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 often demonstrated in artificial gene manipulation studies in model organisms, 4,5 and some examples have been reported in other species,⁶ few examples exist for epistasis amongst natural polymorphisms in human traits.^{7,8} Its absence from empirical findings may simply be due to 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 and computational issues.⁹ Here we show that, using advanced computation¹⁰ 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 7339 gene expression levels measured in peripheral blood, we found 501 significant pairwise interactions between common SNPs influencing the expression of 238 genes $(p < 2.91 \times 10^{-16})$. Replication of these interactions in two independent data sets^{11,12} showed both concordance of direction of epistatic effects $(p = 5.56 \times 10^{-31})$ and enrichment of interaction p-values, with 30 being significant at a conservative threshold of p < 0.05/501. Forty-four of the genetic interactions are located within 2Mb of regions of known physical 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 segregating common polymorphisms interacting to influence human traits.

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. He are to date, though its contribution to phenotypic variance is frequently the subject of debate, here is little empirical exploration of the role that epistasis plays in the architecture of complex traits in humans. Beyond the prism of human association studies there is evidence for epistasis, not only at the molecular scale from artificially induced mutations but also at the evolutionary scale in fitness adaptation. In and speciation.

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 testing ⁹ all make it more difficult to detect epistasis in comparison to additive effects. Thus, 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 arises from 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 and like most complex diseases, these expression traits are typically heritable. ²¹ But unlike complex diseases, genetic associations with gene expression commonly have very large effect sizes that explain large proportions of the genetic variance, ²² making them good candidates to search for epistasis, should it exist.

In our discovery dataset (Brisbane Systems Genetics Study, BSGS²³) of 846 individuals genotyped at 528,509 SNPs, we used a two stage approach to identify genetic interactions. First, we exhaustively test every pair of SNPs for pairwise effects against each of 7339 expression traits in peripheral blood (1.03×10^{15}) statistical tests, family-wise error rate of 5% corresponding to a significance threshold of $p < 2.91 \times 10^{-16}$, Methods). Second, we filtered the SNP pairs from stage 1 on LD and genotype class counts, and tested the remaining pairwise effects for significant interaction terms and used a Bonferroni correction for multiple testing (estimated type 1 error rate $0.05 \le \alpha \le 0.14$, Methods, Supplementary Figure S1). Using this design we identified 501 putative genetic interactions influencing the expression levels of 238 genes (Supplementary Table S1). We used strict quality control measures to avoid statistical associations being driven by technical artifacts (Methods). However it remains possible that unexplained technical artifacts may have led to the significant discovery interactions. 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 (5% significance threshold p < 0.05/501, Table 1). To quantify the similarity of GP maps between the independent datasets (Figure 1) we decomposed the genetic effects of each of the SNP pairs into orthogonal additive, dominance and epistatic effects (A1, A2, D1, D2, A1 \times A2, $A1 \times D2$, $D1 \times A2$, $D1 \times D2$) and tested for concordance of the sign of the most signicant effect (Supplementary Table S3, Methods). Sign concordance between the discovery and both replication datasets was observed in 22 out of the 30 significantly replicated interactions (expected value = 7.5 under the null hypothesis of no interactions, $p = 3.76 \times 10^{-8}$).

In addition, using the meta analysis from the replication samples only, we observed that 316 of the remaining 404 discovery SNP pairs had replication

interaction p-values more extreme than the 2.5% confidence interval of the quantile-quantile plot against the null hypothesis of no interactions where p-values are assumed to be uniformly distributed ($p << 1.0 \times 10^{-16}$, Figure 2 and Supplementary Figure S2). Concordance of the direction of the effect of the largest variance component was also highly significant ($p = 5.71 \times 10^{-31}$, Supplementary Table S3). The congruence of the epistatic networks in discovery and replication datasets is shown in Figure 3, 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,²⁴ but only 20 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 (Supplementary Figure S6). It should be noted that although it is a necessary step to establish the veracity of the interactions from the discovery set, replication of epistatic effects in independent samples is difficult in practice due to LD (Methods).

Though seldom the focus of association studies, SNPs with known main effects are often tested for $A \times A$ genetic interactions, but our analysis suggests this is unlikely to be the best 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 (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 $A \times A$, $A \times D$, $D \times A$ and $D \times D$ at the discovery stage (p = 0.22 for departure from expectation). This is not surprising because these patterns of epistasis used for statistical decomposition are simply convenient orthogonal parameterisations of a two locus model, and are not intended to model biological function.

Of the discovery interactions, 26 were cis-cis acting (within 1Mb of the transcription start site, mean distance between SNPs was 0.53Mb), 462 were cis-trans-acting, and 13 were trans-trans-acting. We observed a wide range of significant GP maps (Figure 1) 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 splicing²⁶) 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 S10). Each of these interactions has evidence for replication in at least one dataset and six are significantly replicated at the Bonferroni level (Supplementary Figure S3). We see similar epistatic networks involving multiple (eight or more) trans-acting SNPs for other gene expresson levels too, for example TMEM149 (Supplementary Figure S11), NAPRT1 (Supplementary Figure S12), TRAPPC5 (Supplementary Figure S13), and CAST (Supplementary Figure S14). We observed that from pedigree analysis these five gene expression phenotypes had non-additive variance component estimates within the 95th percentile of the 17,994 gene expression phenotypes that were analysed previously²² (Supplementary Table S2, Methods).

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,tri-methylation (H3K4me3) chromatin marks, in 34 cell types²⁷ (Supplementary Figure S5). 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 epistatic interactions where tissue specificity is provided by the *cis* SNPs. There is also enrichment for *cis*-SNPs to be localised in regions with regulatory genomic features as measured by chromatin states²⁸ (Supplementary Figure S4).

We also demonstrate physical organisation of interacting loci within the cell, 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. We cross-referenced our epistatic SNPs with a map of chromosome interacting regions (n=96,139) in K562 blood cell lines (Methods) and found that 44 epistatic interactions mapped to within 5Mb ($p<1.8\times10^{-10}$), (Supplementary Figure S15). 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. (30)

Quantifying the importance of epistasis in complex traits in humans remains an open question. Here we are able to identify 238 gene expression traits with at least one significant interaction given our experiment-wide threshold, where the minimum estimated variance explained by the epistatic effects of any interaction was 2.1% of phenotypic variance. Taking results from our previously published eQTL²³ we calculated that 1848 of the 7339 gene expression levels analysed were influenced by additive effects where the estimated additive variance of a locus was 2.1% or greater. Thus, we can infer that the number of instances of large additive effects is significantly greater than the number of instances of large epistatic effects.

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 Taking all additive effects detected in Powell et al (2012) that have additive variance explaining 2.1% or greater of phenotypic variance, we calculated that the proportion of total phenotypic variance of all 7339 gene expression levels explained by additive effects alone was 2.16%. By contrast, the estimated epistatic variance from the interacting SNPs detected in this study on average explain a total of 0.22% of phenotypic variance, approximately ten times lower than the estimated additive variance. There are several caveats to this comparison which we discuss in the Methods.

Overall, we have demonstrated that it is possible to identify and replicate epistasis in complex traits amongst common human variants, despite the rela-

tive contribution of pairwise epistasis to phenotypic variation being small. 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 for 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.

Methods Summary

We searched for pairwise epistasis exhaustively in the BSGS discovery dataset, ²³ which comprises 846 individuals who are genotyped at 528,509 autosomal SNPs. Each individual had gene expression levels measured in peripheral blood at 7,339 probes representing 6,158 RefSeq genes (significant expression in $\geq 90\%$ of individuals). SNP pairs were modelled for full genetic effects, including marginal additive and dominance at both SNPs plus four interaction terms. We used permutation analysis to calculate an experiment-wide significance threshold of $T_e = 2.91 \times 10^{-16}$ at the 5% family-wise error rate (FWER). 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. The 501 significant SNP pairs were carried forward for replication in two independent datasets that used the same expression assays for analysing transcription in peripheral blood Fehrmann, n = 1240; EGCUT, n = 891. A meta analysis on the interaction p-values from each replication dataset was performed to provide an overall replication statistic for each putative interaction.

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Author contributions

G.H., J.E.P., P.M.V., and G.W.M. conceived and designed the study. G.H., J.E.P., K.S., H-J.W., and J.Y. performed the analysis. T.E. and A.M. provided the EGCUT data. A.K.H., A.F.M., G.W.M., N.G.M., and J.E.P. provided the BSGS data. H-J.W. and L.F. provided the Fehrmann data. G.H. and J.E.P. wrote the manuscript with the participation of all authors.

Author information

The authors declare no financial competing interests.

Tables

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

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	Gene (chr.)	SNP 1 (chr.)	SNP 2 (chr.)	BSGS^2			$Meta^4$
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

 $^{^{1}}$ - log₁₀ 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

Figures

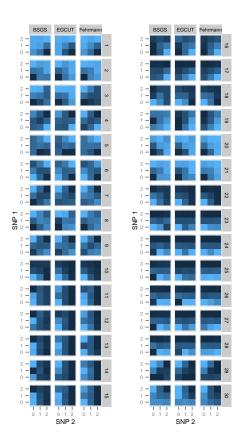


Figure 1: Replication of GP maps in two independent populations. The GP maps for each epistatic interaction that is significant at the Bonferroni level in both replication datasets are shown. Each GP map consists of nine tiles where each tile represents the expression level for that two-locus genotype class. Phenotypes are for gene transcript levels (dark coloured tiles = high expression, light coloured tiles = low expression). Columns of GP maps are for each independent dataset. 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.

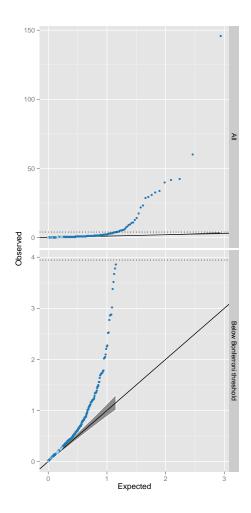


Figure 2: \mathbf{Q} - \mathbf{Q} plots of interaction p-values from replication datasets. The top panel shows all 434 discovery SNPs that were tested for interactions. Observed p-values (y-axis, $-\log_{10}$ scale) are plotted against the expected p-values (x-axis, $-\log_{10}$ scale). The multiple 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.

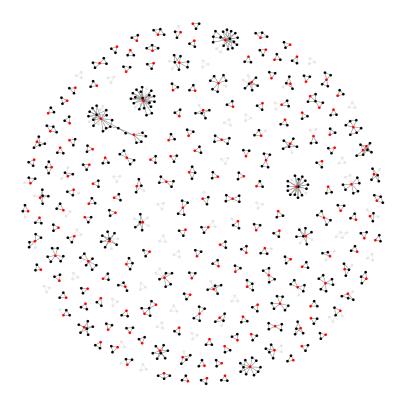


Figure 3: **Discovery and replication of epistatic networks** All 434 putative genetic interactions (edges) with data common to discovery and replication sets is shown, where black nodes represent SNPs and red nodes represent traits (gene expression probes). Three hundred and forty-five interactions had p-values exceeding the 2.5% confidence interval following meta analysis of the replication data 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. An interactive version of this graph can be found here: http://kn3in.github.io/detecting_epi/

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. *Bioin-formatics (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 Schadt, E. *et al.* Genetics of gene expression surveyed in maize, mouse and man. *Nature* **422**, 297–302 (2003).
- ²² 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).
- ²³ Powell, J. E. et al. The Brisbane Systems Genetics Study: genetical genomics meets complex trait genetics. PloS one 7, e35430 (2012).
- ²⁴ Preininger, M. *et al.* Blood-informative transcripts define nine common axes of peripheral blood gene expression. *PLoS genetics* **9**, e1003362 (2013).
- ²⁵ 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).
- ²⁶ Ho, T. H. et al. Muscleblind proteins regulate alternative splicing. The EMBO journal 23, 3103–12 (2004).
- ²⁷ Trynka, G. et al. Chromatin marks identify critical cell types for fine mapping complex trait variants. Nature genetics 45, 124–30 (2013).
- ²⁸ Hoffman, M., Buske, O., Wang, J. & Weng, Z. Unsupervised pattern discovery in human chromatin structure through genomic segmentation. *Nature Methods* 9, 473–476 (2012).

 $^{^{29}\,\}mathrm{Lan},$ X. et al. Integration of Hi-C and ChIP-seq data reveals distinct types of chromatin linkages. Nucleic acids research 40, 7690–704 (2012).

 $^{^{30}}$ Rieder, D., Trajanoski, Z. & McNally, J. G. Transcription factories. Frontiers in genetics ${\bf 3},\,221$ (2012).

Supplementary Figures

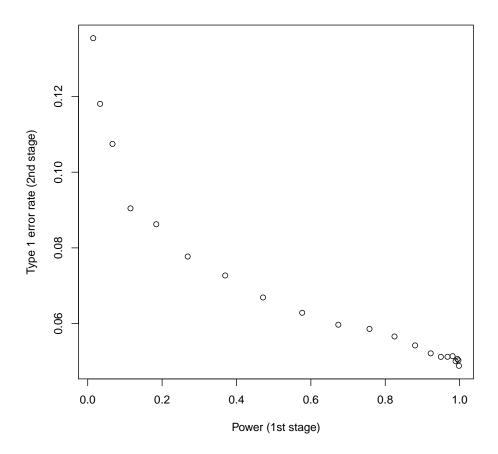


Figure S1: Type 1 error rate of two stage design assuming a null model of one large additive effect and no epistasis In stage 1 SNPs are tested for full genetic effects (8 d.f.) and those that surpass a threshold for multiple testing are then tested for significant interaction terms in stage 2. These interaction p-values are then adjusted (Bonferroni) for the total number of tests that passed stage 1. The type 1 error rate of this two stage design is dependent on the power, which is not known empirically.

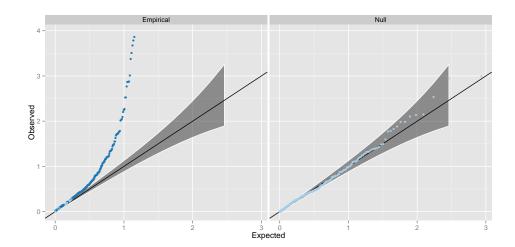


Figure S2: Q-Q plots of interaction p-values from replication datasets, excluding the 30 points significant at the Bonferroni level The right panel (Null) shows the interaction p-values from a meta analysis across two independent datasets on 434 SNP pairs where one SNP has a marginal effect. The left 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 2.

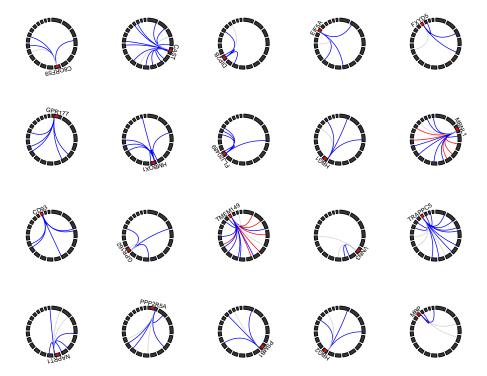


Figure S3: Gene expression traits with four or more genetic interactions Circle plots represent the genomic positions for SNPs (linking lines) and expression probes (red points). Chromosomes are represented by black blocks and ordered from 1 to 22 clockwise, starting from the top. Grey lines represent no evidence for replication, blue lines denote interactions that are outside the 97.5% confidence interval or the Q-Q plot (Figure 2), and red lines denote replication at the Bonferroni correction level. Most interactions are characterised as being cis-trans to the expression probe.



Figure S4: Location of SNPs relative to genomic features We used chromatin segmentation 28 as a method for labelling 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: E = Predicted enhancer, E CTCF enriched element, E Predicted weak enhancer or open chromatin cis regulatory element, E Predicted promoter flanking region, E Predicted promoter region including transcriptional start site, E Predicted transcribed region, E Predicted Repressed or Low Activity region

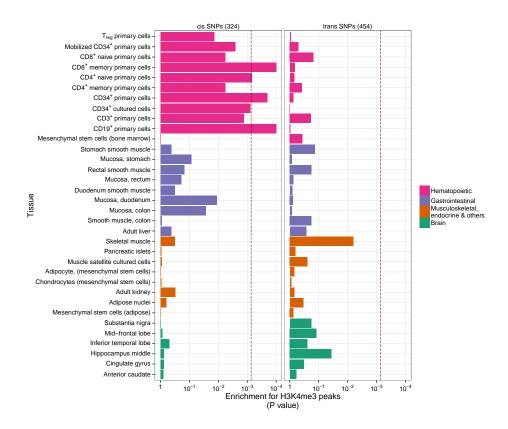


Figure S5: Tissue specific enrichment of SNPs in transcriptionally active regions The locations of transcriptional activity can be predicted by chromatin marks, assayed by H3K4me3.²⁷ Enrichment *p*-values are calculated using permutation analysis for 34 different cell types (*y*-axis) in four tissue types (Rows of boxes). The dotted red line denotes significance (Bonferroni correction for 34 cell types, *x*-axis). There is enrichment for *cis*-acting SNPs in Haematopoietic tissue types only. *Trans*-acting SNPs have no tissue specificity.

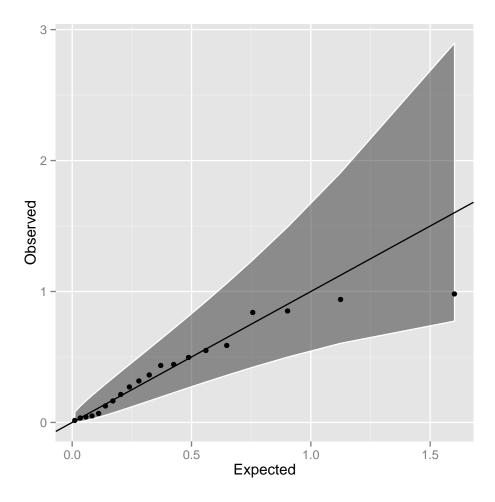


Figure S6: Q-Q plot of interaction p-values in the CDHWB dataset Twenty of the 501 discovery SNP pairs passed filtering in the CDHWB dataset (mainly due to small sample size). There is no evidence for enrichment of interaction terms, most likely due to insufficient power given the limited sample size.

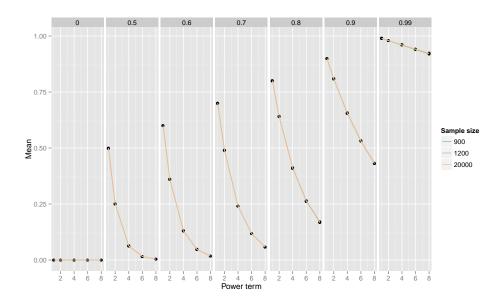


Figure S7: Sampling mean for different power terms of population r values Power of detection and replication of epistatic interactions depends not on r^2 between causal variants and observed SNPs, but on r^4, r^6, r^8 . For a given population value of LD r (columns of plots), plotted is the sample mean (y-axis) of \hat{r} , \hat{r}^2 (additive), \hat{r}^4 (dominance, A×A), \hat{r}^6 (A×D), \hat{r}^8 (D×D) (x-axis) for different sample sizes (coloured lines). As true r reduces the statistical power to detect epistatic variants drops dramatically under the assumption that statistical power is proportional to higher moments of r.

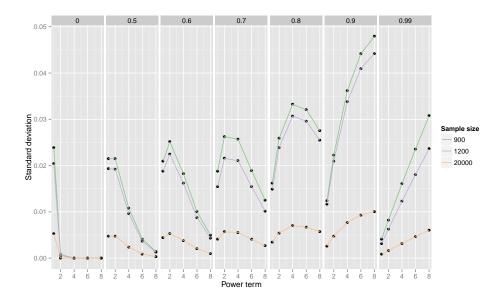


Figure S8: Sampling standard deviation for different power terms of population r values Power of detection and replication of epistatic interactions depends not on r^2 between causal variants and observed SNPs, but on r^4 , r^6 , r^8 . For a given a population value of LD r (columns of plots), plotted is the sampling standard deviation (y-axis) of \hat{r} , \hat{r}^2 (additive), \hat{r}^4 (dominance, A×A), \hat{r}^6 (A×D), \hat{r}^8 (D×D) (x-axis) for different sample sizes (coloured lines). As the power term of r increases the sampling variance also increases. Supposing that there is sufficiently high r^x in the discovery sample for detection of epistasis, the replication sample is less likely to have similarly high r^x as x increases, leading to an expectation of reduced replication rates.

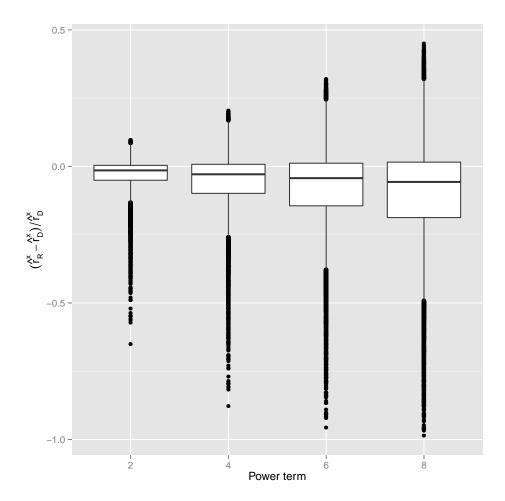


Figure S9: Reduction in LD as estimated in replication data after ascertaining for high LD in discovery data 100,000 "unobserved" causal variants (CVs) were tested for LD against a panel of 528,509 "observed" discovery markers (DMs). DM/CV pairs with LD $r^2 > 0.9$ were then tested in an independent sample. Simulation results of the proportional decrease between discovery and replication datasets in LD (y-axis) of $\hat{r}^2, \hat{r}^4, \hat{r}^6, \hat{r}^8$ (x-axis) are shown, where \hat{r}_D^x and \hat{r}_R^x are the sample LD measurements in the discovery and replication datasets, respectively. The average proportional decrease in the replication \hat{r}_R^x was 2.8%, 5.3%, 7.4% and 9.2% for x=2,4,6 and 8, respectively.

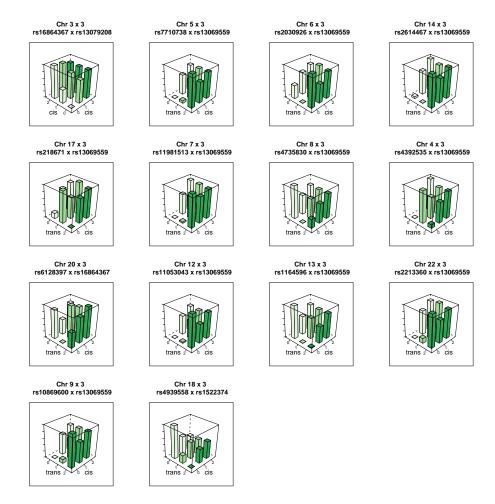


Figure S10: Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1 Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions the *cis* effect is masked when the *trans* SNP is homozygous for the masking allele.



Figure S11: 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 for the masking allele.

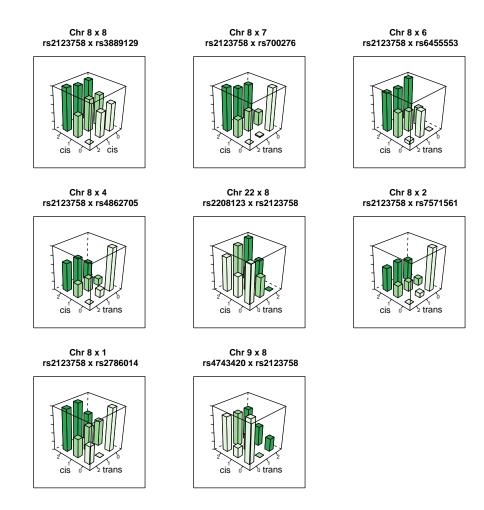


Figure S12: Genotype-phenotype maps for 8 interactions influencing the expression of NAPRT1 Each bar represents the mean phenotypic value for individuals in that genotype class.

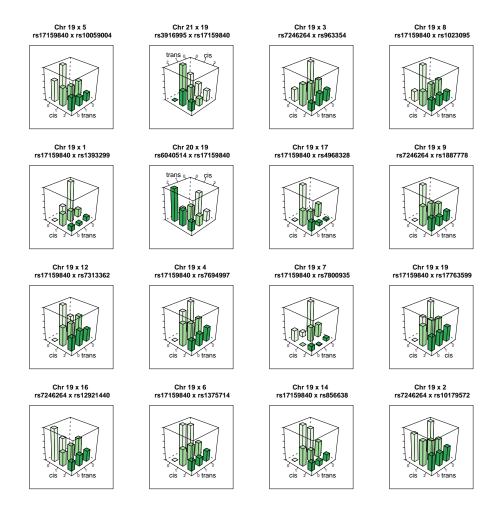


Figure S13: Genotype-phenotype maps for 16 interactions influencing the expression of TRAPPC5 Each bar represents the mean phenotypic value for individuals in that genotype class.

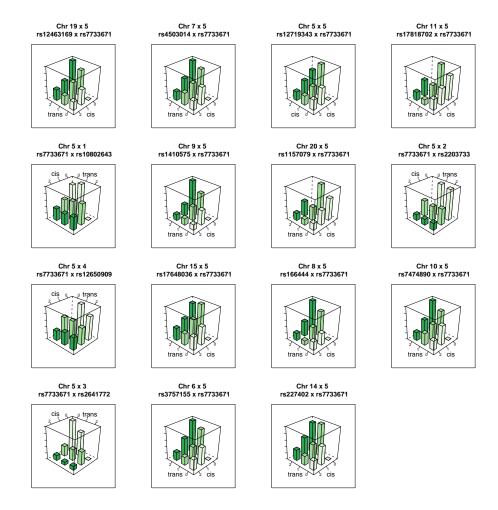


Figure S14: Genotype-phenotype maps for 15 interactions influencing the expression of CAST Each bar represents the mean phenotypic value for individuals in that genotype class.

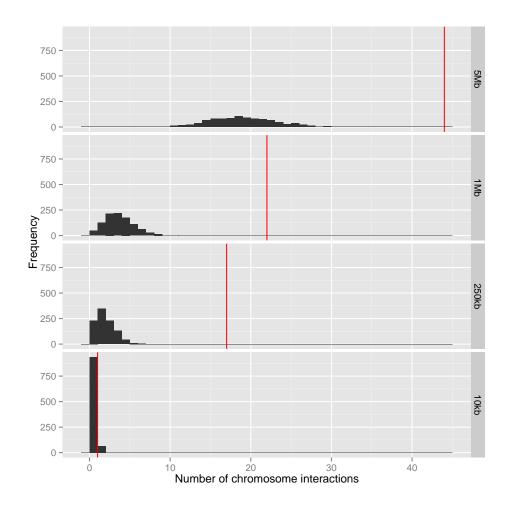


Figure S15: Number of overlaps between chromosome interactions and epistatic interactions Interacting chromosome regions may be a possible mechanism underlying epistatic interactions. The number of epistatic interactions within 20kb, 500kb, 2Mb and 10Mb of known chromosome interacting regions are shown by red vertical lines. The histograms represent the null distribution based on random sampling of 1,000 datasets for each window size.

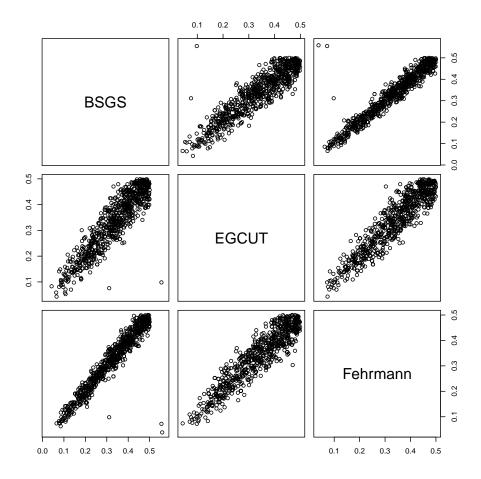


Figure S16: Comparison of allele frequencies for 781 SNPs involved in genetic interactions across independent populations Outliers were removed from the analysis as part of the filtering stage during replication.

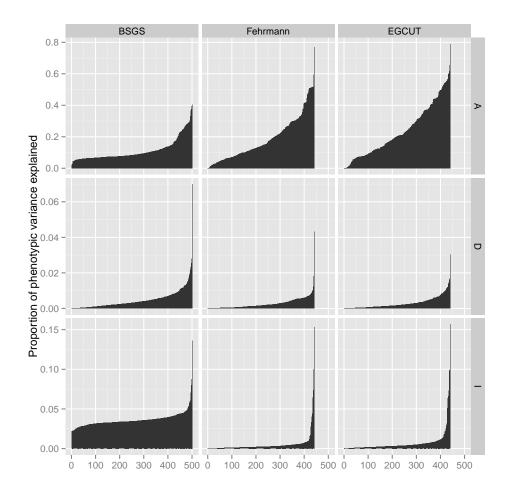


Figure S17: Comparison of variance explained by additive, dominant and epistatic effects from different cohorts How does the estimated variance decomposition change in different cohorts? The proportion of the phenotypic variance that is additive (A), dominant (D), or epistatic (I) for each putative interaction is shown on the y-axis (Note: different scales for each row). BSGS has 501 interactions whereas Fehrmann and EGCUT have 434 (x-axis). The variance estimates in each plot are ordered from lowest additive to highest. This is done independently for each cohort to depict the distribution of estimated effects.

Supplementary Tables

Table S1: Details on 501 interactions discovered in BSGS dataset

Probe ID D Other ID	rs ID rs3752237 rs3752237 rs9455 rs227664 rs12431896 rs8058066 rs8058066 rs2395095 rs23151512 rs10881585	Chr. 19	Pos/Mbc	Association		,		-					
		19		*****	rs ID	CITY:	Pos/Mbc	Association	BSGSe	Fehrmann ¹	EGCUT.	Metag	Distance / Mb
			1047161	ABCA7	rs596183	9	158100199		5.82	0.38^{1}	0.02^{1}	0.09j	
		1 5	1047161	ABCA7	rs914737	10	139522101		5.50	0		1	
		11	108207303	A DC CS	rs4/32202	- 0	72001517		6.10	1.02	1.01	0.83	
		14	7808813	ADCK1	rs4833241	0 4	122933691		2.20	0.36	1.14	0.87	
		16	88462550		rs12431896	14	78088813	ADCK1	6.58	2.04	0.83	2.05	
		10	76446305	ADK	rs10824092	10	75929517		69.9	18.33	21.21	39.82	0.517
		10	51515534	AGAP8	rs2547996	Ю	95174319		6.22				
	_	6	137112421		rs842647	2	61119471		7.15	1.83	1.93	2.88	
		9	29938258	HLA-G	rs1177303	2	61388355	AHSA2	5.45	0.92	0.64	0.94	
		16	57721127		rs13332406	16	53489705	AKTIP	6.91	0.16	0.99	0.57	4.231
	_	16	53536345	AKTIP	rs1362032	7	125543391		5.93	0.71	0.20	0.42	
		16	53536345	AKTIP	rs1473017	4	179323762		6.18	0.27	0.30	0.23	
	rs3760489	17	19581009	ALDH3A2	rs11720112	က	161996349		6.26	0.33	1.37	1.01	
	rs9322855	14	21153299	ANG	rs4866516	IJ	3032625		5.75	0.02	0.20	0.04	
	rs11073891	15	90363995	ANPEP	rs3823523	-	154511163		5.85	0.44	1.09	06.0	
ILMN_1763837 15	rs11073891	15	90363995	ANPEP	rs6846031	4	178019148		6.31	0.47	0.17	0.26	
ILMN_1768867 5	rs6453374	ю	77508159	AP3B1	rs4684443	က	4818792		5.94	0.05			
_		12	105580918	APPL2	rs2769594	6	87918528		5.60	0.80	1.02	1.16	
ILMN_3231952 17	rs12947580	17	75768225		rs8079215	17	44064851	ARL17B	5.96				31.703
ILMN_3231952 17	rs2834541	21	35932619		rs8079215	17	44064851	ARL17B	6.65				
ILMN_3231952 17	_	17	44064851	ARL17B	rs1950646	14	94722497		7.64				
ILMN_3231952 17	rs8079215	17	44064851	ARL17B	rs2197777	12	125831219		6.26				
ILMN_3231952 17	rs8079215	17	44064851	ARL17B	rs2684789	15	99492045		5.98				
	_	17	44064851	ARL17B	rs9834627	က	191203546		5.72				
	_	19	19810050		rs873870	19	19738554		5.30	12.18	3.25	14.23	0.071
	_	22	18213057	BID	rs9804943	12	129906275		5.84	90.0	0.40	0.14	
•••	_	22	18233000		rs10888267	-	248059423		09.9	0.87	0.16	0.20	
	_	11	8886260	C11ORF17	rs6553184	4	189150656		5.66	1.15	0.04	0.54	
	_	16	6259852	0	rs674754	13	46913416	C13ORF18	6.66	0.28	0.28	0.22	
	_	13	46913416	C13ORF18	rs6857876	4 ;	153610164		3.80	0.38	0.50	0.43	
	_	55	37575398		rs4983382	14	105189504	C140RF173	6.02	09.0	0.84	0.85	
	_	15	92276674	0.10	rs4983382	14	105189504	C14ORF173	10.08	0.31	0.28	0.24	
ILMIN_2393450 14	TS4900002	10	19810679	CI4ORF1/3	FSIU/54644	1.	77574400		7.10	0.47	0.34	0.33	
	_	14	77574438		rs10972462	* G	35427324		4.32				
	_	14	77574438		rs6445340	n	63371601		4.40				
ILMN_1804396 14	rs2655991	14	77574438		rs9787151	-1	63179138		4.05				
ILMN_1804396 14	rs4793445	17	70416307		rs2655991	14	77574438		3.85				
	_	22	51151724		rs2655991	14	77574438		4.61				
		61	52083552		rs2655991	41.	77574438	0	4.69	0	i c		
ILMIN_1/4/34/ 1/	rs9907897	17	110577053		rs/405659	1,	00000	CIORFO	0.0	0.03	0.00	91.0	
TI MAN 20027200	F82554525	0 9	10011201		FS223/102	٠,	2002300	CIORFOR	0.90	0.01	0.00	0.13	
0077200 NW:II	1044-04-4	16	25711258		18240002	-	2119833	CIOBES6	. r	06.0	0.00	0.37	
11.MN 1795836 21	_	2.5	48052838		rs901964	12	48676038	ZNF641	4 91	0.00	80.0	80.0	
	_	212	48027084		rs11701361	21	47764477		9.42	6.08	16.36	21.67	0.263
		18	45866512		rs286595	ı D	154348552	C5ORF4	5.55	0.72	0.04	0.27	
		13	36577930		rs2896452	00	86102223	CSORF59	5.49	0.29	0.02	0.07	
ILMN_1653205	8 rs12454561	18	31272238		rs2896452	œ	86102223	CSORF59	5.45	0.31			
	_	œ	86102223	CSORF59	rs1004564	4	55242625		7.62	0.38	0.18	0.21	
ILMN_1653205 8	rs7152284	14	52273663		rs2896452	œ	86102223	CSORF59	5.67	2.18	0.07	1.33	

	цq							6																							۲-					-												-
	Distance / Mb ^h							29.369																							14.697					15.781												
values	Metag	0.87	0.34		0.42	1 75		1.20	0.78	0.37	0.41	1.09	0.01		0.12	1.72	0.23	0.03	0.50	0.54	0.15	0.22	0.31	0.02	0.02	1.20	0.42	80.0	1.16	0.45	0.81				0.11	0.45	0.48	1.44	0.12	0.0	0.44	0.36	0.67	0.73		0.02	1.39	
$-\log_{10} p$ -values	\mathtt{EGCUT}^{f}	0.18	0.00		0.86	0.96		1.57	1.34	0.52	0.03	0.59	0.01		0.33	1.56	0.12	0.78	0.78	0.87	0.26	0.30	0.57	0.10	0.03	0.24	0.80	0.27	1.67	0.22	0.75				0.14	0.07	0.12	0.16	0.24	0.10	0.20	0.02	1.28	0.36	0.27	0.07	0.28	
Interaction statistic /	$Fehrmann^{f}$	1.39	0.94		0.09	0.23		0.36	0.13	0.27	0.97	1.15	0.11		0.07	0.92	0.49	0.75	0.23	0.22	0.19	0.26	0.00	0.23	0.08	1.74	0.13	0.04	0.24	0.71	0.64				0.21	0.95	0.90	2.16	0.15	07:0	0.72	0.92	0.07	0.95		0.07	1.92	0.0
Interactic	BSGS ^e F	5.79	6.36	5.81	6.61	7.07	7.00	7.68	6.55	7.01	7.81	6.62	6.12	6.87	7.24	5.88	6.74	7.42	7.42	6.07	6.93	0.4I	00.00	0.00	5.09	6.06	5.71	5.56	6.31	7.88	5.71	7.43	6.13	6.08	5.46	5.47	6.15	6.67	5.75	0 .0 0 .0 0 .0	5.74	4.75	5.55	7.54	5.55	7.56	6.33	
	Associationd	C8ORF59	CABCI		INPPSE	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST				E	CAT	CCDCssb	VAMPS	CD55						CD93				CDC16	CDK5R1	CEACAM21		0120474	ANALCIO	CHPT1		CLEC12A		CLTB			
SNP 2	Pos/Mb ^c	86102223	227174210	82128660	139266496	96000269	_	_	_	96000269		96000269	_			_	_	238120177	170192890	224093101		34447586	04125142	85816334	207502534	157182040	7992632	196721395	125145394		_	238899903	74439542	77264482	115008038		42066556	158943044	180265266	13424//00	102087844	81937002	10132283	134236688	175595960	63121080	67713633	10000010
SIS	Chr.	∞ -		1	6	υĸ	ı.c	10	ю	ю	ю	ю	ю	ю	ю	ю	ıo.	.,,	4.0	. 7 .	n -	1:	110	70	- 1	. 1	4	3		13	50	- · ·	, ,	17		1.7	19	0.4	4.0	00	10		12	10 1		16	13	,
	rs ID	rs2896452	rs3738725	rs684040	rs4077515	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs10802643	rs12650909	rs2203733	rs2641772	rs11032695	rs541207	rs1254900	rs6700168	rs10255470	rs4696726	rs7622580	rs838875	rs9576388	rs1884655	rs10925747	rs4328531	rs4789981	rs7324744	rs11655031	rs4803481	rs2421050	rs13132719	rs15079012	rs2695290	rs867578	rs7313235	rs3903088	rs6863172	rs169130	rs7336017	0000111
	Associationd	COORE72		INPP5E														CAST	CAST	CAST	CAST		0000000	T C C C C C C C C C C C C C C C C C C C		CD93	CD93	CD93	CD93	CD93		CD93	CD93	CD93		HOXB2		CEACAM21	CEFISZ	CES1	CEST					ABCA7	ABCA7	
SNP 1	Pos/Mb^{C}	7188323	4353908	139289825	6026661	17321669	81840122	125369113	78255630	78392770	27311111	86107920	70496867	15166804	136458593	31149140	59590078	96000269	96000269	96000269	96000269	1700000	64007333	80280117	76033374	23074375	23074375	23074375	23074375	23074375	37771578	23076914	23076914	23076914	104162263	46614102	51956250	42066556	13069782			102277782	84471642	10156646	96929337	1047161	1047161	1010011
S	Chr.	16	10	6	Ξ:	07-	16	10	6	œ	12	11	14	21	9	-	10	ı, n	ı, n	ລາ	0 0	0 0	S -	11	11	20	20	20	20	20	20	0.70	20	20	14	17	20	5.	× -	14	13	17	16	12	11	19	19	(
	rs ID	rs8051751	rs12765847	rs4266763	rs4573661	rs1157079	rs12599264	rs12719343	rs1410575	rs166444	rs17648036	rs17818702	rs227402	rs2822124	rs3757155	rs4503014	rs7474890	rs7733671	rs7733671	rs7733671	rs7733671	rs872311	rs2555205	rs3211834	rs750801	rs1884655	rs1884655	rs1884655	rs1884655	rs1884655	rs2868504	rs4813479	rs4813479	rs4813479	rs861544	rs9905940	rs200609	rs4803481	rs6505780	rs3825569	rs591967	rs6539014	rs429790	rs7305054	rs17129799	rs3752237	rs3752237	400001
	Chr.	o o	o	6	6	οıc	, rü	10	r0	r0	10	ю	r0	ю	10	ın.	ıņ i	ıo ı	ıo ı	o,	o :	1:	1:	11	-	20	20	20	20	20	50	0.00	20	20	13	17	19	10		o 1	15	17	12	12	r0	19	16	•
Expression trait	Probe ID ^b	ILMN_1653205	ILMN_1731064	ILMN_1712532	ILMN_1712532	ILMN-1717234 II.MN 1717234	ILMN_1717234	ILMN-1717234	ILMN_1717234	ILMN-1717234	ILMN-1717234	ILMN-1717234	ILMIN-1717234	ILMIN_1651705	ILMIN_1772208	II.MN 1784863	ILMN_1800540	ILMN_1704730	ILMN_1704730	ILMN_1704730	ILMN_1704730	ILMN_1704730	ILMN-1704730	ILMN-1704730	II.MN 1704730	ILMN_1704730	ILMN_2339796	ILMN_1730928	ILMN_1745949	ILMIN_1745949	ILMIN_1703754	ILMN-1787808	II.MN 2202940	ILMN_2202940	ILMN_1663142	ILMN_2403228	ILMN_1674609	ILMN_1770290	ILMN_1770290	TINGS TOTAL								
Exp	Gene ID ^a	CSORF59	CABC1	CARD9	CARD9	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CASI	CAI	10000000000000000000000000000000000000	CD36	CD55	CD93	CD93	CDC16	CDK5R1	CEACAM21	CEACAM21	CEFISZ	CEFES	CHPT1	CHPT1	CLEC12A	CLEC12A	CLTB	CNN2	CNNZ	ינוכנכ							

	Distance / Mb ^h			0.033			0.040						12.255																66,920	0.052																		10.736	0.23
alues	Metag	0.04	0.15	42.27	0.11	1.03	33.53	0.03	0.34	0.04	1.47	0.36	0.44	09.0	0.44	0.14	0.42	0.44	0.16	0.29	0.58	0.32	0.37	0.03	0.10	01	0.13	0.01	0.11	0.97	1.12	0.70	0.22	0.35	0.79	0.10	0.41	0.02	0.53	0.11	0.41		0.35	0.81	0.09	0.08	0.44	F	0.23
- log10 p-values	$EGCUT^{f}$	0.03	0.36	16.72	0.41	0.74	15.06	0.01	0.53	0.02	1.87	0.83	0.10	98.0	0.41	0.58	0.25	0.29	0.41	0.02	1.17	0.34	0.04	0.11	0.00	0.00	0.52	0.02	0.00	1.45	0.27	1.18	0.35	0.16	0.47	0.11	0.59	0.05	1.12	0.04	0.40		0.58	1.20	0.11	0.04	0.19	1.38	0.30
	Fehrmann ^f]	0.19	0.10	25.20	0.02	0.92	18.76	0.21	0.23	0.20	0.39	0.05	0.87	0.29	0.48	0.00	0.64	0.61	80.0	0.77	90.0	0.37	88.0	0.05	0.32	0.80	0.30	60:0	0.48	0.23	1.58	0.15	0.22	0.64	0.90	0.43	0.28	0.08	0.05	0.36	0.45		0.20	0.25	0.20	0.29	0.74	H -	0.27
Interaction statistic	BSGS ^e Fel	5.55	6.18	11.99	5.74	5.67 8.4	7.16	5.42	5.89	5.68	5.81	5.53	5.85	5.42	5.44	9.12	5.62	5.31	5.47	6.39	0.00	6.48	5.51	7.64	4.00	4. n	4.40	5.03	5.92	5.79	6.17	4.81	6.19	22.28	5.50	5.30 7.44	5.55	6.36	5.52	6.51	5.56	6.03	5.70	5.43	6.11	0.00	0.00	5.61	6.33
	Associationd	CPVL			CTNNA1	Carc		CWF19L1	CYBRD1	CYBRD1	CYBRD1	CYBRD1		CYP27A1	DAB2					COQ10A	DHRS9	DHRS9	DHRS9	L A SSE	LASSS	A O O A	LASSS		LASS5	DNAJB6	DPH3		ECHDC2	ECHDC2	EHD4	DIF 2D2				EMR2	EMR2		EPHX2	ERICH1	ERICH1	ERICHI	EXOC3	FAHD1	COQ10A
SNP 2	Pos/Mb ^c	29188475 46843631	62406408	45198355	138226767	108679892	88077479	102027407	172368120	172368120	172368120	172368120	160112881	219650616	39381357	82076988	187475208	32451144	88204888	137810259	169960422	169960422	169893419	169893419	153134888	50730458	61971140	115214154	51074199	157163614	16320360	64004670	53402552	53402552	42192040	0.0590540	49359676	129624067	126387391	14879034	14879034	102480759	27400604	578742	607161	5,000,000,000	428236	1972548	137810259
	Chr.	r c	ıю	21	10	10	11	10	7	7	61	61	7	73	10	9	က	6	7	6	7	01 (01 (2 5	1 17	- 61	1 oc	0 -	12	7	8	18		Η;	1.5 1.4	1.4	7 7	00	11	19	19	13	œ	∞	x 0 0	x0 =	# LC	16	6
	rs ID	rs245884 rs1531133	rs1473927	rs3761385	rs176382	rs7079264	rs556895	rs12784396	rs888427	rs888427	rs888427	rs888427	rs7591849	rs933994	rs835223	rs1343244	rs2378341	rs7042042	rs2519515	rs10120023	rs7566044	rs7566044	rs2161037	rs2161037	1811109322	rsz8/2008	rs1808634	rs4532958	rs12427378	rs3779589	rs1566972	rs4891884	rs11206043	rs11206043	rs1048166	rs1769096	rs1553474	rs2197210	rs4471434	rs9305048	rs9305048	rs3007765	rs13269963	rs12115088	rs4735900	rs12115088	rs12188164	rs344363	rs10120023
	Associationd		CRLS1		i E	CISC							CYBRD1				DDT		COQ10A						A 0.0 A	LASSS	LASSE	LASSE				ECGF1				FIFEA	EIF5A	EIF5A	EIF5A			EMR2				11171	PRICEI		
SNP 1	Pos/Mb ^c	39202070 188859908	5986234	45230974	69500505	26250645	88117962	11456027	129994690	140698856	12318284	23344590	172368120	36571928	110451383	43111688	24248761	125962645	137810259	106703727	89468283	147132505	29959453	187776431	50636364	71711815	50730458	50744171	117994348	157216093	93409054	50971266	241911027	17675900	53244938	70212034	7221707	7221707	7221707	23196249	18761714	14879034	127909396	134611176	45337329	31187910	55228462	12708208	129591144
01	Chr.	21	20	21	18	116	11	11	4	6	10	20	73	20	7	17	22	11	6	11	12	2	21	4 1	13	7 0	12	2 5	12	1	15	22	7	55	19	1 0	17	17	17	21	20	19	11	11	5 5	× 0	° 0	16	12
	rs ID	rs2835998	rs6139887	rs9979356	rs924943	rs2457684	rs7930237	rs7108734	rs2592948	rs7852475	rs11257679	rs6137908	rs888427	rs6021982	rs7778910	rs9900173	rs5760102	rs4937097	rs10120023	rs12363827	rs1519956	rs1528529	rs2831914	rs7661304	rs11160325	rsillosco	rs7134595	rs7312252	rs871257	rs2286842	rs12232308	rs140522	rs4234091	rs5992637	rs10403312	rs030724	rs7216490	rs7216490	rs7216490	rs2827076	rs6132112	rs9305048	rs1107764	rs10894861	rs5766218	rs/20145	rs4755855 rs187076	rs1560104	rs12580388
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Expression trait	Probe ID ^b	ILMN_1682928 ILMN_1813256	ILMN_1737685	ILMN_1761797	ILMN_1804854	ILMN-1696347	ILMN_2242463	ILMN_1651886	ILMN_1712305	ILMN_1712305	ILMN_2087692	ILMN_2087692	ILMN_2087692	ILMN_1704985	ILMN_2128428	ILMN_1811648	ILMN_1690982	ILMN_1797001	ILMN_1783996	ILMN_1783996	ILMN_1733998	ILMN_1733998	ILMN_2384181	ILMN-2384181	ILMIN-1755559	ILMIN_1755559	ILMN 1755589	II.MN 1755589	ILMN_1755589	ILMN_1793770	ILMN_2349610	ILMN_2109708	ILMN_1671568	ILMN_1671568	ILMIN_1720083	ILMN 1794599	ILMN 1794522	ILMN_1794522	ILMN_1794522	ILMN_2353633	ILMN_2353633	ILMN_2353633	ILMN_1709237	ILMN_1731001	ILMN_1731001	ILMIN-1731001	ILMN 1789419	ILMN_2246661	ILMN_1668063
Ex	Gene IDa	CPVL	CRLS1	CSTB	CTNNA1	CIRC	CISC	CWF19L1	CYBRD1	CYBRD1	CYBRD1	CYBRD1	CYBRD1	CYP27A1	DAB2	DCAKD	DDT	DDX58	DEM1	DEM1	DHRS9	DHRS9	DHRS9	DHRS9	DIFZE	DIFZB	DIP2B	DIP2B	DIP2B	DNAJB6	DPH3	ECGF1	ECHDC2	ECHDC2	EHD4	EIF 2D2	EIF5A	EIF5A	EIF5A	EMR2	EMR2	EMR2	EPHX2	ERICH1	ERICHI	ERICHI	EXOCA	FAHD1	FCN1

313.001546 2 36701326 FEEZZ 6.78 0.14 0.33 0.16 313.001546 6 3 36701326 FEEZZ 6.78 0.14 0.23 0.16 313.001546 6 3 3670132 FEEZZ 6.58 0.14 0.23 0.11 313.001546 6 5 3670132 FEEZZ 6.59 0.13 0.02 0.01 313.001546 6 1000561 FLIZOMAS 6.54 0.01 0.02 0.01 315.00252 FLIZOMAS 6.44 0.03 0.01 0.02 0.01 315.0025 FLIZOMAS 6.44 0.03 0.04 0.03 0.04 315.0025 FLIZOMAS 6.44 0.03 0.04 0.03 0.04 315.0025 FLIZOMAS FLIZOMAS 6.44 0.03 0.04 0.03 0.04 315.0025 FLIZOMAS 6.44 0.03 0.04 0.03 0.04 0.03 315.0025 FLIZOMAS 6.44 0.03 0.04 0.03	SNP 1 Pos/Mb ^c
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Expression trait Probe ID ^b Chr.	Chr.	\vdash	rs ID	Chr.	SNP 1 Pos/Mb ^c	Associationd	rs ID	Chr.	SNP 2 Pos/Mb ^c	Associationd	Interact	Interaction statistic /	$-\log_{10} p$ -values	values Metag	Distance / Mbh
CIII. IS ID CIII. FOS/MD	IS ID CITIC LOS/MD	The contract of the contract o	FOS/MID		1	Association	15 11		r Os/ MID	Tipos		Lemmann	10051	Meta	Distance / MD
LLMIN_2084825 11 rs12975066 19 35723501 ILMN_2084825 11 rs2855039 11 5271671 HB	19 35723501	19 35723501	35723501 5271671		Н	HBG2	rs2855039	11	5271671 213088494	HBG2 LOK1	5.77	80.0 0.0 0.0	0.13	0.05	
11 rs2855039 11 5271671	rs2855039 11 5271671	11 5271671	5271671		HBG	1 21	rs12503379	4	141533832		5.98	0.00	0.46	0.10	
ILMN-3266186 12 rs2109029 16 6036851	rs2109029 16 6036851	16 6036851	6036851		1001	-	rs4760636	12	48173352	HDAC7	5.75 0.75	5	G H	0	
17 rs1942719 18 71237270	rs1942719 18 71237270	12 13143613	71237270		D D		rs7213057	17	80378939	HEXDC	5.81	1.61	0.34	1.22	
6 rs4899635	rs4899635 14	14		77532672			rs7192	9	32411646	HLA-DRB6	5.94	0.90	0.16	0.52	
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8 rs2837803 21	rs2837803 21	21		42112794			rs4732890	000	28751381	HMBOX1	6.62	0.05	1.01	0.46	
8 rs4765451 12 1	rs4765451 12 1	12 1	_	127237464			rs8180944	œ	28904086	HMBOX1	5.80	0.39	3.13	2.52	
8 rs587639 8 132725731	8 132725731	8 132725731	132725731				rs7837237	oo i	28876221	HMBOX1	6.58	0.55	0.34	0.44	103.850
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5 rs6894268 5 1	52	52	. –	179032488			rs4700810	'n	178991794		15.38	8.55	3.01	10.37	0.041
1 rs555812 16	16	16		88882257			rs4654783	1	22439520	HSPC157	5.51				
1 rs6063164 20	20	20		46486900			rs4654783	-1	22439520	HSPC157	6.51				
1 rs662739 12 121229893	12 121229893	12 121229893	121229893		(rs4654783		22439520	HSPC157	6.61				
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9 rs8044524 16 8	rs8044524 16 8	4 16 8	00	81603771			rs1127152	6	139335599	INPP5E	5.58	1.46	0.84	1.55	
7 rs757355 12 47970693	rs757355 12 47970693	12 47970693	47970693				rs849341	-1	28288174		8.16	0.02	0.26	0.05	
21 rs2186344 21 39606769	rs2186344 21 39606769	21 39606769	39606769		X	KCNJ15	rs424299	11	5570771		5.64	0.65	0.13	0.33	
19 rs649216 19 55324635	rs649216 19 55324635	19 55324635	55324635		Σ,	KIR2DL1	rs6419960	4 0	189055298	.0	4.74	0.46	0.89	0.77	
1LMN-1811104 3 rs4349034 13 84597119	rs4349034 13	13	-	84597119			rs727905	n m	119119433	KTELCI	5.53 8.53	0.08	08.0	0.37	
22 rs4822006 22 41519362	rs4822006 22 41519362	22 41519362	41519362		Н	L3MBTL2	rs1294338	·	233438952	IVI EFFO	80.10	0.33	0.04	0.00	
4 rs7042087 9	9	9	_	132602868			rs7658240	4	17588950	LAP3	5.72	0.24	0.47	0.31	
1 rs1891432 1 2			CI	203877662			rs10900520		203780591		19.16	18.60	11.22	29.24	0.097
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19 rs3859532 19	rs3859532 19	19		54827248		LILRAS	rs714789	18	71561497		6.13	0.23	0.03	0.02	
15 rs11247226 15 1	rs11247226 15 1	15 1	1	101120963		LINS1	rs1278387	10	127804531		5.89		0.13		
19 rs6009951 22 5	rs6009951 22	1 22		51151350			rs8101804	19	18496107	LRRC25	5.68	0.11	0.35	0.15	
6 rs977785 6	rs977785 6	9		6588881		LY86	rs1543675	I	78946879		5.61	0.13	0.15	0.07	
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12 EST/1820 10 (72/0904 19 rs9168099 19 69734641	EST(1020 10 (1210904 12 co.2168090 12 60734641	19 69734641	69734641			1.7.2	rs2105029	7 0	130319560	717	6.71	0.43	0.03	0.10	
7 187783715 7	rs7783715 7	1 1-	,	1923385		MADILI	rs6414306	. m	127011798		5.62	0.25	0.88	0.59	
6 rs7983718 13 1	rs7983718 13	13		103203146			rs1096699	9	43528441	MAD2L1BP	5.93	0.63	1.11	1.09	
20 rs974607 21	rs974607 21	21	•	29435869			rs6060034	20	33351864	MAP1LC3A	5.78	1.18			
3 rs10869600 9 7	rs10869600 9	6		78225815			rs13069559	က	152187431	MBNL1	7.96	0.79	0.27	0.54	
3 rs11053043 12	3 12	3 12		9932070			rs13069559	က	152187431	MBNL1	6.70	0.08	2.21	1.37	
3 rs1164596 13	rs1164596 13	13		97100681			rs13069559	က	152187431	MBNL1	7.38	1.43	0.63	1.34	
3 rs11981513 7	rs11981513 7	7	7 94648239	94648239			rs13069559	က	152187431	MBNL1	7.71	0.43	5.36	4.58	
3 rs16864367 3 1	rs16864367 3 1	. 3	3 152234166	152234166			rs13079208	က	152116652		13.49	16.25	24.74	41.56	0.118
3 rs2030926 6 11	rs2030926 6 11	6 11	11	114067127			rs13069559	က	152187431	MBNL1	7.10	0.91	5.80	5.53	
3 rs218671 17	17	17		6604708			rs13069559	က	152187431	MBNL1	7.63	0.62	5.82	5.23	
ILMN_2313158 3 rs2213360 22 34291750 ILMN_2313158 3 rc2305802 10 16038535	252	252		34291750			rs13069559	ကက	152187431	MBNL1 MBNL1	6.05	0.52	0.72	0.70	
3 rs2614467 14	14	14		99770138			rs13069559	ာက	152187431	MBNL1	5.74	4.13	2.22	5.30	
										•				Continu	Continued on next page

	Distance / Mb ^h											0.015																		10 401	13.431			38.948				0.050									0.010				
alues	Metag	L	3.38	0.07	1.73	9.28	0.02	0.05	0.27	0.26	0.14	28.73	1.71	0.41	0.14	0.50	0.02	0.02	0.40	0.04	1.35	0.19		0.22	0.64	0.46	0.28	2.86	0.50	0.23	0.00	0.43	0.02	1.77	0.04	0.30	0.18	30.77	0.81	1.01	2.5	0.23	0.03	0.00	1.12	1.71	12.70	0.22	0.35	90.0	
- log10 p-values	$\mathtt{EGCUT}^{\mathrm{f}}$	4.33	4.21	0.27	1.15	7.89	0.03	0.23	0.76	0.50	0.47	21.91	1.33	0.25	0.30	1.03	0.12	80.0	0.27	0.23	1.08	0.18		0.44	0.70	0.63	0.25	1.87	0.52	0.50	0.92	0.40	0.00	0.59	0.03	0.43	0.48	16.08	0.19	0.76	2.58	0.47	0.00	0.10	1.10	0.44	6.33	0.18	0.34	0.04	
\mathbb{L}	Fehrmann ^f 1	0.02	0.32	0.03	1.34	2.55	0.10	0.03	0.02	0.15	0.03	7.06	1.13	0.61	0.13	0.07	0.11	0.02	0.57	0.01	0.97	0.34	0.26	0.14	0.46	0.31	0.41	1.87	0.46	0.11	0.29	0.13	0.04	2,00	0.20	0.27	0.07	15.12	1.27	0.87	1.10	0.13	0.13	21.0	0.67	2.11	7.51	0.39	0.42	0.24	
Interaction statistic	BSGS ^e Fe		6.74	7.72	7.22	7.92	6.26	5.56	5.79	6.03	5.82	5.40	4.63	5.76	5.81	5.57	7.05	4.17	5.45	5.90	5.64	6.89	5.71	6.56	7.48	6.85	6.21	5.18	6.31	0.00 10.00 10.00	0 10 10 10 10 10 10 10 10 10 10 10 10 10	0.00 70	07.0	25.55	5.65	5.46	80.9	8.45	5.62	6.12	0.80	6.03	0.00 70 10	. n	0 10	0 10	7.31	3.88	6.84	5.90	5.45
	Association	MBNL1	MBNL1			MBNL1	MBP	MBP			MBP		MEGF9	MFN2		MGC13057	MGC13057		MGST3		MPZL2	MRPL36	MRPL43	MRPL52	MRPS10	MRPS10	MRPS10				0000000	MYDDCS	MIDIO	N4BP1	NAAA	NAAA						1000	NAFRII	T THE TOTAL				NDUFA12		NOD2	NRBF2 NRBF2
SNP 2	Pos/Mb^{C}	152187431	152187431	152235530	152234166	152187431	74715653	74715653	155204939	55097534	74715653	74732087	123453281	12050634	171860973	50428445	50428445	137526799	165600146	154708716	118076069	1782046	102746503		42194916	42158596	42164401	42068689	95514596	26706382	29363604	4 7 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	134485237	48632478	76870229	76870229	234897243	144613680	187445552	167811764	146189057	213386267	144003001	08301111	95976932	234721287	232291471	95386791	183114008	50719103	65133822 65133822
	Chr.	8	က	က	က	က	18	18	n	r0	18	18	6	1	4	7	4	œ	-1	-	11	ro.	10	14	9	9	9 ;	14	14	ω .	7 -	1.	- ×	16	4	4	1	00	4	9 1	- 0	21 0	0 o	0 0	10	2 2	61	12	8	16	10
	rs ID	rs13069559	rs13069559	rs1522374	rs16864367	rs13069559	rs2051344	rs2051344	rs1125539	rs2619046	rs2051344	rs4890876	rs966396	rs4846085	rs11725347	rs12718598	rs12718598	rs2660665	rs4147592	rs11771552	rs1805	rs750495	rs2863095	rs3811188	rs722269	rs2395803	rs13217993	rs12431444	rs11160227	rs4973801	rs8130120	rs151/149	re9737499	rs11649236	rs6826085	rs6826085	rs2786014	rs3889129	rs4862705	rs645553	rs/00276	rs/5/1561	182123130	201020303	rs10882406	rs7577137	rs4973397	rs11107847	rs12490878	rs9302752	rs7923609 rs7923609
	Associationd								MBP	MBP					MGC13057			MGC72104		MPZL2								MTMR10					MVOWI				NAPRT1	NAPRT1	NAPRTI	NAPRI	NAPKII	NAPKII		NADGB	NAPSB	NAPSB			NMT2		
SNP 1	Pos/Mb^{c}	41513423	895841	46278591	57253132	22101322	15462611	42210985	74715653	74715653	33436367	74747424	51922071	109401737	50428445	69070772	82628245	26197931	55779644	118076069	19953193	8436432	80641040	26710271	110202230	15063214	52453567	31215935	42795027	42795027	61503110	100550551	3247256	87580855	147638723	37770630	144663661	144663661	144663661	144663661	144663661	144663661	102788080	5088989	50882619	50882619	232301670	37101890	15239498	7067773	5209048 69876894
S	Chr.	4	œ	18	20	Ю	20	22	18	18	19	18	20	13	-1	18	16	20	17	11	12	10	16	14	00	20	91	12	77	5 5	77 -	10	2 0	16	-1	22	œ	00	00 (x 0 (x0 0	000	4 0		61	161	61	22	10	19	11
	rs ID	rs4392535	rs4735830	rs4939558	rs6128397	rs7710738	rs6079849	rs139568	rs2051344	rs2051344	rs4805021	rs8092433	rs13039689	rs7989895	rs12718598	rs674608	rs8058318	rs845787	rs740441	rs1805	rs7316716	rs17469061	rs6564769	rs1950857	rs10955512	rs11698155	rs1420537	rs7178375	rs459498	rs459498	rs459498	"57255766	rs4798075	rs12444224	rs2707575	rs2071856	rs2123758	rs2123758	rs2123758	rs2123758	rs2123758	rs2123758	rs4200123	154143420 161405655	rs1405655	rs1405655	rs7563453	rs2746971	rs10906857	rs2967636	rs11063498 rs2375269
	Chr.	3	e	ო	က	33	18	18	18	18	18	18	6		61	61	73	20		11	11	r0	10	14	9	9	9 !	15	77	27	7 -	1.	3 2	16	4	4	œ	00	00 (x 0 (x0 0	x0 0	0 a	0 0	61	61	61	12	10	16	10
Expression trait	Probe ID ^b	ILMN_2313158	ILMN_2313158	ILMN_2313158	ILMN_2313158	ILMN_2313158	ILMN_2331544	ILMN_2398939	ILMN_2398939	ILMN_2398939	ILMN_2398939	ILMN_2398939	ILMN_2290118	ILMN_1651385	ILMN_1787526	ILMN_1787526	ILMN_1787526	ILMN-1688318	ILMN_1751956	ILMN_1752932	ILMN_1752932	ILMN_1800197	ILMN_2258774	ILMN_1713966	ILMN_1663664	ILMN_1663664	ILMN_1663664	ILMN_2152178	ILMN_1662358	ILMN_1662358	ILMIN_1602358	ILMIN-1/01104	II.MN 1680344	ILMN_2201966	ILMN_1668605	ILMN_2391512	ILMN_1710752	ILMN_1710752	ILMN_1710752	ILMN_1710752	ILMN-1710752	ILMN-1710752	ILMIN-1710752	II MN 1784040	ILMN 2109416	ILMN_2109416	ILMN_2121437	ILMN_1737738	ILMN_1656378	ILMN_1762594	ILMN_3237385 ILMN_3237385
Exi	Gene ID ^a	MBNL1	MBNL1	MBNL1	MBNL1	MBNL1	MBP	MBP	MBP	MBP	MBP	MBP	MEGF9	MFN2	MGC13057	MGC13057	MGC13057	MGC72104	MGST3	MPZL2	MPZL2	MRPL36	MRPL43	MRPL52	MRPS10	MRPS10	MRPS10	MTMR15	MXI	MXI	MAI	MYDDCS	MYOMI	N4BP1	NAAA	NAAA	NAPRT1	NAPRT1	NAPRTI	NAPRII	NAPRII	NAPRII	NAPPTI	NADGA	NAPSB	NAPSB	NCL	NDUFA12	NMT2	NOD2	NRBF2 NRBF2

Ex	Expression trait				SNP 1				SNP 2		Interacti	Interaction statistic /	- log10 p-values	values	
Gene IDa	Probe ID ^b	Chr.	rs ID	Chr.	Pos/Mb ^c	Associationd	rs ID	Chr.	Pos/Mb ^c	Associationd	BSGS _e	Fehrmann ^f	$EGCUT^{f}$	Metag	Distance / Mb ^h
NRBF2 NRBF2	ILMN_3237385 ILMN 3237385	10	rs6025645	20	56157341		rs7923609	10	65133822	NRBF2 NRBF2	5.45				
NRD1	ILMN_1800897	1	rs4852124	- 61	240680022		rs6588415	1	52334047	MILLE	6.13	0.47	0.02	0.17	
NUDT18	ILMN_1787885	œ	rs5017351	11	25453482		rs1005901	œ	21964378	NUDT18	5.44	0.03	0.46	0.15	
OAS1	ILMN_1658247	12	rs11613438	12	113480510		rs1047944	9	163997467		8.59	1.27	1.55	2.03	
OASI	ILMN_1658247	7 7	rs13311	7 7	113448652		rs2072133	7 7	113409260	200	4.13	4.12	0.81	3.86	0.039
OPTN	ILMN 2381899	101	rs7192613	16	74286646		rs17512962	7 0	13169066	OPTN	5.64	0.42	0.06	0.10	
OSBPL5	ILMN_2307032	11	rs2829679	21	26662543		rs998639	11	3149249	OSBPL5	5.00	0.36	0.00	0.07	
OSTF1	ILMN_1742456	6	rs17780195	17	70624189		rs2273770	6	77755469	OSTF1	5.42	0.16	0.87	0.49	
OSTF1	ILMN_1742456	6	rs2273770	6	77755469	OSTF1	rs7718088	10	179590952		5.42	1.20	80.0	0.62	
OVGP1	ILMN_1734542		rs10802822	-	240132968		rs1264898		111992823	OVGP1	5.43	0.13	1.48	0.88	128.140
OVGP1	ILMN_1734542	⊣ 1	rs347331	က၊	140148107		rs1264894	٠,	111969719	OVGP1	6.04	0.25	1.21	0.82	
PAM	ILMN-2313901	οĸ	rs28092	οĸ	102149795	PAM	rs784600	- 6	2139553	HPCAL4	5.59	0.66	0.44	0.59	
PEX5	ILMN_1660232	12	rs10444467	17	128052636		rs4329748	17	7364442	PEX5	0.00	0.09	0.71	0.32	120,688
PEX5	ILMN_1660232	12	rs7495797	12	27246462		rs4329748	12	7364442	PEX5	5.74	0.34	0.00	0.13	
PFAAP5	ILMN_1797893	13	rs131969	22	49151303		rs7328733	13	33126737	PFAAP5	5.64	0.87	0.36	0.67	
PGLYRP1	ILMN_1704870	19	rs12982353	19	46529456	PGLYRP1	rs1263806	14	21982957		6.51	0.03	0.65	0.24	
PHCA	ILMN_1812552	11	rs493642	11	123097386		rs10736812	11	76708086	PHCA	5.51	0.36	0.90	0.70	46.389
PIK3IP1	ILMN_1719986	55	rs4141404	55	31675185	PIK3IP1	rs2065841	;	61728597		5.60	0.20	0.01	0.03	
PISD	ILMN-1793934	55	rs470072	7.7	32263131	PISD	rs10498313	14	30398876		5.23	0.02	0.87	0.33	
PISD	ILMN_1793934	55	rs6518752	7.7.5	31999127	PISD	rs954627	- 0	18236681	400	7.11	0.00	1.19	84.0	
PISD	ILMN_1793934	7.7	rs715572	77.	33234931		rs6518754	77 0	32097775	PISD	4.12	0.05	0.42	0.15	1.137
PNRD	ILMIN_1/4504	N C	rs0809411	o 1	158/81604		rs4012004	NI C	140467106	PINED PINED A7	0.50 0.50 0.50	0.10	0.04	0.04	
PPFIRD2	ILMN 1675656	n =	rs011019	30	432/109		rs4758001	. .	7559930	PDFIRDS	0.10	0.01	0.70	0.00	
PPP9R3C	II.MN 1662617	17	re12914603	4 -	58350896		re11156875	14	35619816	PPP9R3C	+ - x	0.13	0.00	07:0	
PPP2R5A	ILMN 1738784	<u> </u>	rs10930170	27 67	166399467		rs12120009		212447167	PPP2R5A	5.63	0.72	0.48	0.66	
PPP2R5A	ILMN_1738784	-	rs12423255	12	123595064		rs12120009	-	212447167	PPP2R5A	5.72	0.08	0.95	0.46	
PPP2R5A	ILMN_1738784	1	rs1889083	13	66222691		rs12120009	Т	212447167	PPP2R5A	5.61	0.36	0.13	0.17	
PPP2R5A	ILMN_1738784	1	rs682334	11	107417238		rs12120009		212447167	PPP2R5A	5.65	1.69	0.28	1.21	
PPP2R5A	ILMN-1738784	1	rs7757871	9	135030045		rs12120009		212447167	PPP2R5A	5.95	0.37	90.0	0.12	
PPP2R5A	ILMN_1738784	- ;	rs7871178	6	27148475		rs12120009	;	212447167	PPP2R5A	5.72	0.16	0.30	0.16	
PRDX5	ILMN-1711606	Ι.	rs8019823	14	95040482		rs11600990		64082807	PRDX5	6.43	0.81	0.14	0.44	
PRKCBI	ILMIN_1713603	16	rs2188355	16	23867776	10000	rs10492793	16	12639800		7.34	0.53	0.11	0.25	11.228
PRMT2	ILMN 1675038	21.	rs2839372	21	48063862	CTIONE OF	rs11701058	21	47776382	C21ORF57	6.87	0.69	4.47	4.06	0.287
PSMB1	ILMN_1789176	9	rs3862607	11	121774705		rs13207114	9	170877444	PSMB1	5.79		0.44		
PSMB1	ILMN_1789176	9	rs4890648	18	43983954		rs6928843	9	170890384	PSMB1	5.14	0.00	0.26	0.04	
PSMB1	ILMN_1789176	9	rs6060930	50	30347832		rs9295415	9	170823379	PSMB1	5.44	0.44	0.21	0.27	
PSMB1	ILMN_1789176	9	rs6928843	9	170890384	PSMB1	rs2769689		225797957		4.58	1.95	0.64	1.78	
PSMB1	ILMN_1789176	9 9	rs7299749	15	131727816		rs13207114	9 ;	170877444	PSMB1	5.42	1.18	0.32	0.86	
PWP1	ILMN_1743049	12	rs2353567	14	95478823		rs11036212	Ξ;	5221825	PTDSS1	5.00	0.03	0.48	0.15	
PWP1	ILMN-1743049	7 7	rs4969205	17	76598123		rs11036212	11	5221825	PTDSSI	5.90	0.80	0.08	85.0	
1 W 7 I	ILMN 1679443	7 7	18031302	1 9	106348946		re10000212		17596689	ODDB	7 C	0.02		 	
RABSIP	ILMN 1803197	13	rs241730	2.5	33375704		rs7305307	15	70235726	11 17		0.25	80.0	50.0	
RABAC1	ILMN_2207363	13	rs1075728	19	42462788	RABAC1	rs7951628	11	120161117		6.42	0.28	0.84	0.59	
RBL2	ILMN_1756999	16	rs9931702	16	53526551	AKTIP	rs1863464	15	26938488		6.38	0.03	0.31	0.08	
RCN1	ILMN_1800276	11	rs10879131	12	41147155		rs4922579	11	32136436	RCN1	5.23	0.58	0.37	0.47	
RCN1	ILMN_1800276	11	rs4922579	11	32136436	RCN1	rs11166957	∞ -	141177468		4.32	0.41	0.09	0.17	
1				:				4					1	Continu	Continued on next page

Table S1 - continued from previous page

Exp	Expression trait				SNP 1				SNP 2		Interac	Interaction statistic /	$-\log_{10} p$ -values	ralues	
Gene ID ^a	Probe ID ^b	Chr.	rs ID	Chr.	Pos/Mb^{c}	Associationd	rs ID	Chr.	Pos/Mb^{c}	Associationd	BSGSe	Fehrmann ^f	$\mathtt{EGCUT}^{\mathrm{f}}$	Metag	Distance / Mb ^h
RERE	ILMN_1802380	1	rs4982958	14	24987865		rs301819	-1	8501786	RERE	5.66	0.61	1.23	1.17	
RERE	ILMN_1802380		rs7697290	4.	135248366		rs301819	·	8501786	RERE	5.74	0.14	0.10	0.06	
KEKE	ILMIN-2327795		rs11085829	61	113874312		rs301819		8501786	7,57,57 7,07,0 7,07,0	5.12	0.21	0.33	0.21	
RNASE6	ILMN 1780533	141	rs11628398	. 4	21182800	BNASE6	rs7324365	- 2	100601327	TOTAL	4 4 5	0.08	0.21	0.26	
RNASE6	ILMN_1780533	14	rs6603134	19	8106521		rs11628398	14	21182800	RN ASE6	5.11	60.0	0.22	0.08	
RNF167	ILMN_1794726	17	rs238230	17	4875566		rs4884857	13	54668512		4.37				
RNF167	ILMN_1794726	17	rs400688	17	4839930	RNF167	rs11706900	က	36348968		5.59	0.71	0.46	0.64	
RNPEP	ILMN_1738347	1	rs1107121	21	46127549		rs2819365	1	201983242		6.27	0.11	0.30	0.13	
RNPEP	ILMN_1738347	1	rs8071611	17	67153386		rs2819365	1	201983242		4.32	1.48	0.52	1.28	
RPL13	ILMN_2413278	16	rs352935	16	89648580		rs2965817	16	89513234		4.98	3.79	14.41	17.24	0.135
RPL23AP7	ILMN_22222750	61	rs1401202	16	80320056		rs4849261	73	114450028	RPL23AP7	5.55	0.13	0.73	0.38	
RPL36AL	ILMN_2189933	14	rs3007033	14	50103816	RPL36AL	rs17495030	6	138038093		5.46	0.09	90.0	0.02	
RPL36AL	ILMN_2189936	14	rs4900928	14	50020817	RPL36AL	rs1502991	9	66137260		5.86	0.32	0.20	0.19	
RPL8	ILMN_1764721	∞ ∞	rs2958482	œ	145984615	RPL8	rs1619856	1	234585790		4.59	0.10	0.37	0.15	
RPL8	ILMN-1764721	œ	rs4143674	20	4741304		rs2958482	œ	145984615	RPL8	4.33	0.13	0.45	0.22	
SEC13	ILMN-3297880	8	rs4889214	16	80913946		rs696221	3	10342876	SEC13	6.48				
SEMA4A	ILMN_1702787	-	rs17085428	n	95388015		rs7695	1	156147326	SEMA4A	5.70	0.22	1.73	1.17	
SESN3	ILMN_1694027	111	rs12147460	14	104412137		rs684856	11	94906111	SESN3	5.50	0.02	0.51	0.15	
SESN3	ILMN_1694027	11	rs355391	15	46591793		rs684856	11	94906111	SESN3	5.67	0.31	90.0	0.10	
SESN3	ILMN_1694027	11	rs684856	11	94906111	NENN3	rs7004947	00	134606425		5.60	0.21	0.51	0.31	
SH3BGRL2	ILMN_1762764	9 0	rs10838191	Ξ,	43893658		rs1354034	က	56849749	PPBP	5.52	0.70	0.12	0.35	
SHSBGRL2	ILMN_1762764	9	rs2545385	٠.	66383979		rs1354034	n	56849749	PPBP	5.97	0.20	0.51	0.30	
SHSBGRLZ	ILMIN_1762764	۰ ۵	rsb845304	4.0	88280502		rs1354034	n	56849749	PFBF	5.23	0.32	0.71	0.53	
SH3GLB2	ILMIN_2158336	5 6	rs1034120	17.0	18196922	Segre	rsI/4555I/	D 4	131785369	SH3GLB2	7.40	0.22	0.18	0.13	
01 A 20 A 10	ILMIN-LITTOUT	0 -	181000000	07	1012013	PIRE	150042139 1196709E	* :	01060#00	OT 600 10	H C.	00.0	0.10	100	
SLC22A18	ILMIN-2382505	1 :	rs116/3260	E -	2023826	ST.C22 A 18	rs56/055	11	153224179	SUCZZAIS	0.4 70.7	0.09	0.24	0.00	
SI.C22A18	II.MN 2382505		re367035	1:	2023826	ST.C22A18	rs3772054	۰.	241678528			0.39	0.10	00:0	
SLC41A3	ILMN_2356111	-	rs1912136	11	24616743		rs6771703	1 00	125801067	SLC41A3	8 8 8	1.10	0.82	1.24	
SLC45A4	ILMN_1745778	00	rs6985508	œ	142337734	SLC45A4	rs7701916	n	174598073		5.95	0.86	0.07	0.40	
SLC46A3	ILMN_1658639	13	rs949805	17	55602091		rs7981190	13	29259349	SLC46A3	5.52	0.09	0.58	0.26	
SMG7	ILMN_1706553	-	rs8035259	15	97403923		rs10911353	1	183489203	SMG7	6.52	0.17	0.09	90.0	
SMOX	ILMN_1775380	20	rs8118315	20	4161500	SMOX	rs11677815	2	65800982		5.68	0.39	0.62	0.52	
SNHG8	ILMN_3309349	4	rs1105621	6	133050233		rs705837	4	119225940	SNHG8	6.11		,	1	
SNORD14A	ILMN_1799381	===	rs1520429	12	46259108		rs214097	11	17291499	SNORD14A	6.60	0.29	10.08	0.72	7660
SNORD89	II.MN 3238662	7.7	rs10445863	7.7	115929241		rs750783	7.7	101889306	SNOBD89	20.9	11.01	10.30	9	14 040
SNORD89	ILMN_3238662	1 (7)	rs11605822	11	122986326		rs750783	1 (7)	101889306	SNORD89	5.96				
SNORD89	ILMN_3238662	2	rs2135064	ъ	26778066		rs750783	2	101889306	SNORD89	6.33				
SNUPN	ILMN_1733932	12	rs8134646	21	46376528	SNUPN	rs7185362	16	81888905		6.45	0.13	1.41	0.83	
SNUPN	ILMN_2364535	12	rs8134646	21	46376528	SNUPN	rs1472075	က	193706323		5.59	0.34	0.00	90.0	
SPATA5L1	ILMN_1729179	12	rs1131620	13	41117869		rs4774580	12	45652086	SPATA5L1	5.44	1		0	
STARDIO	ILMIN_I717052	1 1	rs2221406	27 -	901/4526		rs1000620	1 1	72509713	1127	0.00 0.00	0.67	0.12	0.33	
SIIALI SIII.F2	ILMIN-2210/29	06	rs40/3164	20	46153148	SIII.F2	rs1/685	- 4	180439236	SITALI	0 10 0 10 0 10	0.57	0.17	0.30	
SULT1A4	ILMN_2336133	1 91	rs1463965	8	74332954	1	rs3785354	16	28550667	TUFM	7.05	0.01	0.05	0.00	
SULT1A4	ILMN_2336133	16	rs2836657	21	40119768		rs3785354	16	28550667	TUFM	5.83				
SURF6	ILMN_1778032	6	rs6099626	20	56013994		rs3118663	6	136281753	SURF6	6.14	0.26	0.16	0.14	
SYTL2	ILMN_2336609	11	rs1375719	13	103410782		rs485485	11	85495269	SYTL2	5.47	0.28	0.31	0.24	
THBS3	ILMN_1804663	-	rs1939875	11	95422867		rs4072037	-	155162067	THBS3	5.55	0.03	0.15	0.03	
THBS3	ILMN_1804663		rs8014956	14	20687978		rs2049805	·	155194980	THBS3	5.65	0.31	0.76	0.55	
ILUT	TEIMIN-1.101407	-	LSZ0Z0Z40	17	10/40020		rs1520995	7	100104033	IIFND	0.22	0.07	0.40	01.0	

	Distance / Mb ^{II}					0.122																				0	0.031	12.131				1	5.389														45.345		
8	Meta ⁸ Dist	0.70	0.26			- 28	3.67	08.0	78	2.52	0.03	87	00.9	00	27	19	.51	7.36	10.72	2.10	9.20	4.47		0.32	0.07	0.62	4.09	0.29	1.07	0.68	0.08	0.59	0.16	0.44	0.22	0.16	80.0		1.01	0.02	0.13	0.40	0.69	0.11	1.69 0.30	0.06			
						14													_																														
Test	EGCUT	1.34	0.48			45.78	3.09	0.99	1.18	1.00	0.07	0.77	3.33	9.61	1.52	0.33	3.62	5.15	8.80	3.14	96.9	5.75		0.12	0.15	0.17	1.89	0.40	1.60	0.87	0.18	0.47	0.24	0.38	0.36	0.33	0.07	i	0.78	0.02	0.26	0.86	06.0	0.25	1.23	0.18			
3	Fehrmann ¹	90.0	0.16		0.76	81.55	1.55	0.40	3.61	2.41	0.08	3.06	3.72	0.04	1.57	0.19	0.00	3.31	3.06	0.07	3.36	0.10		0.64	0.11	1.03	3.19	0.50	0.21	0.37	0.12	0.63	0.21	0.50	0.20	0.15	0.24	0	0.85	0.14	0.14	80.0	0.36	0.11	1.20	0.07			
	BSGSc	5.70	8.11	6.79	11.09	12.16	8.12	8.02	8.39	7.37	6.95	6.93	6.21	7.30	6.70	5.92	8.89	8.55	5.80	5.49	6.22	9.44	5.60	5.79	5.61	5.52	80 E	5.52	5.97	6.92	7.79	6.43	6.38	6.51	5.86	6.27	6.73	7.58	5.73 10	6.71	7.34	7.05	7.41	5.42	0.92	0.00	5.01	5.51	6.34
7	Association	TMED4	TMEM149	TMEM149	TMEM149	TMEM149																	TMEM63A	TMEM80	IRF5	IRF5	TD A DDCA	TRAPPC4										TRAPPC5	TRAPPCS	CO I IVIII		RAPGEF1		TREMI	TRIMIS	TSPAN14	TSPAN32		
	Pos/Mb^{c}	44581986	36219525	36219525	36219525	36147315	4799159	133025756	188359436	128884559	64268976	90932598	13822381	113317583	147619772	171792273	129595460	233879066	161683974	80357420	242889492	21473952	226027323	656845	128593948	128593948	23498358	118887887	166970604	132022957	156404902	242329791	2369415	57495457	9947811	146690926	85439550	7758194	7758194	228504503	30408765	134635088	157393770	41264577	26044369	82273079	2317951	137947208	238746880
	Chr.	2	19	19	19	19	10	6	က	12	18	14	œ	4	7	10	11	7	9	17	1	13	1	11	7	⊳ 1	- 1-	1 [20	œ	9	- !	19	12	4	-	14	19	S - C	2	16	6	en 1	9 9	0 9	10	11	9	7
	rs ID	rs17725246	rs8106959	rs8106959	rs8106959	rs7254601	rs10508289	rs10819626	rs10937361	rs1401098	rs1557335	rs17719594	rs1843357	rs2351458	rs2539000	rs2731711	rs471728	rs6718480	rs6926382	rs7213338	rs914940	rs9509428	rs4149226	rs4963126	rs10488630	rs10488630	rs11770192	rs3916581	rs10059004	rs1023095	rs1375714	rs1393299	rs17763599	rs4968328	rs7694997	rs7800935	rs856638	rs17159840	rs17159840	rs10179572	rs12921440	rs1887778	rs963354	rs2395771	rs2393771	rs10748526	rs12800998	rs620607	rs1198819
	Association					SNX26	TMEM149							TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5										MYBPC3	TSPAN32	ECGF1															
0	Pos/Mb^{c}	132389627	47248981	27925288	45207005	36268923	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	72890603	58058246	4859303	22287303	112521675	131018917	7758194	7758194	7758194	7758194	7758194	7758194	7758194	7758194	7758194	22740855	45128454	7762978	7762978	7762978	7762978	85749398	158808416	27194634	47663049	2317951	50971266
	Chr.	11	21	22	20	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	13	19	6	50	- 2	3 =	19	19	19	19	13	61	19	19	19	5 5	27	61	19	19	19	12	10	17	11	11	22
	rs ID	rs1940400	rs2839013	rs5762235	rs6090518	rs807491	rs8106959	rs1254086	rs1548475	rs1537146	rs199793	rs7776572	rs1793823	rs17159840	rs380708	rs3916995	rs7246264	rs7246264	rs7246264	rs7246264	rs10862975	rs12412964	rs968726	rs10838738	rs12800998	rs140522																							
1	Chr.	7	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	1	11	7	r- 1	11		19	19	19	19	10	61 61	13	19	19	19	 61 7	61	19	19	19	9 9	- u	01	11	11	22
4	Probe ID	ILMN_1804148	ILMN_1786426	ILMN_1719649	ILMN_1708482	ILMN_1683811	ILMN_1683811	ILMN_1731043	II.MN 1814650	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN-2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN-2372639	ILMN 2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN_1688231	ILMN-1695651	ILMN_1785060	ILMN_1718621	ILMN_2389970	ILMN_3223126																			
ı	Gene ID ^a	TMED4	TMEM149	TMEM63A	TMEM80	TNP03	TNPO3	TRAZA TPAPPCA	TRAPPC4	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAFFC5	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TREMI	TRIMIS	TSPAN14	TSPAN32	TSPAN32	TYMP																			

	/ Mp _p			1.643	0.088																					
	Distance																									
values	Metag	0.52	1.10	0.03	4.95	0.46	0.57		0.19	0.41	0.31	0.17	0.04	1.21	0.16	0.57	0.26	1.47	0.09	1.22	0.35	2.25	1.63	0.15	0.46	0.05
$-\log_{10} p$ -values	$\mathtt{EGCUT}^{\mathrm{f}}$	0.42	1.29	0.14	5.14	0.15	0.69		0.19	0.74	0.48	0.17	0.19	1.15	0.05	0.54	0.17	1.38	0.13	1.35	0.61	1.43	0.17	0.36	0.27	0.01
Interaction statistic /	$Fehrmann^{f}$	0.59	0.48	0.03	0.94	0.84	0.39		0.33	0.16	0.23	0.31	0.03	0.73	0.46	0.53	0.48	0.81	0.19	0.57	0.18	1.64	2.38	0.09	0.67	0.26
Interact	$BSGS^{e}$	5.91	6.01	5.71	5.09	5.64	5.44	5.72	5.77	6.44	5.74	6.44	5.82	6.12	4.83	5.60	5.71	5.88	5.88	6.34	5.85	4.86	5.48	5.79	5.29	6.04
	Associationd					VNN2	VNN2	VNN2	VNN2	VNN3	VNN3	VNN3	VNN3	VNN3	VNN3			VSTM1	WDR48	WDR48	WDR48	WDR6		ZFP90	ZNF500	ZYX
SNP 2	$^{ m Pos/Mb^c}$	83600397	214514361	75151717	45974668	133077063	133072650	133072650	133072650	133067782	133067782	133067782	133067782	133067782	133067782	71024750	123098249	54553697	39091812	39067925	39044116	49194331	93119799	68573945	4799041	143093824
	Chr.	16	1	17	19	9	9	9	9	9	9	9	9	9	9	18	10	19	က	က	က	က	15	16	16	7
	rs ID	rs7201194	rs7512594	rs7225546	rs2276470	rs1883613	rs1883617	rs1883617	rs1883617	rs2267952	rs2267952	rs2267952	rs2267952	rs2267952	rs2267952	rs4552100	rs7895870	rs10500316	rs6778963	rs883349	rs7619193	rs11715581	rs12591171	rs1182968	rs2290560	rs2242601
	Association ^d	UBASH3A	UBASH3A	USP36												VSTM1	VSTM1			RAPGEF1			XAF1			
SNP 1	Pos/Mb^{c}	43855067	43855067	76794981	46063167	105252718	9116155	49927332	16834510	151662184	73006453	75547169	83262064	16594253	51692548	54553697	54553697	30261219	188927822	134635088	102624790	123371708	6673170	37040648	48283177	8935312
0.	Chr.	21	21	17	19	-1	20	22	11	-1	œ	6	14	21	13	19	19	22	4	6	13	11	17	21	22	20
	rs ID	rs1893592	rs1893592	rs2279308	rs1264226	rs10435352	rs13044386	rs134447	rs216495	rs10278073	rs1443946	rs348462	rs7157055	rs2823165	rs9596457	rs10500316	rs10500316	rs9625870	rs1388935	rs1887778	rs9554833	rs12362253	rs1533031	rs909446	rs4823723	rs6056281
	Chr.	21	21	17	19	9	9	9	9	9	9	9	9	9	9	19	19	19	n	n	n	n	17	16	16	7
Expression trait	Probe ID ^b	ILMN_2338348	ILMN_2338348	ILMN_1697227	ILMN_1743646	ILMN_1678939	ILMN_1678939	ILMN_1678939	ILMN_1678939	ILMN_1804935	ILMN_1804935	ILMN_1804935	ILMN_1804935	ILMN_2387680	ILMN_2387680	ILMN_1763455	ILMN_1763455	ILMN_1763455	ILMN_1762103	ILMN_1762103	ILMN_1762103	ILMN_1669484	ILMN_2370573	ILMN_1684628	ILMN_1700238	ILMN_1701875
Ex	Gene IDa	UBASH3A	UBASH3A	USP36	VASP	VNN2	VNN2	VNN2	VNN2	VNN3	VNN3	VNN3	VNN3	VNN3	VNN3	VSTM1	VSTM1	VSTM1	WDR48	WDR48	WDR48	WDR6	XAF1	ZFP90	ZNF500	ZYX

Table S1 - continued from previous page

a Phenotypes are expression levels of RefSeq Genes
Dilumina probe ID used to measure gene expression
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)
Interaction - log₁₀ p-value from discovery dataset
Interaction - log₁₀ p-value from meta analysis of replication datasets on the statement of the

Table S2: Estimation of additive and non-additive variance components from pedigree information Taken from previous analysis in Powell et al 2013^{22}

		Additi	ve	Non-add	itive
Gene	Probe	Variance	s.e.	Variance	s.e.
NAPRT1	ILMN_1710752	0.37	0.03	0.14	0.05
TMEM149	$ILMN_1786426$	0.41	0.04	0.09	0.04
MBNL1	ILMN_2313158	0.18	0.03	0.11	0.04
TRAPPC5	$ILMN_2372639$	0.32	0.04	0.13	0.05
CAST	ILMN_1717234	0.31	0.03	0.10	0.04

Table S3: Concordance of sign of epistatic variance components between discovery and replication datasets

	T	D	b	D + 10	01 1d	
Test	Interactions ^a	Dataset	n^{b}	Expected ^c	Observed ^d	<i>p</i> -value
1^{e}	All	EGCUT	434	217.00	306	6.69×10^{-18}
		Fehrmann	434	217.00	278	5.04×10^{-9}
		Both	434	108.50	221	5.56×10^{-31}
	Significant	EGCUT	30	15.00	25	3.25×10^{-4}
		Fehrmann	30	15.00	24	1.43×10^{-3}
		Both	30	7.50	22	3.76×10^{-8}
2^{f}	All	EGCUT	434	54.25	92	4.22×10^{-7}
		Fehrmann	434	54.25	79	6.18×10^{-4}
		Both	434	6.78	30	2.55×10^{-11}
	Significant	EGCUT	30	3.75	19	9.46×10^{-11}
		Fehrmann	30	3.75	19	9.46×10^{-11}
		Both	30	0.47	18	2.23×10^{-25}
$\overline{3^{\mathrm{g}}}$	All	EGCUT	1133	566.50	775	7.10×10^{-36}
		Fehrmann	1133	566.50	726	1.90×10^{-21}
		Both	1133	283.25	562	1.39×10^{-70}
	Significant	EGCUT	73	36.50	55	1.69×10^{-5}
		Fehrmann	73	36.50	55	1.69×10^{-5}
		Both	73	18.25	46	7.86×10^{-12}

 $^{^{\}rm a}$ "All" denotes 434 discovery interactions and "Significant" denotes 30 interactions with significant replication $p\text{-}{\rm values}$

^b Number of tests for concordance

 $^{^{\}rm c}$ Expected number of concordant cases under the null hypothesis of no interactions

^d Observed number of concordant cases

^e The sign of the most significant epistatic variance component in discovery is the same as the corresponding variance component in the replication data.

^f The largest epistatic variance component in the discovery is the same as in the replication with the same sign in both.

^g The sign of all epistatic variance components in the discovery with p < 0.05 are the same as the corresponding variance components in the replication data.

Table S4: Concordance of sign of epistatic variance components between discovery and replication datasets using test 4

Interactions ^a	Dataset	$n^{ m b}$	$0_{\rm c}$	1^{c}	2^{c}	3^{c}	4^{c}	p
Expected ^d	-	-	0.06	0.25	0.38	0.25	0.06	-
All	EGCUT	434	0.06	0.22	0.41	0.23	0.08	0.194
All	Fehrmann	434	0.07	0.22	0.39	0.24	0.08	0.385
All	Combined	868	0.07	0.22	0.40	0.23	0.08	0.0448
Significant	EGCUT	30	0.07	0.03	0.30	0.33	0.27	4.72×10^{-4}
Significant	Fehrmann	30	0.03	0.07	0.33	0.27	0.30	6.69×10^{-4}
Significant	Combined	60	0.05	0.05	0.32	0.30	0.28	5.49×10^{-8}

 $^{^{\}rm a}$ "All" denotes 434 discovery interactions and "Significant" denotes 30 interactions with significant replication $p\text{-}{\rm values}.$

^b Number of tests for concordance.

 $^{^{\}rm c}$ Proportion of tests that have 0, 1, 2, 3 or 4 concordant signs between discovery and replication.

^d Expected proportion of concordant signs under the null hypothesis of no epistasis.

 ${\it Table~S5:~} \textbf{Details~on~linkage~disequilibrium~and~relative~positions~of~all~discovery~interactions~with~SNPs~on~the~same~chromosome$

TMEMI49	Chr	Gene	SNP 1	SNP 2	Position 1	Position 2	Distance / Mb	R^2	D'
CSTB									
MBNL1			rs898095	rs9892064	80890638	80827903		0.063	
10	21		rs9979356	rs3761385	45230974	45198355	0.033	0.041	0.066
Transfer	3	MBNL1	rs16864367	rs13079208	152234166	152116652	0.118	0.041	0.117
17	10		rs2395095	rs10824092	76446305	75929517	0.517	0.013	
NAPRT1	11	CTSC	rs7930237	rs556895	88117962	88077479	0.040	0.012	0.045
LAX1	17	GAA	rs11150847	rs12602462	78153130	78146016	0.007	0.000	0.001
MBP	8	NAPRT1	rs2123758	rs3889129	144663661	144613680	0.050	0.053	0.060
SNORD14A	1	LAX1	rs1891432	rs10900520	203877662	203780591	0.097	0.065	0.106
21 C210RF57 rs9978658 rs11701361 48027084 47764477 0.263 0.032 0.065 16 RPL13 rs352935 rs2965817 89648580 89513234 0.135 0.054 0.060 19 ATP13A1 rs4284750 rs873870 19810050 19738554 0.071 0.008 0.015 2 NCL rs7563453 rs4973397 232301670 232291471 0.010 0.027 0.029 5 HNRPH1 rs6894268 rs4700810 179032488 178991794 0.041 0.000 0.001 19 VASP rs1264226 rs2276470 46063167 45974668 0.088 0.018 0.022 7 TRA2A rs776572 rs11701058 48063862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs1244224 rs11649236 8758055 48	18	MBP	rs8092433	rs4890876	74747424	74732087	0.015	0.035	0.053
16 RPL13 rs352935 rs2965817 89648580 89513234 0.135 0.054 0.060 19 ATP13A1 rs4284750 rs873870 19810050 19738554 0.071 0.008 0.015 2 NCL rs7563453 rs4973397 232201670 232291471 0.010 0.027 0.029 5 HNRPHI rs6894268 rs4700810 179032488 178991794 0.041 0.000 0.001 19 VASP rs1264226 rs2276470 46063167 45974668 0.088 0.018 0.022 7 TRA2A rs7776572 rs1177101058 48663862 47776882 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs773589 157216093 1	11	SNORD14A	rs2634462	rs6486334	17339127	17015557	0.324	0.008	0.012
NCL	21	C21ORF57	rs9978658	rs11701361	48027084	47764477	0.263	0.032	0.065
2 NCL rs7563453 rs4973397 232301670 232291471 0.010 0.027 0.029 5 HNRPH1 rs6894268 rs4700810 179032488 178991794 0.041 0.000 0.001 19 VASP rs1264226 rs2276470 46063167 45974668 0.088 0.018 0.022 7 TRA2A rs7775672 rs11770192 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs11701058 48063862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12749343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs2286842 rs3779589 157216093 <td< td=""><td>16</td><td>RPL13</td><td>rs352935</td><td>rs2965817</td><td>89648580</td><td>89513234</td><td>0.135</td><td>0.054</td><td>0.060</td></td<>	16	RPL13	rs352935	rs2965817	89648580	89513234	0.135	0.054	0.060
5 HNRPH1 rs6894268 rs4700810 179032488 178991794 0.041 0.000 0.001 19 VASP rs1264226 rs2276470 46063167 45974668 0.088 0.018 0.022 7 TRA2A rs7776572 rs11770192 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs11701058 48063862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs2286842 rs3779589 157216093 157166014 0.052 0.005 0.006 1 OVGP1 rs10802822 rs184655 37771578 <t< td=""><td>19</td><td>ATP13A1</td><td>rs4284750</td><td>rs873870</td><td>19810050</td><td>19738554</td><td>0.071</td><td>0.008</td><td>0.015</td></t<>	19	ATP13A1	rs4284750	rs873870	19810050	19738554	0.071	0.008	0.015
19 VASP rs1264226 rs2276470 46063167 45974668 0.088 0.018 0.022 7 TRA2A rs7776572 rs11770192 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs11701058 48063862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs2286842 rs3779589 157216093 157163614 0.052 0.005 0.005 0.006 1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.00 0.00 11 PHCA rs493642 rs10736812 1	2	NCL	rs7563453	rs4973397	232301670	232291471	0.010	0.027	0.029
7 TRA2A rs7776572 rs11770192 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs11701058 48063862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs2286842 rs3779589 157216093 157163614 0.052 0.005 0.006 1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.008 0.030 20 CD93 rs28668504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386	5	HNRPH1	rs6894268	rs4700810	179032488	178991794	0.041	0.000	0.001
21 PRMT2 rs2839372 rs11701058 48063862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs286842 rs3779589 157216093 157163614 0.052 0.005 0.006 1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.008 0.030 20 CD93 rs2868504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs2896940 rs13332406 57721127	19		rs1264226	rs2276470	46063167	45974668	0.088	0.018	0.022
12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs2286842 rs3779589 157216093 157163614 0.052 0.005 0.006 1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.008 0.030 20 CD93 rs2868504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.001 16 AKTIP rs2886940 rs13332406 57721127	7	TRA2A	rs7776572	rs11770192	23528927	23498358	0.031	0.064	0.064
16 N4BP1 rs12444224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs2286842 rs3779589 157216093 157163614 0.052 0.005 0.006 1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.008 0.030 20 CD93 rs2868504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.000 16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs1655031 46614102	21	PRMT2	rs2839372	rs11701058	48063862	47776382	0.287	0.100	0.122
5 CAST rs12719343 rs7733671 125369113 96000269 29.369 0.001 0.001 7 DNAJB6 rs2286842 rs3779589 157216093 157163614 0.052 0.005 0.006 1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.008 0.030 20 CD93 rs2868504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.000 16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs1655031 46614102 30833162 15.781 0.000 0.000 2 CYBRD1 rs888427 rs7591849 172368120	12	OAS1	rs13311	rs2072133	113448652	113409260	0.039	0.002	0.016
7 DNAJB6 rs2286842 rs3779589 157216093 157163614 0.052 0.005 0.006 1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.008 0.030 20 CD93 rs2868504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.000 16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs11655031 46614102 30833162 15.781 0.000 0.000 2 CYBRD1 rs888427 rs7591849 172368120 160112881 12.255 0.000 0.000 8 HMBOX1 rs587639 rs7837237 132725731	16	N4BP1	rs12444224	rs11649236	87580855	48632478	38.948	0.007	0.021
1 OVGP1 rs10802822 rs1264898 240132968 111992823 128.140 0.008 0.030 20 CD93 rs2868504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.000 16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs1655031 46614102 30833162 15.781 0.000 0.001 2 CYBRD1 rs88427 rs7591849 172368120 160112881 12.255 0.000 0.000 2 CYBRD1 rs88427 rs7591849 172368120 160112881 12.255 0.000 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917	5	CAST	rs12719343	rs7733671	125369113	96000269	29.369	0.001	0.001
20 CD93 rs2868504 rs1884655 37771578 23074375 14.697 0.000 0.002 11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.000 16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs11655031 46614102 30833162 15.781 0.000 0.000 2 CYBRD1 rs888427 rs7591849 172368120 160112881 12.255 0.000 0.000 8 HMBOX1 rs587639 rs7837237 132725731 28876221 103.850 0.001 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636	7	DNAJB6	rs2286842	rs3779589	157216093	157163614	0.052	0.005	0.006
11 PHCA rs493642 rs10736812 123097386 76708086 46.389 0.002 0.008 21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.000 16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs11655031 46614102 30833162 15.781 0.000 0.000 2 CYBRD1 rs88427 rs7591849 172368120 160112881 12.255 0.000 0.000 8 HMBOX1 rs587639 rs7837237 132725731 28876221 103.850 0.001 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 <td>1</td> <td>OVGP1</td> <td>rs10802822</td> <td>rs1264898</td> <td>240132968</td> <td>111992823</td> <td>128.140</td> <td>0.008</td> <td>0.030</td>	1	OVGP1	rs10802822	rs1264898	240132968	111992823	128.140	0.008	0.030
21 MX1 rs459498 rs8130120 42795027 29363604 13.431 0.000 0.000 16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs11655031 46614102 30833162 15.781 0.000 0.000 2 CYBRD1 rs888427 rs7591849 172368120 160112881 12.255 0.000 0.000 8 HMBOX1 rs587639 rs7837237 132725731 28876221 103.850 0.001 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776<	20	CD93	rs2868504	rs1884655	37771578	23074375	14.697	0.000	0.002
16 AKTIP rs2896940 rs13332406 57721127 53489705 4.231 0.000 0.001 17 CDK5R1 rs9905940 rs11655031 46614102 30833162 15.781 0.000 0.000 2 CYBRD1 rs888427 rs7591849 172368120 160112881 12.255 0.000 0.000 8 HMBOX1 rs587639 rs7837237 132725731 28876221 103.850 0.001 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3411188 26710	11	PHCA	rs493642	rs10736812	123097386	76708086	46.389	0.002	0.008
17 CDK5R1 rs9905940 rs11655031 46614102 30833162 15.781 0.000 0.000 2 CYBRD1 rs888427 rs7591849 172368120 160112881 12.255 0.000 0.000 8 HMBOX1 rs587639 rs7837237 132725731 28876221 103.850 0.001 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C17ORF60 rs9907897 rs7405659 635	21	MX1	rs459498	rs8130120	42795027	29363604	13.431	0.000	0.000
2 CYBRD1 rs888427 rs7591849 172368120 160112881 12.255 0.000 0.000 8 HMBOX1 rs587639 rs7837237 132725731 28876221 103.850 0.001 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C170RF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 19 TRAPPC5 rs17159840 rs17763599 77	16	AKTIP	rs2896940	rs13332406	57721127	53489705	4.231	0.000	0.001
8 HMBOX1 rs587639 rs7837237 132725731 28876221 103.850 0.001 0.001 11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C170RF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7	17	CDK5R1	rs9905940	rs11655031	46614102	30833162	15.781	0.000	0.000
11 TRAPPC4 rs1793823 rs3916581 131018917 118887887 12.131 0.001 0.002 12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C17ORF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 3323493	2	CYBRD1	rs888427	rs7591849	172368120	160112881	12.255	0.000	0.000
12 PEX5 rs10444467 rs4329748 128052636 7364442 120.688 0.000 0.000 12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C17ORF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.003 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 GPR162 rs27272500 rs2707210 79685913 </td <td>8</td> <td>HMBOX1</td> <td>rs587639</td> <td>rs7837237</td> <td>132725731</td> <td>28876221</td> <td>103.850</td> <td>0.001</td> <td>0.001</td>	8	HMBOX1	rs587639	rs7837237	132725731	28876221	103.850	0.001	0.001
12 FLJ20489 rs17615703 rs3782908 117036766 48169526 68.867 0.001 0.002 16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C170RF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 <td>11</td> <td>TRAPPC4</td> <td>rs1793823</td> <td>rs3916581</td> <td>131018917</td> <td>118887887</td> <td>12.131</td> <td>0.001</td> <td>0.002</td>	11	TRAPPC4	rs1793823	rs3916581	131018917	118887887	12.131	0.001	0.002
16 PRKCB1 rs2188355 rs10492793 23867776 12639800 11.228 0.000 0.000 14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C17ORF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	12	PEX5	rs10444467	rs4329748	128052636	7364442	120.688	0.000	0.000
14 MRPL52 rs1950857 rs3811188 26710271 23299135 3.411 0.002 0.004 17 C17ORF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	12	FLJ20489	rs17615703	rs3782908	117036766	48169526	68.867	0.001	0.002
17 C17ORF60 rs9907897 rs7405659 63502633 59874129 3.629 0.004 0.011 6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	16	PRKCB1	rs2188355	rs10492793	23867776	12639800	11.228	0.000	0.000
6 FLJ43093 rs6906101 rs13214069 36667610 32705248 3.962 0.000 0.000 19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	14	MRPL52	rs1950857	rs3811188	26710271	23299135	3.411	0.002	0.004
19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	17	C17ORF60	rs9907897	rs7405659	63502633	59874129	3.629	0.004	0.011
19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000 22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003 12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	6	FLJ43093	rs6906101	rs13214069	36667610	32705248	3.962	0.000	0.000
12 DIP2B rs871257 rs12427378 117994348 51074199 66.920 0.001 0.001 12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	19	TRAPPC5	rs17159840		7758194		5.389	0.000	0.000
12 GPR162 rs2272500 rs2707210 79685913 6902002 72.784 0.003 0.005	22	PISD	rs715572	rs6518754	33234931	32097775	1.137	0.001	0.003
	12	DIP2B	rs871257	rs12427378	117994348	51074199	66.920	0.001	0.001
17 USP36 rs2279308 rs7225546 76794981 75151717 1.643 0.000 0.000	12	GPR162	rs2272500	rs2707210	79685913	6902002	72.784	0.003	0.005
	17	USP36	rs2279308	rs7225546	76794981	75151717	1.643	0.000	0.000