMEM149	11.09	0.76			
TMEM149	ILMN_1786426	19	rs8074491	36268923	SNX26	rs7254601	19	36147315	TMEM149	12.16	81.55	45.78	145.78	0.122
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs10508289	10	4799159		8.12	1.55	3.09	3.67	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs10819626	9	133025756		8.02	0.40	0.99	0.80	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs10937361	3	183359436		8.39	3.61	1.18	3.78	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs1401098	12	128884559		7.37	2.41	1.00	2.52	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs1557335	18	64268976		6.95	0.08	0.07	0.03	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs17719594	14	90932598		6.93	3.06	0.77	2.87	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs1843357	8	13822381		6.21	3.72	3.33	6.00	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs2351458	4	113317583		7.30	0.04	9.61	8.00	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs2539000	7	147619772		6.70	1.57	1.52	2.27	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs2731711	5	171792273		5.92	0.19	0.33	0.19	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs471728	11	129595460		8.89	0.90	3.62	3.51	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs6718480	2	233879066		8.55	3.31	5.15	7.36	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs6926382	6	161683974		5.80	3.06	8.80	10.72	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs7213338	17	80357420		5.49	0.07	3.14	2.10	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs914940	1	242889492		6.22	3.36	6.96	9.20	
TMEM149	ILMN_1786426	19	rs8106959	36219525	TMEM149	rs9509428	13	21473952		9.44	0.10	5.75	4.47	
TMEM63A	ILMN_1719649	11	rs1254086	72900603		rs4149226	1	226027323	TMEM63A	5.60				
TMEM80	ILMN_1708482	11	rs1548475	58058246		rs4963126	11	656845	TMEM80	5.79	0.64	0.12	0.32	
TNPO3	ILMN_1683811	7	rs1537146	4859303		rs10488630	7	128593948	IRF5	5.61	0.11	0.15	0.07	
TNPO3	ILMN_1683811	7	rs199793	22287303		rs10488630	7	128593948	IRF5	5.52	1.03	0.17	0.62	
TRA2A	ILMN_1731043	7	rs7776572	23528927		rs11770192	7	23498358		8.23	3.19	1.89	4.09	0.031
TRAPPC4	ILMN_1814650	11	rs1278760	135531675		rs3916581	11	118887887	TRAPPC4	5.61	0.28	0.40	0.29	
TRAPPC4	ILMN_1814650	11	rs1793823	131018917		rs3916581	11	118887887	TRAPPC4	5.52	0.93	0.01	0.36	12.131
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs10059004	5	166970604		5.97	0.21	1.60	1.07	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs10230095	8	132022957		6.92	0.37	0.87	0.68	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs1375714	6	156404902		7.79	0.12	0.18	0.08	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs1393299	1	242329791		6.43	0.63	0.47	0.59	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs17763599	19	2369415		6.38	0.21	0.24	0.16	5.389
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs4968328	17	57495457		6.51	0.50	0.38	0.44	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs7313362	12	129644342		7.08	0.04	0.65	0.25	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs7694997	4	9947811		5.86	0.20	0.36	0.22	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs7800935	7	146690926		6.27	0.15	0.33	0.16	
TRAPPC5	ILMN_2372639	19	rs17159840	7758194	TRAPPC5	rs856638	14	85439550		6.73	0.24	0.07	0.08	
TRAPPC5	ILMN_2372639	19	rs380708	22740835		rs17159840	19	7758194	TRAPPC5	7.58				
TRAPPC5	ILMN_2372639	19	rs39916995	45128454		rs17159840	19	7758194	TRAPPC5	7.73	0.85	0.78	1.01	
TRAPPC5	ILMN_2372639	19	rs6040514	112728861		rs17159840	19	7758194	TRAPPC5	8.10	0.51	0.55	0.56	
TRAPPC5	ILMN_2372639	19	rs7246264	7762978		rs10179572	2	228540503		6.71	0.14	0.02	0.02	
TRAPPC5	ILMN_2372639	19	rs7246264	7762978		rs12921440	16	30440876		7.34	0.14	0.26	0.13	
TRAPPC5	ILMN_2372639	19	rs7246264	7762978		rs1887778	9	134635088	RAPGEF1	7.05	0.08	0.86	0.40	
TRAPPC5	ILMN_2372639	19	rs7246264	7762978		rs963354	3	157339377		7.41	0.36	0.90	0.69	
TREM1	ILMN_1688231	6	rs10862975	85749398		rs2395771	6	41264577	TREM1	5.42	0.11	0.25	0.11	
TREM1	ILMN_1688231	6	rs12412964	108256422		rs2395771	6	41264577	TREM1	5.92	1.20	1.23	1.69	
TRIM38	ILMN_1697971	6	rs2527180	158808416		rs2032447	6	26044369	TRIM38	6.46	0.04	0.91	0.39	
TSPAN14	ILMN_1785060	10	rs968726	27194634		rs10748526	10	82273079	TSPAN14	6.00	0.07	0.18	0.06	
TSPAN32	ILMN_1718621	11	rs10838738	47663049	MYBPC3	rs620607	11	23177951	TSPAN32	5.01				45.345
TSPAN32	ILMN_2389970	11	rs12800998	2317951	TSPAN32	rs1198819	2	237947208		5.51				
TYMP	ILMN_3223126	22	rs140522	509712666	ECGF1	rs4783126	16	85147633		6.34				
TYMP	ILMN_3223126	22	rs470119	50966914	ECGF1					6.13				

33

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[f]	Meta[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	1.643
VASP	ILMN_1743646	19	rs1264226	19	46063167		rs2276470	19	45974668		5.09	0.94	5.14	4.95	0.088
VNN2	ILMN_1678939	6	rs10435352	7	105252718		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	rs1344447	22	49927332		rs1883617	6	133072650	VNN2	5.72				
VNN2	ILMN_1678939	6	rs216495	11	16345510		rs1883617	6	133072650	VNN2	5.77	0.33	0.19	0.41	
VNN3	ILMN_1804935	6	rs10278073	7	151662184		rs2267952	6	133067782	VNN3	6.44	0.16	0.74	0.31	
VNN3	ILMN_1804935	6	rs1443946	8	73006453		rs2267952	6	133067782	VNN3	5.74	0.23	0.48	0.17	
VNN3	ILMN_1804935	6	rs348462	9	755471169		rs2267952	6	133067782	VNN3	6.44	0.31	0.17	0.04	
VNN3	ILMN_1804935	6	rs7157055	14	83262064		rs2267952	6	133067782	VNN3	5.82	0.03	0.19	0.04	
VNN3	ILMN_2387680	6	rs2823165	21	16594253		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	123098249		5.71	0.48	0.17	0.26	
VSTM1	ILMN_1763455	19	rs9625870	22	302612219		rs10500316	19	54533697	VSTM1	5.88	0.81	1.38	1.47	
WDR48	ILMN_1762103	3	rs1388935	4	188927822		rs6778963	3	39091812	WDR48	5.88	0.19	0.13	0.09	
WDR48	ILMN_1762103	3	rs1887778	9	134635088	RAPGEF1	rs883349	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	123371708		rs11715581	3	49194331	WDR6	4.86	1.64	1.43	2.25	
XAF1	ILMN_2370573	17	rs1533031	17	6673170	XAF1	rs12591171	15	93119799		5.48	2.38	0.17	1.63	
ZFP90	ILMN_1684628	16	rs909446	21	37040648		rs1182968	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 $-\log_{10}$ p-value from discovery dataset

[f] Interaction $-\log_{10}$ p-value from replication dataset

[g] Interaction $-\log_{10}$ p-value from meta analysis of replication datasets only

[h] Distance in Mb between interacting SNPs for cis-cis acting SNP pairs

References

[1] Carlborg, O. & Haley, C. S. Epistasis: too often neglected in complex trait studies? *Nature Reviews Genetics* **5**, 618–25 (2004).

[2] Hill, W. G., Goddard, M. E. & Visscher, P. M. Data and Theory Point to Mainly Additive Genetic Variance for Complex Traits. *PLoS Genetics* **4** (2008).

[3] Crow, J. F. On epistasis: why it is unimportant in polygenic directional selection. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences* **365**, 1241–4 (2010).

[4] Costanzo, M. *et al.* The genetic landscape of a cell. *Science (New York, N.Y.)* **327**, 425–31 (2010).

[5] Bloom, J. S., Ehrenreich, I. M., Loo, W. T., Lite, T.-L. V. o. & Kruglyak, L. Finding the sources of missing heritability in a yeast cross. *Nature* 1–6 (2013).

[6] Carlborg, O., Jacobsson, L., Ahgren, P., Siegel, P. & Andersson, L. Epistasis and the release of genetic variation during long-term selection. *Nature Genetics* **38**, 418–420 (2006).

[7] Strange, A. *et al.* A genome-wide association study identifies new psoriasis susceptibility loci and an interaction between HLA-C and ERAP1. *Nature Genetics* **42**, 985–90 (2010).

[8] Evans, D. M. *et al.* Interaction between ERAP1 and HLA-B27 in ankylosing spondylitis implicates peptide handling in the mechanism for HLA-B27 in disease susceptibility. *Nature Genetics* **43** (2011).

[9] Cordell, H. J. Detecting gene-gene interactions that underlie human diseases. *Nature Reviews Genetics* **10**, 392–404 (2009).

[10] Hemani, G., Theocharidis, A., Wei, W. & Haley, C. EpiGPU: exhaustive pairwise epistasis scans parallelized on consumer level graphics cards. *Bioinformatics (Oxford, England)* **27**, 1462–5 (2011).

[11] Metspalu, A. The Estonian Genome Project. *Drug Development Research* **62**, 97–101 (2004).

[12] Fehrmann, R. S. N. *et al.* Trans-eQTLs reveal that independent genetic variants associated with a complex phenotype converge on intermediate genes, with a major role for the HLA. *PLoS genetics* **7**, e1002197 (2011).

[13] Lieberman-Aiden, E. *et al.* Comprehensive mapping of long-range interactions reveals folding principles of the human genome. *Science (New York, N.Y.)* **326**, 289–93 (2009).

14 Visscher, P. M., Brown, M. a., McCarthy, M. I. & Yang, J. Five years of GWAS discovery. *American journal of human genetics* **90**, 7–24 (2012).

15 Weinreich, D. M., Delaney, N. F., Depristo, M. a. & Hartl, D. L. Darwinian evolution can follow only very few mutational paths to fitter proteins. *Science (New York, N.Y.)* **312**, 111–4 (2006).

16 Breen, M. S., Kemena, C., Vlasov, P. K., Notredame, C. & Kondrashov, F. a. Epistasis as the primary factor in molecular evolution. *Nature* **490**, 535–538 (2012).

17 Weir, B. S. Linkage disequilibrium and association mapping. *Annual review of genomics and human genetics* **9**, 129–42 (2008).

18 Hemani, G., Knott, S. & Haley, C. An Evolutionary Perspective on Epistasis and the Missing Heritability. *PLoS Genetics* **9**, e1003295 (2013).

19 Marchini, J., Donnelly, P. & Cardon, L. R. Genome-wide strategies for detecting multiple loci that influence complex diseases. *Nature Genetics* **37**, 413–417 (2005).

20 Lango Allen, H. *et al.* Hundreds of variants clustered in genomic loci and biological pathways affect human height. *Nature* **467**, 832–8 (2010).

21 Powell, J. E. *et al.* Congruence of Additive and Non-Additive Effects on Gene Expression Estimated from Pedigree and SNP Data. *PLoS Genetics* **9**, e1003502 (2013).

22 Powell, J. E. *et al.* The Brisbane Systems Genetics Study: genetical genomics meets complex trait genetics. *PloS one* **7**, e35430 (2012).

23 Preininger, M. *et al.* Blood-informative transcripts define nine common axes of peripheral blood gene expression. *PLoS genetics* **9**, e1003362 (2013).

24 Cockerham, C. C. An extension of the concept of partitioning hereditary variance for analysis of covariances among relatives when epistasis is present. *Genetics* **39**, 859–882 (1954).

25 Ho, T. H. *et al.* Muscleblind proteins regulate alternative splicing. *The EMBO journal* **23**, 3103–12 (2004).

26 Trynka, G. *et al.* Chromatin marks identify critical cell types for fine mapping complex trait variants. *Nature genetics* **45**, 124–30 (2013).

27 Ward, L. D. & Kellis, M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic acids research* **40**, D930–4 (2012).

28 Lan, X. *et al.* Integration of Hi-C and ChIP-seq data reveals distinct types of chromatin linkages. *Nucleic acids research* **40**, 7690–704 (2012).

[29] Osborne, C. S. *et al.* Active genes dynamically colocalize to shared sites of ongoing transcription. *Nature genetics* **36**, 1065–71 (2004).

[30] Rieder, D., Trajanoski, Z. & McNally, J. G. Transcription factories. *Frontiers in genetics* **3**, 221 (2012).

[31] Visscher, P. M., Hill, W. G. & Wray, N. R. Heritability in the genomics era– concepts and misconceptions. *Nature Reviews Genetics* **9**, 255–66 (2008).

[32] Churchill, G. A. & Doerge, R. W. Empirical threshold values for quantitative trait mapping. *Genetics* **138**, 963–71 (1994).