# 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. extent to which epistasis influences complex traits<sup>1</sup> and contributes to their variation<sup>2,3</sup> is a fundamental question in evolution and human genetics. Though often demonstrated in artificial gene manipulation studies in model organisms<sup>4,5</sup>, and some examples have been reported in other species<sup>6</sup>, few examples exist for epistasis amongst natural polymorphisms in human traits<sup>7,8</sup>. Its absence from empirical findings may simply be due to low incidence in the genetic control of complex traits<sup>2,3</sup>, but an alternative view is that it has previously been too technically challenging to detect due to statistical and computational issues<sup>9</sup>. Here we show that, using advanced computation<sup>10</sup> 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<sup>11,12</sup> 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 interactions<sup>13</sup> ( $p = 1.8 \times 10^{-10}$ ). 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<sup>14</sup>. But to date, though its contribution to phenotypic variance is frequently the subject of debate<sup>1–3</sup>, there is little empirical exploration of the role that epistasis plays in the architecture of complex traits in humans<sup>7,8</sup>. Beyond the prism of human association studies there is evidence for epistasis, not only at the molecular scale from artificially induced mutations<sup>4</sup> but also at the evolutionary scale in fitness adaptation<sup>15</sup> and speciation<sup>16</sup>.

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<sup>17,18</sup>, increased model

complexity in fitting interaction terms<sup>19</sup>, and more extreme significance thresholds to account for increased multiple testing<sup>9</sup> 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<sup>14</sup>, the power to detect epistasis diminishes rapidly. There are two simple ways to overcome this problem. One is by using extremely large sample sizes<sup>20</sup>; 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<sup>21</sup>. But unlike complex diseases, genetic associations with gene expression commonly have very large effect sizes that explain large proportions of the genetic variance<sup>22</sup>, making them good candidates to search for epistasis, should it exist.

In our discovery dataset (Brisbane Systems Genetics Study, BSGS<sup>23</sup>) 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  $(1.03 \times 10^{15})$ 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, Fehrmann<sup>12</sup> and the Estonian Genomics Centre University of Tartu (EGCUT)<sup>11</sup>, 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<sup>24</sup>, 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<sup>9</sup>, 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<sup>22</sup> (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<sup>25</sup>.

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 splicing<sup>26</sup>) 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 previously<sup>22</sup> (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 types<sup>27</sup> (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 states<sup>28</sup> (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 <sup>13</sup>. We cross-referenced our epistatic SNPs with a map of chromosome interacting regions (n=96,139) in K562 blood cell lines <sup>29</sup> (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 <sup>30</sup>.

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 eQTL<sup>23</sup> 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<sup>2</sup>. 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<sup>23</sup>. 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<sup>12</sup>, n = 1240; EGCUT<sup>11</sup>, (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. G.G. provided the CHDWB 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.)	$\mathrm{BSGS}^2$			$Meta^4$
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

 $<sup>^{1}</sup>$  - log<sub>10</sub> p-values for 4 d.f. interaction tests  $^{2}$  Discovery dataset

 <sup>&</sup>lt;sup>3</sup> Independent replication dataset
 <sup>4</sup> Meta analysis of interaction terms between replication datasets only

# **Figures**

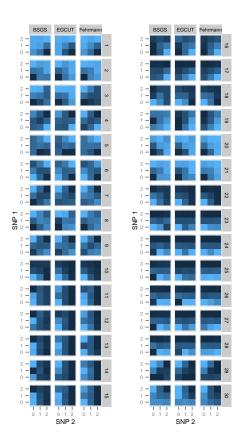


Figure 1: Replication of GP maps in two independent populations. The GP maps for each epistatic interaction that is significant at the Bonferroni level in both replication datasets are shown. Each GP map consists of nine tiles where each tile represents the expression level for that two-locus genotype 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.

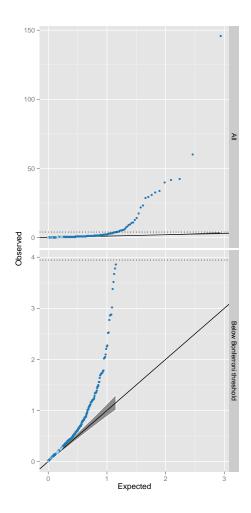


Figure 2:  $\mathbf{Q}$ - $\mathbf{Q}$  plots of interaction p-values from replication datasets. The top panel shows all 434 discovery SNPs that were tested for interactions. Observed p-values (y-axis,  $-\log_{10}$  scale) are plotted against the expected p-values (x-axis,  $-\log_{10}$  scale). The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

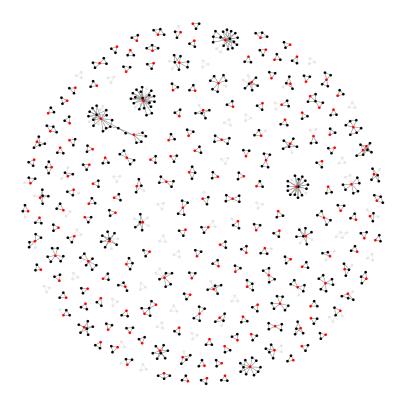


Figure 3: **Discovery and replication of epistatic networks** All 434 putative genetic interactions (edges) with data common to discovery and replication sets is shown, where black nodes represent SNPs and red nodes represent traits (gene expression probes). Three hundred and forty-five interactions 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/

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## Online methods

# 1 Discovery data

## 1.1 Data description

The Brisbane Systems Genetics Study (BSGS) comprises 846 individuals of European descent from 274 independent families<sup>23</sup>. DNA samples from each individual were genotyped on the Illumina 610-Quad Beadchip by the Scientific Services Division at deCODE Genetics Iceland. Full details of genotyping procedures are given in Medland et al.<sup>31</sup> Standard quality control (QC) filters were applied and the remaining 528,509 autosomal SNPs were carried forward for further analysis.

Gene expression profiles were generated from peripheral blood collected with PAXgene TM tubes (QIAGEN, Valencia, CA) using Illumina HT12-v4.0 bead arrays. The Illumina HT-12 v4.0 chip contains 47,323 probes, although some probes are not assigned to RefSeq genes. We removed any probes that did not match the following criteria: contained a SNP within the probe sequence with MAF > 0.05 within 1000 genomes data; did not map to a listed RefSeq gene; were not significantly expressed (based on a detection p-value < 0.05) in at least 90% of samples. After this stringent QC 7339 probes remained for 2D-eQTL mapping. These data are accessible through GEO Series accession number GSE53195.

#### 1.2 Normalisation

Gene expression profiles were normalised and adjusted for batch and polygenic effects. Profiles were first adjusted for raw background expression in each sample. Expression levels were then adjusted using quantile and  $\log_2$  transformation to standardise distributions between samples. Batch and polygenic effects were adjusted using the linear model

$$y = \mu + \beta_1 c + \beta_2 p + \beta_3 s + \beta_4 a + g + e \tag{1}$$

where  $\mu$  is the population mean expression levels, c, p, s and a are vectors of chip, chip position, sex and generation respectively, fitted as fixed effects; and g is a random additive polygenic effect with a variance covariance matrix

$$G_{jk} = \begin{cases} \sigma_a^2 & j = k \\ 2\phi_{jk}\sigma_a^2 & j \neq k \end{cases}$$
 (2)

The parameter  $\sigma_a^2$  is the variance component for additive background genetic. Here, we are using family based pedigree information rather than SNP based IBD to account for relationships between individuals and so  $\phi_{jk}$  is the kinship coefficient between individuals j and k. The residual, e, from equation 1 is assumed to follow a multivariate normal distribution with a mean of zero.

Residuals were normalised by rank transformation and used as the adjusted phenotype for the pairwise epistasis scan to remove any skewness and avoid results being driven by outliers. The GenABEL package for R was used to perform the normalisation<sup>32</sup>.

# 2 Exhaustive 2D-eQTL analysis

#### 2.1 Two stage search

We used epiGPU<sup>10</sup> software to perform an exhaustive scan for pairwise interactions, such that each SNP is tested against all other SNPs for statistical association with the expression values for each of the 7339 probes. This uses the massively parallel computational architecture of graphical processing units (GPUs) to speed up the exhaustive search. For each SNP pair there are 9 possible genotype classes. We treat each genotype class as a fixed effect and fit an 8 d.f. F-test to test the following hypotheses:

$$H_0: \sum_{i=1}^{3} \sum_{j=1}^{3} (\bar{x}_{ij} - \mu)^2 = 0;$$
(3)

$$H_1: \sum_{i=1}^{3} \sum_{j=1}^{3} (\bar{x}_{ij} - \mu)^2 > 0;$$
 (4)

where  $\mu$  is the mean expression level and  $x_{ij}$  is the pairwise genotype class mean for genotype i at SNP 1 and genotype j at SNP 2. This type of test does not parameterize for specific types of epistasis, rather it tests for the joint genetic effects at two loci. This has been demonstrated to be statistically more efficient when searching for a wide range of epistatic patterns, although will also include any marginal effects of SNPs which must be dealt with post-hoc<sup>18</sup>.

#### 2.1.1 Stage 1

The complete exhaustive scan for 7339 probes comprises  $1.03 \times 10^{15}~F$ -tests. We used permutation analysis to estimate an appropriate significance threshold for the study. To do this we performed a further 1600 exhaustive 2D scans on permuted phenotypes to generate a null distribution of the extreme p-values expected to be obtained from this number of multiple tests given the correlation structure between the SNPs. We took the most extreme p-value from each of the 1600 scans and set the 5% FWER to be the 95% most extreme of these p-values,  $T_* = 2.13 \times 10^{-12}$ . The effective number of tests in one 2D scan being performed is therefore  $N_* = 0.05/T_* \approx 2.33 \times 10^{10}$ . To correct for the testing of multiple traits we established an experiment wide threshold of  $T_e = 0.05/(N_* \times 7339) = 2.91 \times 10^{-16}$ . This is likely to be conservative as it assumes independence between probes.

**Filtering** We used two approaches to filter SNPs from stage 1 to be tested for significant interaction effects in stage 2.

Filter 1 After keeping SNP pairs that surpassed the  $2.91 \times 10^{-16}$  threshold in stage 1 only SNP pairs with at least 5 data points in all 9 genotype classes were kept. We then calculated the LD between interacting SNPs (amongst unrelated individuals within the discovery sample and also from 1000 genomes data) and removed any pairs with  $r^2 > 0.1$  or  $D'^2 > 0.1$  to avoid the inclusion of haplotype effects and to increase the accuracy of genetic variance decomposition. If multiple SNP pairs were present on the same chromosomes for a particular expression trait then only the sentinel SNP pair was retained, *i.e.* if a probe had multiple SNP pairs that were on chromosomes one and two then only the SNP pair with the most significant p-value was retained. At this stage 6404 filtered SNP pairs remained.

Filter 2 We also performed a second filtering screen applied to the list of SNP pairs from stage 1 that was identical to filter 1 but an additional step was included where any SNPs that had previously been shown to have a significant additive or dominant effect  $(p < 1.29 \times 10^{-11})$  were removed<sup>22</sup>, creating a second set of 4751 unique filtered SNP pairs.

#### 2.1.2 Stage 2

To ensure that interacting SNPs were driven by epistasis and not marginal effects we performed a nested ANOVA on each pair in the filtered set to test if the interaction terms were significant. We did this by contrasting the full genetic model (8 d.f.) against the reduced marginal effects model which included the additive and dominance terms at both SNPs (4 d.f.). Thus, a 4 d.f. F-test was performed on the residual genetic variation, representing the contribution of epistatic variance. Significance of epistasis was determined using a Bonferroni threshold of  $0.05/(6404+4751) = 4.48 \times 10^{-6}$ . This resulted in 406 and 95 SNP pairs with significant interaction terms from filters 1 and 2, respectively.

#### 2.2 Type 1 error rate

Using a Bonferroni correction of 0.05 in the second stage of the two stage discovery scan implies a type 1 error rate of  $\alpha=0.05$ . However, this could be underestimated because the number tests performed in the second stage depends on the number of tests in the first stage, and this depends on statistical power and model choice. We performed simulations to estimate the type 1 error rate of this study design.

We assumed a null model where there was one true additive effect and 7 other terms with no effect. To simulate a test statistic we simulated 8 z-scores,  $z_1 \sim N(\sqrt{NCP}, 1)$  and  $z_{2...8} \sim N(0, 1)$ . Thus  $z_{full} = \sum_{i=1}^8 z_i \sim \chi_8^2$  (representing the 8 d.f. test) and  $z_{int} = \sum_{i=5}^8 z_i \sim \chi_4^2$  (representing the 4 d.f. test where the null hypothesis of no epistasis is true). For a particular value of NCP we simulated

100,000~z values, and calculated the  $p_{full}$ -value for the  $z_{full}$  test statistic. The  $n_{int}$  test statistics with  $p_{full} < 2.31 \times 10^{-16}$  were kept for the second stage, where the type 1 error rate of stage 2 was calculated as the proportion of  $p_{int} < 0.05/n_{int}$ . The power at stage 1 was calculated as  $n_{int}/100,000$ . This procedure was performed for a range of NCP parameters that represented power ranging from  $\sim 0$  to  $\sim 1$ .

#### 2.3 Population stratification

We ruled out population stratification as a possible cause of inflated test statistics. To test for cryptic relatedness driving the interaction terms we tested for increased LD among the SNPs<sup>33</sup>. We calculated the mean of the off-diagonal elements of the correlation matrix of all unique SNPs from the 501 interactions (731 SNPs) using only unrelated individuals,  $\bar{r}^2 = 0.0039$ . This is not significantly different from the null hypothesis of zero (sampling error =  $1/n_{\rm unrelated} = 0.0039$ ).

## 2.4 Probe mapping

To avoid possibility that epistatic signals might arise due to expression probes hybridising in multiple locations we verified that probe sequences for genes with significant interactions mapped to only a single location. As an initial verification we performed a BLAST search of the full probe sequence against 1000 genomes phase 1 version 3 human genome reference and ensured that only one genomic location aligned significantly (p < 0.05). As a second step, to mitigate the possibility of weak hybridisation elsewhere in the genome we divided the probe sequence into three sections (1-25bp, 13-37bp, 26-50bp) and performed a BLAST search of these probe sequence fragments. No probe sequences or probe sequence fragments mapped to positions other than the single expected genomic target (p < 0.05).

# 3 Replication

#### 3.1 Data description

We attempted replication of the 501 significant interactions from the discovery set using three independent cohorts; Fehrmann, EGCUT, and CHDWB. It was required that LD  $r^2 < 0.1$  and  $D'^2 < 0.1$  between interacting SNPs (as measured in the replication sample directly), and all nine genotype classes had at least 5 individuals present in order to proceed with statistical testing for replication in both datasets. We also excluded any putative SNPs that had discordant allele frequencies in any of the datasets. Details of the cohorts are as follows.

**Fehrmann:** n = 1240 The Fehrmann dataset<sup>12</sup> consists of peripheral blood samples of 1240 unrelated individuals from the United Kingdom and the Netherlands. Some of these individuals are patients, while others are healthy controls.

Individuals were genotyped using the Illumina HumanHap300, Illumina HumanHap370CNV, and Illumina 610 Quad platforms. RNA levels were quantified using the Illumina HT-12 V3.0 platform. These data are accessible through GEO Series accession numbers GSE20332 and GSE20142.

**EGCUT:** n=891 The Estonian Genome Center of the University of Tartu (EGCUT) study<sup>11</sup> consists of peripheral blood samples of 891 unrelated individuals from Estonia. They were genotyped using the Illumina HumanHap370CNV platform. RNA levels were quantified using the Illumina HT-12 V3.0 platform. These data are accessible through GEO Series accession number GSE48348.

**CDHWB:** n=139 The Center for Health Discovery and Well Being (CD-HWB) Study<sup>24</sup> is a population based cohort consisting of 139 individuals of European descent collected in Atlanta USA. Gene expression profiles were generated with Illumina HT-12 V3.0 arrays from peripheral blood collected from Tempus tubes that preserve RNA. Whole genome genotypes were measured using Illumina OmniQuad arrays. Due to the small sample size, most SNP pairs did not pass filtering in this dataset (20 SNP pairs remained) and so we have excluded it from the rest of the analysis.

#### 3.2 Meta Analysis

The 4 d.f. interaction p-values for each independent replication dataset were calculated using the same statistical test as was performed in the discovery dataset. We then took the interaction p-values from EGCUT and Fehrmann and calculated a joint p-value using Fisher's method of combining p-values for a meta analysis as  $-2 \ln p_1 - 2 \ln p_2 \sim \chi_{4d.f.}^2$ . As in the discovery analysis, all gene expression levels were normalised using rank transformation to avoid skew or outliers in the distribution<sup>34</sup>.

#### 3.3 Concordance of direction of effects

We used four methods to calculate the concordance of the direction of effects between the discovery and replication datasets.

**Test 1** Is the most significant epistatic effect in the discovery set in the same direction as the same epistatic effect in the replication sets? We decomposed the genetic variance into 8 orthogonal effects, four of which are epistatic  $(A \times A, A \times D, D \times A, D \times D)$ . The sign of the epistatic effect that had the largest variance in the discovery was recorded, and then was compared to the same epistatic effect in the two replication datasets (regardless of whether or not the same epistatic effect was the largest in the replication datasets). The probability of the sign being the same in one dataset is 1/2. The probability of the sign being the same in two is 1/4.

**Test 2** Is the most significant epistatic effect in the discovery the same as the largest epistatic effect in the replication set with the sign being concordant. As in Test 1, but this time we required that the largest effect was the same in the discovery and the replication, and that they had the same sign (e.g. if the largest effect in the discovery is  $A \times A$ , with a positive effect, then concordance is achieved if the same is true in the replication). The probability of one replication dataset being concordant by chance is 1/8, and concordance in both is 1/64.

Test 3 Do the epistatic effects that are significant at nominal p < 0.05 in the discovery have the same direction of effect as in the replication? Here we count all the epistatic variance components in the discovery that have p < 0.05 (1133 amongst the 434 discovery SNP pairs, *i.e.* each SNP pair has at least 1 and at most 4 significant epistatic variance components). Then we compare the direction of the effect in the replication dataset. The probability of the sign being the same in one dataset for any one significant effect is 1/2. The probability of the sign being the same in two is 1/4.

Test 4 If we count how many of the 4 epistatic effects are concordant between the discovery and replication data for each interaction then is this significant from what we expect by chance? There can be either 0, 1, 2, 3 or 4 concordant signs at each interaction, each with expectation of p = 1/16, 4/16, 6/16, 4/16, 1/16 under the null, respectively. Observed counts are multinomially distributed, and we tested if the observed proportions were statistically different from the expected proportions using an approximation of the multinomial test  $^{35}$ .

The probability of observing the number of concordant signs in tests 1-3 is calculated using a binomial test. All variance decompositions were calculated using the NOIA method $^{36}$ .

# 4 Effects of LD on detection and replication

The power to detect genetic effects, when the observed markers are in LD with the causal variants, is proportional to  $r^x$ . For additive effects x=2, but for non-additive effects x is larger, i.e. x=4 for dominance or  $A\times A$ , x=6 for  $A\times D$  or  $D\times A$ , and x=8 for  $D\times D$ . Many biologically realistic GP maps may be comprised of all 8 variance components<sup>18</sup>.

This is important for both detection and for replication of epistasis. For detection, if the epistatic effect includes the  $D \times D$  term then if the two causal variants are tagged by observed markers that are each in LD r=0.9, then if the true variance is  $V_t$  then the observed variance  $V_o$  at the markers will be  $0.9^8V_t=0.43V_t$ . Therefore, it is important to consider the sampling variation of  $\hat{r}^x$  in a sample given some true population value of r.

#### 4.1 Simulation 1

For some values of fixed population parameters,  $p_1$  (minor allele frequency at observed marker),  $q_1$  (minor allele frequency at causal variant), and r (LD between marker and causal variant), the expected haplotype frequencies are

$$h_{11} = r\sqrt{p_1q_1p_2q_2} + p_1q_1 \tag{5}$$

$$h_{12} = p_1 q_2 - r \sqrt{p_1 q_1 p_2 q_2} \tag{6}$$

$$h_{21} = p_2 q_1 - r \sqrt{p_1 q_1 p_2 q_2} \tag{7}$$

$$h_{22} = r\sqrt{p_1 q_1 p_2 q_2} + p_2 q_2 \tag{8}$$

where  $p_2 = 1 - p_1$  and  $q_2 = 1 - q_1$ . For a range of population parameters we randomly sampled 2n haplotypes where the expected haplotype frequencies were  $h_{11}, h_{12}, h_{21}, h_{22}$ . From the sample haplotype frequencies we then calculated sample estimates of  $\hat{r}$  where

$$\hat{r} = \frac{\hat{h}_{11} - \hat{p}_1 \hat{q}_1}{\sqrt{\hat{p}_1 \hat{q}_1 \hat{p}_2 \hat{q}_2}} \tag{9}$$

For each value of combination of the parameters  $p_1, q_1, r, n$  1000 simulations were performed and the sampling mean and sampling standard deviation of  $\hat{r}, \hat{r}^2, \hat{r}^4, \hat{r}^6, \hat{r}^8$  were recorded. It was observed that sampling variance increases for increasing x in  $\hat{r}^x$ .

#### 4.2 Simulation 2

We assume that the discovery SNP pairs are ascertained (from a very large number of tests) have high  $\hat{r}$  between observed SNPs and causal variants because otherwise power of detection would be low. We can hypothesis that the distribution of  $\hat{r}$  in this ascertained sample will be a mixture of r that is high and r that is lower but with ascertained higher values from sampling. Therefore, we would expect those with truly high r to have a higher replication rate in independent datasets, and those with ascertained high  $\hat{r}$  to have lower replication because resampling is unlikely to result in the same extreme ascertainment. To obtain empirical estimates of  $\hat{r}$  in discovery and replication datasets we conducted the following simulation.

- 1. Using 1000 genomes data (phase 1, version 3, 379 European samples) we selected the 528,509 "markers" used in the original discovery analysis, plus 100,000 randomly chosen "causal variants" (CVs) with minor allele frequence > 0.05.
- 2. The 379 individuals were split into discovery (190) and replication (189) sets
- 3. For each CV the marker with the maximum  $\hat{r}_D^2$  from the marker panel was recorded in the discovery set. This marker was known as the "discovery marker" (DM).

4. The  $\hat{r}_R^2$  for each CV/DM pair was then calculated in the replication set where the discovery LD was ascertained to be high, such that  $\hat{r}_D^2 > 0.9$ .

We observed that there was an average decrease in  $\hat{r}_R^x$  relative to  $\hat{r}_D^x$ , and that this decrease was larger with increasing x. We observed that  $(\hat{r}_R^2 - \hat{r}_D^2)/\hat{r}_D^2 = 0.029$  whereas  $(\hat{r}_R^8 - \hat{r}_D^8)/\hat{r}_D^8 = 0.092$ . The average drop in in replication  $\hat{r}^8$  was 3 times higher than the drop in  $\hat{r}^2$ .

#### 4.3 Interpretation

Simulation 1 shows that sampling variance of  $r^x$  increases as x increases. Detection of epistatis is highly dependent upon high  $\hat{r}$ . Amongst the discovery SNPs there will be a mixture of interactions where observed SNPs are either in true high LD with causal variants, or will have highly inflated sample  $\hat{r}^x$  compared to the population  $r^x$ . Simulation 2 shows that as x gets larger, the average decrease in  $\hat{r}^x$  between discovery and replication becomes larger, likely to be a result of ascertained high  $\hat{r}$  in the discovery and increased sampling variance with increasing x in the replication. These results demonstrate that if all else is equal, the impact of sampling variance of r alone will reduce the replication rate of epistatic effects compared to additive effects.

#### 5 Additive and non-additive variance estimation

#### 5.1 Fixed effects

To compare the relative contribution to the phenotypic variance of gene expression levels between additive and epistatic effects we are constrained by the problem that non-additive variance components for a phenotype cannot be calculated directly. Here, we only have SNP pairs that exceed a threshold of  $p < 2.91 \times 10^{-16} = T_e$ . A strong conclusion cannot be made about the genomewide variance contribution, but we can compare the variance explained by SNP effects at this threshold for additive scans and epistatic scans.

In Powell et al  $2012^{23}$  an expression quantitative trait locus (eQTL) study was performed searching for additive effects in the same BSGS dataset as was used for the discovery here. Using the threshold  $T_e$  for the additive eQTL study, 453 of the 7339 probes analysed here had at least one significant additive effect. Assuming that the phenotypic variance for each of the probes is normalised to 1, the total phenotypic variance of all 7339 explained by the significant additive effects was 1.73%.

Following the same procedure, at the threshold  $T_e$  there were 238 gene expression probes with at least one significant pairwise epistatic interaction out of the 7339 tested. In total the proportion of the phenotypic variance explained by the epistatic effects at these SNP pairs was 0.25%.

## 5.2 Limitations of this type of comparison

### 5.3 Pedigree estimates

The gene expression levels for MBNL1, TMEM149, NAPRT1, TRAPPC5 and CAST are influenced by large cis-trans epistatic networks (eight interactions or more). Though it is not possible to orthogonally estimate the non-additive genetic variance for non-clonal populations, an approximation of a component of non-additive variance can be estimated using pedigree information. The BSGS data is comprised of some related individuals and standard quantitative genetic analysis was used to calculate the additive and dominance variance components for each gene expression phenotype in Powell  $et\ al\ 2013^{22}$ . The dominance effect is likely to capture additive  $\times$  additive genetic variance plus some fraction of other epistatic variance components. We found that the aforementioned genes had dominance variance component estimates within the top 5% of all 17,994 gene expression probes that were analysed in Powell  $et\ al\ 2013$ .

# 6 Functional enrichment analysis

#### 6.1 Tissue specific transcriptionally active regions

We employed a recently published method (http://www.broadinstitute.org/mpg/epigwas/)<sup>27</sup> that tests for cell-type-specific enrichment of active chromatin, measured through H3K4me3 chromatin marks<sup>37</sup> in regions surrounding the 731 SNPs that comprise the 501 discovery interactions. The exact method used to perform this analysis has been described previously<sup>38</sup>. Briefly, we tested the hypothesis that the 731 SNPs were more likely to be in transcriptionally active regions (as measured by chromatin marks) than a random set of SNPs selected from the same SNP chip. This hypothesis was tested for 34 cell types across four broad tissue types (haematopoietic, gastrointenstinal, musculoskeletal and endocrine, and brain).

#### 6.2 Chromosome interactions

It has been shown<sup>13</sup> that different regions on different chromosomes or within chromosomes spatially colocalise within the cell. We shall refer to the colocalisation of two chromosome regions as a chromosome interaction. A map of pairwise chromosome interactions for K562 blood cell lines was recently produced<sup>29</sup>, and we hypothesised that part of the underlying biological mechanism behind some of the 501 epistatic interactions may arise from chromosome interactions. We found that 44 of the putative epistatic interactions were amongst SNPs that were within 5Mb of known chromosome interactions. This means that SNP A was no more than 2.5Mb from the focal point of the chromosome interaction on chromosome A, and SNP B was no more than 2.5Mb from the focal point on chromosome B.

We performed simulations to test how extreme the observation of 44 epistatic interactions overlapping with chromosome interactions is compared to chance. Chromosome interactions fall within functional genomic regions<sup>13,29</sup>, and the SNPs in our epistatic interactions are enriched for functional genomic regions. Therefore, we designed the simulations to ensure that the null distribution was of chromosome interactions between SNPs enriched for functional genomic regions but with no known epistatic interactions. To do this we used the 731 SNPs that form the 501 putative epistatic interactions and randomly shuffled them to create new sets of 501 pairs, disallowing any SNP combinations that were in the original set. Therefore, each new random set was enriched for functional regions but had no genetic interactions. We scanned the map of chromosome interactions for overlaps with the new sets and then repeated the random shuffling process. We performed 1,000 such permutations to generate a null distribution of chromosome interaction overlaps.

We repeated this process, searching for overlaps within 1Mb, 250kb, and  $10\mathrm{kb}.$ 

#### 6.3 SNP colocalisation with genomic features

We tested for enrichment of genomic features for the 687 IndexSNPs that comprise the 434 epistatic interactions with data present in discovery and replication datasets. For each of the 687 IndexSNPs we calculated LD with all regional SNPs within a radius of 0.5Mb and kept all regional SNPs with LD  $r^2 > 0.8$ . We then cross-referenced the remaining regional SNPs with the annotated chromatin structure reference<sup>28</sup>) querying whether the regional SNPs fell in Predicted promoter region including TSS (TSS), Predicted promoter flanking region (PF), Predicted enhancer (E), Predicted weak enhancer or open chromatin cis regulatory element (WE), CTCF enriched element (CTCF), Predicted transcribed region (T), or Predicted Repressed or Low Activity region (R) positions. Therefore a particular IndexSNP might cover multiple genomic features through LD.

We then performed the whole querying process for each of the 528,509 SNPs present in the SNP chip used in the scan, and used the results from this second

analysis to establish a null distribution for the expected proportion of SNPs for each genomic feature. We calculated p-values for enrichment of each of the seven genomic features independently, and for cis- and trans-SNPs separately, using a binomial test. For each genomic feature we used the expected proportion of SNPs as the expected probability of "success" (p). Here, a success is defined as an IndexSNP residing in a region that includes the genomic feature. The observed number of successes for each IndexSNP (k) out of the total count of IndexSNPs (n) was then modelled as  $Pr(X = k) = \binom{n}{k} p^k (1-p)^{n-k}$ .

#### 6.4 Transcription factor enrichment

To test for enrichment of transcription factor binding sites (TFBS) we followed a procedure similar to that described in Section 6.3. For each of the 687 IndexSNPs we extracted regional SNPs as previously described. We then used the PWMEnrich package in Bioconductor (http://www.bioconductor.org/packages/2.12/bioc/html/PWMEnrich.html) to identify which TFBSs each of the regional SNPs for one IndexSNP falls in (within a radius of 250bp). Thus, the number of occurrences of a particular TFBS was counted for each IndexSNP. We used the "Threshold-free affinity" method for identifying TFBSs<sup>39</sup>.

We constructed a null distribution of expected TFBS occurrences based on the same null hypothesis as described in Section 6.3 - the probability of an IndexSNP covering a particular TFBS is identical to any of the 528,509 SNPs in the discovery SNP chip. To do this, we performed the same procedure for each SNP in the discovery SNP chip as was performed for each IndexSNP to obtain an expected probability of covering a particular TFBS. We then tested the IndexSNPs for enrichment of each TFBS independently, and for cis- and trans-SNPs separately. p-values were obtained using Z-scores, calculated by using a normal approximation to the sum of binomial random variables representing motif hits along the sequence<sup>40</sup>.

#### 6.5 Defining previously identified SNP associations

The discovery dataset (BSGS) had previously been analysed for additive and dominant marginal effects for all gene expression levels  $^{22,23}$ . To define SNPs that had been previously detected to have effects for a particular gene expression level we used a significance threshold accounting for multiple testing across SNPs and expression probes,  $T_m = 0.05/(528509 \times 7339) = 1.29 \times 10^{-11}$ . From this, we found that only nine of the 501 discovery interactions had known main effects, 64 were between SNPs that had no known marginal effects, and 439 were between a SNP with a known marginal effect and a SNP with no known marginal effect.

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# Supplementary Figures

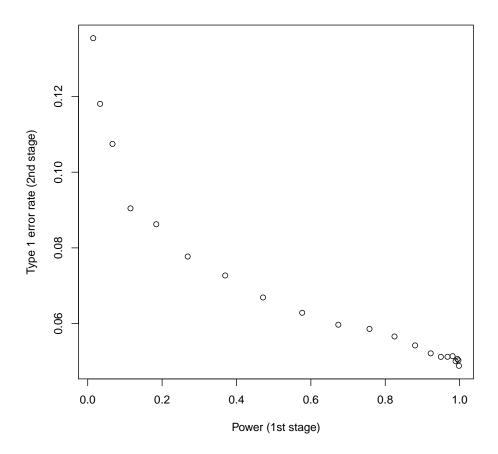


Figure S1: Type 1 error rate of two stage design assuming a null model of one large additive effect and no epistasis In stage 1 SNPs are tested for full genetic effects (8 d.f.) and those that surpass a threshold for multiple testing are then tested for significant interaction terms in stage 2. These 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.

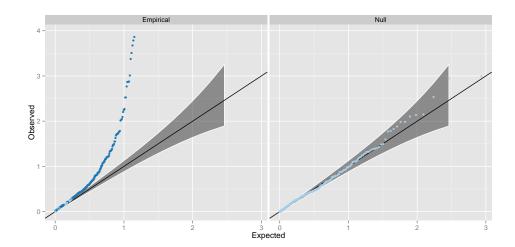


Figure S2: Q-Q plots of interaction p-values from replication datasets, excluding the 30 points significant at the Bonferroni level The right panel (Null) shows the interaction p-values from a meta analysis across two independent datasets on 434 SNP pairs where one SNP has a marginal effect. The left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

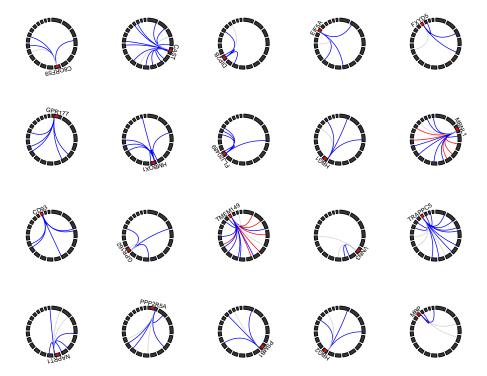


Figure S3: Gene expression traits with four or more genetic interactions Circle plots represent the genomic positions for SNPs (linking lines) and expression probes (red points). Chromosomes are represented by black blocks and ordered from 1 to 22 clockwise, starting from the top. Grey lines represent 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

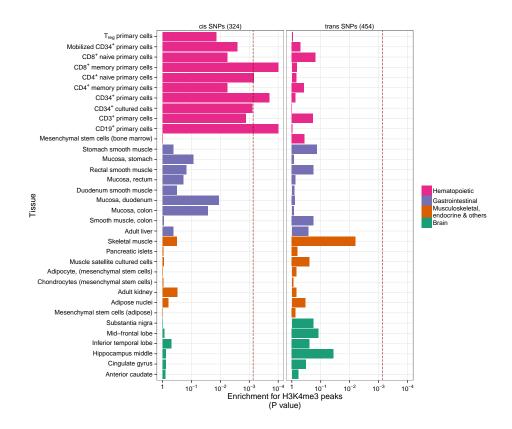


Figure S5: Tissue specific enrichment of SNPs in transcriptionally active regions The locations of transcriptional activity can be predicted by chromatin marks, assayed by  $\rm H3K4me3^{27}$ . Enrichment p-values are calculated using permutation analysis for 34 different cell types (y-axis) in four 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.

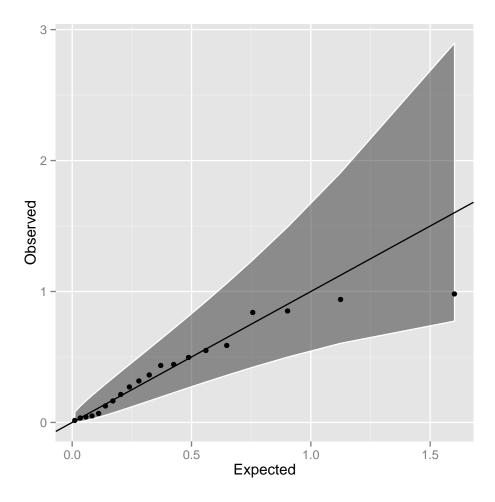


Figure S6: Q-Q plot of interaction p-values in the CDHWB dataset Twenty of the 501 discovery SNP pairs passed filtering in the CDHWB dataset (mainly due to small sample size). There is no evidence for enrichment of interaction terms, most likely due to insufficient power given the limited sample size.

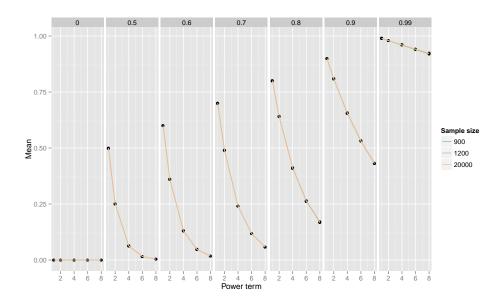


Figure S7: Sampling mean for different power terms of population r values Power of detection and replication of epistatic interactions depends not on  $r^2$  between causal variants and observed SNPs, but on  $r^4, r^6, r^8$ . For a given population value of LD r (columns of plots), plotted is the sample 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.

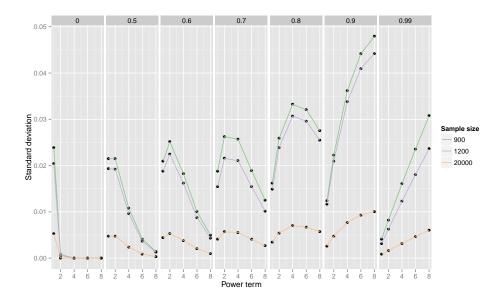


Figure S8: Sampling standard deviation for different power terms of population r values Power of detection and replication of epistatic interactions depends not on  $r^2$  between causal variants and observed SNPs, but on  $r^4$ ,  $r^6$ ,  $r^8$ . For a given a population value of LD r (columns of plots), 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.

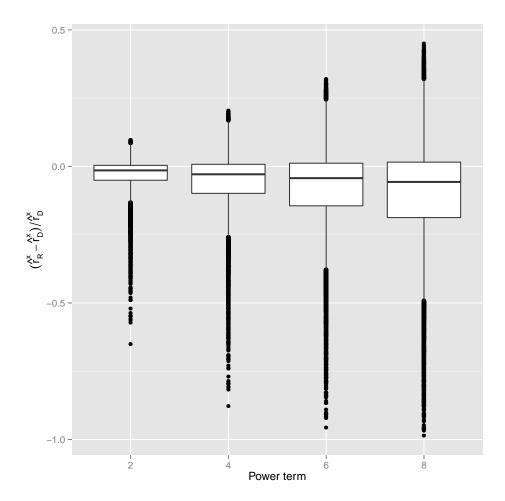


Figure S9: Reduction in LD as estimated in replication data after ascertaining for high LD in discovery data 100,000 "unobserved" causal variants (CVs) were tested for LD against a panel of 528,509 "observed" discovery markers (DMs). DM/CV pairs with LD  $r^2 > 0.9$  were then tested in an independent 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.

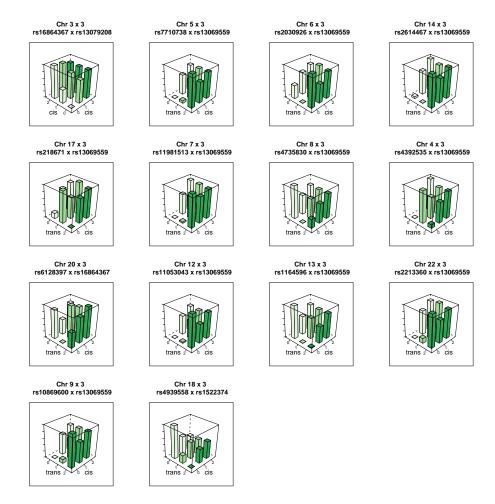


Figure S10: Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1 Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions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

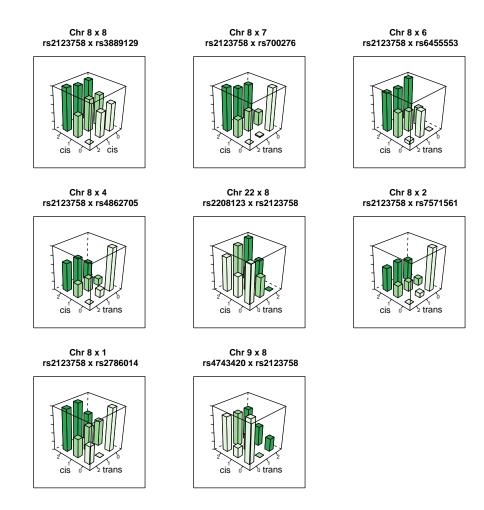


Figure S12: Genotype-phenotype maps for 8 interactions influencing the expression of NAPRT1 Each bar represents the mean phenotypic value for individuals in that genotype class.

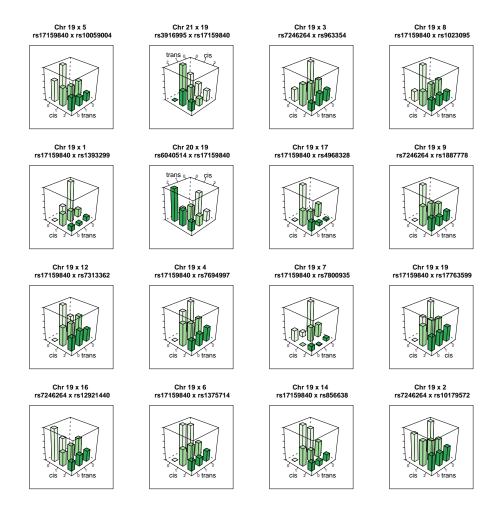


Figure S13: Genotype-phenotype maps for 16 interactions influencing the expression of TRAPPC5 Each bar represents the mean phenotypic value for individuals in that genotype class.

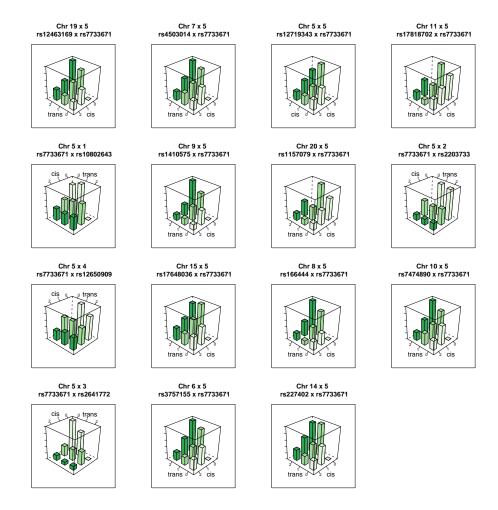


Figure S14: Genotype-phenotype maps for 15 interactions influencing the expression of CAST Each bar represents the mean phenotypic value for individuals in that genotype class.

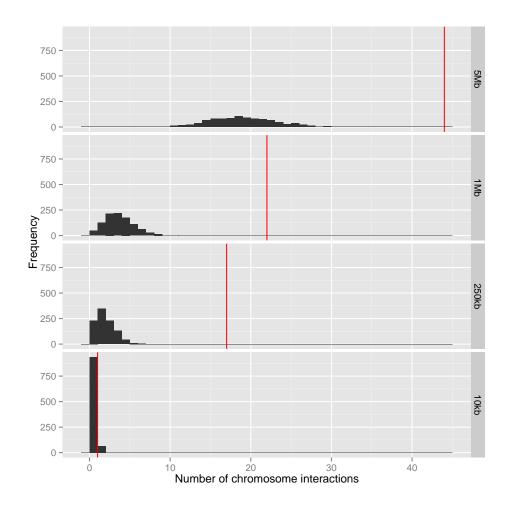


Figure S15: Number of overlaps between chromosome interactions and epistatic interactions Interacting chromosome regions may be a possible mechanism underlying epistatic interactions. The number of epistatic interactions within 20kb, 500kb, 2Mb and 10Mb of known chromosome interacting regions are shown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

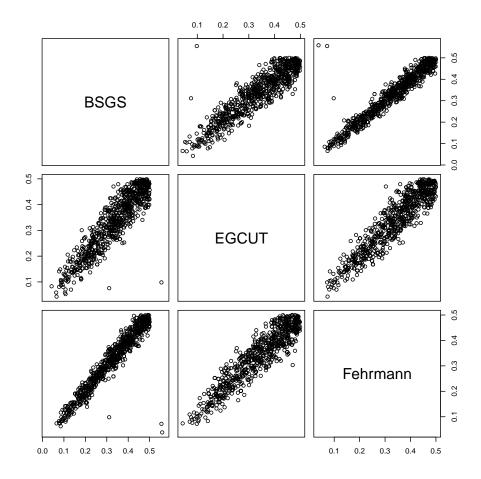


Figure S16: Comparison of allele frequencies for 781 SNPs involved in genetic interactions across independent populations Outliers were removed from the analysis as part of the filtering stage during replication.

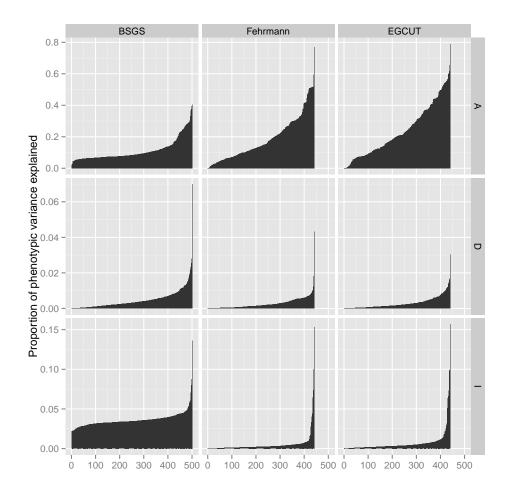


Figure S17: Comparison of variance explained by additive, dominant and epistatic effects from different cohorts How does the estimated variance decomposition change in different cohorts? The proportion of the phenotypic variance that is additive (A), dominant (D), or epistatic (I) for each putative interaction 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/Mpc	Association		,		-					
		19		*****	rs ID	CITY:	Pos/Mbc	Association	BSGSe	Fehrmann <sup>1</sup>	EGCUT.	Metag	Distance / Mb
			1047161	ABCA7	rs596183	9	158100199		5.82	$0.38^{1}$	$0.02^{1}$	0.09j	
		1 2	1047161	ABCA7	rs914737	10	139522101		5.50	0		1	
		11	108207303	A D C C S	rs4/32202	- 0	72001517		6.10	1.02	1.01	0.83	
		14	7808813	ADCK1	rs4833241	0 4	122933691		2.50	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	TS4900001	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	F82004020	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	CIOBES	. 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	

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	Distance / Mb <sup>h</sup>							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 <sup>e</sup> 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 <sup>c</sup>	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	1000001
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	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	CESI	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
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Expression trait	Probe ID <sup>b</sup>	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 <sup>a</sup>	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 <sup>h</sup>			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 <sup>f</sup> ]	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	0.23	0.74	H -	0.27
Interaction statistic	BSGS <sup>e</sup> Fel	5.55	6.18	11.99	5.74	79.0 84	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 <sup>c</sup>	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	<b>∞</b> 0	<b>x</b> 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 i	CISC							CYBRD1				DDT		COQ10A						A 0.0 A	LASSS	LASSE	LASSE				ECGF1				FIFEA	EIF5A	EIF5A	EIF5A			EMR2				11171	PRICEI		
SNP 1	Pos/Mb <sup>c</sup>	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	7	21	4 5	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
	Chr.	r- 0	20	21	ю;	I :	111	10	73	7	61	61	7	61	10	17	22	6		-	7	01 (	01 (	21 5	7 5	7 5	2 6	1 0	12	1-	8	22	-	- ;	1.5	7 1	17	17	17	19	19	19	œ	<b>oo</b> 0	<b>20</b> 0	<b>x</b> 0 0	0 10	16	6
Expression trait	Probe ID <sup>b</sup>	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 <sup>c</sup>
2         30810133         FE222         6.59         0.14         0.28         0.14           1         37001033         FE224         6.69         0.14         0.28         0.11           1         37001035         FGD2         5.69         0.13         0.05         0.01           1         48169526         FL204489         6.49         0.03         0.01         0.05           1         24166026         FL2120489         6.49         0.03         0.01         0.05           1         24166026         FL2120489         6.49         0.03         0.01         0.05           1         481662         FL2120489         6.49         0.03         0.01         0.05           1         48167         0.03         0.04	
6         36999682         FCD2         5.40         1.20         0.10         0.66           1         48169526         FL20489         5.49         1.20         0.11         0.66           1         48169526         FL20489         5.74         0.03         0.11         0.02           1.2         48169526         FL20489         6.74         0.03         0.01         0.02           1.2         48169526         FL20489         6.90         0.31         0.02         0.04           1.2         48169526         FL20489         6.90         0.33         0.01         0.02         0.04           1.2         48169526         FL20489         6.04         0.03         0.01         0.02         0.03           1.2         48169526         FL20489         6.04         0.03         0.01         0.03         0.01         0.02         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.03         0.04         0.0	159963132 rs11691600 46205050
12         48169526         FL/120489         5.81         0.06         0.07         0.29           12         48169526         FL/120489         5.74         0.03         0.11         0.02           12         48169526         FL/120489         5.74         0.03         0.01         0.03           12         48169526         FL/120489         6.74         0.03         0.01         0.02           12         48169526         FL/120489         6.04         0.34         0.07         0.03           16         5000734         FL/120718         6.04         0.34         0.05         0.03           17         80270748         FL/120718         6.00         0.04         0.04         0.05           18         92407044         FL/120718         6.00         0.03         0.05         0.05           19         3700004         PL/1         0.03         0.01         0.05         0.05           11         900000         FL/1         0.03         0.05         0.05         0.05           12         14709663         FL/1         0.03         0.04         0.05         0.05           2         14709663         FL/1	
14         1000000000000000000000000000000000000	007001
12         48169326         FL/J04489         6.49         0.31         0.47         0.86           12         48169326         FL/J04489         6.49         0.38         0.17         0.21           6         501069326         FL/J0489         6.04         0.13         0.01         0.03           1         28705248         FL/J4098         5.48         0.09         0.04         0.13           1         28705248         FL/J4098         5.48         0.09         0.04         0.13           1         28705248         FL/J4098         6.09         0.04         0.01         0.06           1         2870504         FVXDS         6.09         0.04         0.17         0.05           2         47567240         6.00         0.03         0.17         0.05         0.17           2         47567240         6.00         0.03         0.14         0.05         0.17           1         47567240         6.00         0.03         0.14         0.15         0.05           2         4756404         1.04         0.03         0.14         0.15         0.14           2         4756404         1.04         0.03	48109526 FLJZ0489 FS897511 7992118 FLJZ0489 FS897511
12         48169264         FLJ20488         6.90         0.38         0.17         0.21           6         501065261         FLJ20488         6.90         0.38         0.06         0.13           6         32705248         FLJ3093         5.48         0.39         0.06         0.13           1         24068019         FUCA1         6.16         0.01         0.01         0.01           13         98238503         FUCA1         6.01         0.03         0.01         0.01           13         98238503         FUCA1         6.00         0.03         0.04         0.01           2         141709663         FVXYD5         6.58         0.03         0.04         0.01           2         2417667204         FVXYD5         6.00         0.03         0.04         0.01           1         7 59604204         FVXYD5         6.00         0.03         0.04         0.05           1         7 7846016         FVXYD5         6.00         0.03         0.04         0.03           1         7 7846017         FVXYD5         6.00         0.03         0.04         0.03           1         1 8072818         GAPT         6.22 </td <td></td>	
16         50106594         FL/30718         6.04         0.14         0.95         0.53           6         32667610         FL/43093         6.04         0.14         0.95         0.53           1         23667610         FL/43093         6.04         0.09         0.06         0.18           1         24168019         FVCA1         6.41         0.00         0.04         0.18           1.9         3560440         FXVD5         6.58         0.03         0.44         0.17           2         47654604         FXVD5         6.70         0.07         0.17         0.05           1         7816016         GAPT         5.70         0.03         0.48         0.15           2         47654604         6.10         0.03         0.48         0.17         0.05           1         7816016         GAPT         5.72         0.03         0.43         0.17           1         7816016         GAPT         5.72         0.01         0.78         0.17           1         7816016         GAPT         5.72         0.26         0.03         0.44           1         782605228         GAPT         5.72         0.26 </td <td></td>	
6         32006010         FL443093         5.44         0.03         0.04         0.11           1         8022002         FVCA1         6.16         28.24         29.39         59.95           1         80238559         FVYD5         6.58         0.03         0.44         0.15           2         41709563         FXYD5         6.70         0.09         0.44         0.15           3         5532048         FXYD5         6.00         0.09         0.44         0.15           4         7654404         6.00         0.09         0.51         0.22           1         24166016         1.0         0.09         0.51         0.12           1         48572404         6.00         0.09         0.51         0.12           1         48562404         1.0         0.09         0.51         0.02           1         48562404         1.0         0.09         0.04         0.13           1         4856240         6.00         0.09         0.44         0.05           1         4856240         6.00         0.09         0.04         0.13           2         5778610         0.00         0.09 <t< td=""><td></td></t<>	
17         \$0.00000000000000000000000000000000000	07276627 rsb9U6IUI
1         24168019         FUCA1         6.41         0.01         0.30           13         98328563         FXYD5         6.70         0.09         0.41           19         58228655         FXYD5         6.57         0.03         0.48           19         58268656         FXYD5         6.57         0.03         0.48           1         7654604         6.00         0.09         0.51         0.51           1         7784610         GAPT         6.10         0.28         0.51           1         7844606         6.00         0.09         0.51           1         7846010         GAPT         6.10         0.28         0.51           1         79827448         GATS         6.20         0.01         0.78           1         48772811         GAPT         5.75         0.26         0.11           1         48772812         GATS         6.20         0.09         0.41           1         4877281         GATS         6.21         0.25         0.09           1         4877281         GATS         6.22         0.01         0.09           1         111         68723819         GP	FLJ45095
13         98328565         FXYD5         6.58         0.09         0.41           5         141709563         FXYD5         6.58         0.09         0.41           2         4 7654604         6.00         0.07         0.17           12         4 7654604         6.10         0.28         0.31           12         13267808         6.10         0.08         0.31           2         2 55695228         6.10         0.08         0.31           1         4 8572632         6APT         5.72         0.06           5         5 778610         GAPT         5.72         0.03           1         4 8572632         GALS         0.01         0.11           1         4 8572632         GALS         0.02         0.01           1         4 8572632         GALS         6.24         0.83         0.35           1         4 8572632         GALS         5.74         0.83         0.35           1         4 8572632         GALS         5.74         0.83         0.35           1         4 8572632         GALS         5.74         0.83         0.45           1         6 902002         GPR162 <td></td>	
19         35660450         FXYD5         6.58         0.03         0.04           2         147096563         FXYD5         6.58         0.07         0.17           4         77657329         6.00         0.09         0.01           17         78146016         5.19         0.028         0.37           17         78146016         5.19         0.028         0.37           2         255695228         5.65         0.01         0.78           5         577665208         5.65         0.01         0.78           1         485725432         6.05         0.01         0.78           14         485725432         6.07         0.11         0.78           14         48572543         6AT         0.83         0.05           14         48572543         6AT         0.83         0.05           14         48572543         6AT         0.83         0.45           15         1116423         GPNIX         5.78         0.05           16         692002         GPRIX         5.78         0.05           17         692002         GPRIA         5.74         0.25         0.05	35695200 rs788178
5         141709663         5         770         0.07         0.17           2         47567329         6.10         0.08         0.51           1         7 8466044         5.19         0.08         0.51           1         7 8466106         5.19         0.08         0.51           1         1 22678089         5.55         0.01         0.78           2         23565228         5.85         0.01         0.78           7         99827148         GAPS         5.72         0.26         0.11           7         99827148         GATS         6.22         0.01         0.78           1         48572632         GNLS         6.27         0.83         0.63           1         48572632         GNLS         6.27         0.83         0.63           1         48572632         GNLS         6.27         0.83         0.63           1         48572632         GNLS         6.57         0.02         0.42           1         48572632         GNLS         6.57         0.02         0.45           1         48572632         GNLS         6.57         0.02         0.45           1 <td></td>	
3         95331048         6.00         0.09         0.51           4         76544604         6.10         0.09         0.51           1         7.8146016         13.91         19.98         10.9           1         7.8146016         13.91         19.98         10.39           2         2.33695228         6.10         0.08         0.51           5         5.7786120         5.66         0.11         0.39           7         99827148         GATS         6.27         0.83         0.61           1         4.8572632         GALY         6.27         0.83         0.63           4         128972822         GNLY         5.78         0.05         0.45           4         128972822         GNLY         5.78         0.05         0.45           12         6920202         GPR162         5.77         0.25         0.05           12         6920202         GPR162         5.47         0.25         0.05           13         188880113         GPR177         5.46         0.17         0.40           14         48722819         GPR177         5.45         0.25         0.05           1 </td <td>FXYD5</td>	FXYD5
2         47567329         6.10         0.28           17         78146016         5.19         0.028         0.37           112         78146016         5.19         0.028         0.37           12         2256695228         5.66         0.011         0.39           2         2256695228         GAPT         5.86         0.011         0.78           4         487276148         GATS         6.57         0.26         0.011           4         48577373         GATS         6.57         0.38         0.63           14         48577373         GATS         6.57         0.38         0.03           12         11164237         GND         0.25         0.09           12         111164237         GPRIG         5.78         0.02         0.46           12         111164237         GPRIG         5.74         0.25         0.06           <	FXYD5
4         76554604         13.19         0.08         0.37           12         78446016         13.19         19.98         12.99           2         225662089         5.65         0.11         0.38         10.39           5         57786110         GAPT         5.65         0.11         0.78           7         9827148         GATS         6.22         0.11         0.78           1         48572632         GATS         6.27         0.83         0.05           1         48572632         GALY         6.27         0.38         0.05           1         48572632         GNLX         5.78         0.02         0.42           1         6020202         GPR162         5.78         0.05         0.05           1         6020202         GPR162         5.77         0.25         0.05           1         6020202         GPR162         5.77         0.25         0.06           1         68732819         GPR177         5.76         0.17         0.40           1         68732819         GPR177         5.46         0.17         0.40           1         68732819         GPR177         5.46	FXYD5
17         78142015         12391         12391         12391           2         236695228         5.65         0.01         0.39           7         99827148         GATS         6.22         0.01         0.78           14         48767632         GATS         6.57         0.39         0.01         0.78           14         48767632         GATS         6.57         0.38         0.01         0.78           14         48767632         GATS         6.57         0.38         0.03         0.12           14         48767632         GNLX         5.78         0.05         0.45         0.15         0.36         0.45           12         85072285         GNLX         5.78         0.05         0.45         0.45         0.45         0.45         0.45         0.45         0.45         0.45         0.45         0.45         0.06         0.	_
12         132678089         5.65         0.11         0.78           5         236678089         5.85         0.11         0.78           7         99827148         GATS         6.22         0.26         0.11           1         4857632         6.27         0.83         0.63           2         8593224         GALS         6.27         0.35         0.05           1         4857633         GNLY         5.86         0.55         0.00           1         48576432         GNLY         5.78         0.05         0.05           1         6902002         GPR162         5.49         0.36         0.46           1         6902002         GPR162         5.77         0.25         0.05           1         6902002         GPR162         5.77         0.25         0.06           1         6902002         GPR162         5.77         0.25         0.06           1         6902002         GPR162         5.77         0.25         0.06           1         68723819         GPR177         5.47         0.25         0.06           1         68732819         GPR177         5.76         0.17	
2         2330992748         GAPT         5.785         0.01         0.71           7         99827148         GATS         5.72         0.01         0.71           14         48572632         GATS         6.57         0.88         0.63           4         1289723287         GNLY         5.86         0.55         0.09           2         869372387         GNLY         5.78         0.05         0.45           12         611164237         GPR162         5.72         0.36         0.46           12         6902002         GPR162         5.47         0.25         0.03           13         6873819         GPR177         5.46         0.77         0.06           1         68732819         GPR177         5.46         0.77         0.40           1         68732819         GPR177         5.46         0.77         0.40           1         68732819         GPR177         5.46         0.77         0.40           1         68732819         GPR177         5.43         0.21         0.11           1         68732819         GPR177         5.46         0.75         0.40           1         687	GAA
5         9778110         GAFY         5.77         0.26         0.11           7         99827148         GATS         5.47         0.26         0.12           1         4.8572345         GATS         6.22         0.83         0.63           2         8.9323245         GNLX         5.78         0.05         0.09           12         8.9032287         GPN13         5.78         0.02         0.45           12         6.902002         GPR162         5.49         0.25         0.09           12         6.902002         GPR162         5.49         0.26         0.06           1         6.902002         GPR162         5.77         0.25         0.06           3         1.8882019         GPR177         5.47         0.26         0.06           4         1.8732819         GPR177         5.45         0.77         0.40           1         68723819         GPR177         5.43         0.31         0.11           1         68723819         GPR177         5.46         0.24         0.34           1         68723819         GPR177         5.86         0.24         0.24           1         1010	GAPT
7         99827148         GATS         6.23         0.53           14         48572632         GATS         6.24         0.83         0.65           14         18872632         GALS         6.57         0.38         0.65           12         8595282         GNLY         5.78         0.02         0.45           12         6902002         GPR162         5.72         0.05         0.06           12         6902002         GPR162         5.47         0.25         0.06           12         6902002         GPR162         5.47         0.25         0.06           1         68732819         GPR177         5.46         0.17         0.40           1         68732819         GPR177         5.46         0.25         0.21           1         68732819         GPR1	
14         48572632         0.35         0.35           4         128972852         GNLX         5.86         0.35         0.35           12         11104237         GPN3         5.78         0.05         0.46           12         11104237         GPN3         5.77         0.25         0.03           12         6902002         GPR162         5.47         0.25         0.03           1         68732819         GPR162         5.47         0.25         0.03           1         68732819         GPR177         5.45         0.17         0.40           1         68732819         GPR177         5.48         0.21         0.11           1         68732819         GPR177         5.48         0.24         0.21           1         68732819         GPR177         5.48         0.24         0.21           1         68732819         GPR177	85056572 rs2950520
4         128972357         5.86         0.55         0.09           2         85935287         GPN3         5.78         0.05         0.045           12         11116237         GPN3         5.77         0.25         0.045           12         6902002         GPR162         5.07         0.25         0.03           1         6972020         GPR162         5.47         0.25         0.05           3         18888013         GPR162         5.47         0.25         0.06           1         68723819         GPR177         5.45         0.72         0.67           1         68732819         GPR177         6.50         0.77         0.67           1         68732819         GPR177         6.50         0.77         0.67           1         68732819         GPR177         6.50         0.01         0.24           1         68732819         GPR177         5.86         0.24         0.24           1         68732819         GPR177         5.86         0.24         0.24           1         1010266754         GSTM1         6.10         0.01         0.24           1         110266754 <td< td=""><td>GDPD3</td></td<>	GDPD3
2         85935282         GNLY         5.78         0.02         0.45           112         6902002         GPR162         5.77         0.25         0.06           12         6902002         GPR162         5.49         0.36         0.06           12         6902002         GPR162         5.47         0.25         0.06           3         188880113         6.21         0.96         0.06           1         68732819         GPR177         5.45         0.17         0.40           1         68732819         GPR177         5.46         0.17         0.40           1         68732819         GPR177         5.43         0.31         0.11           1         68732819         GPR177         5.46         0.24         0.34           1         68732819         GPR177         5.86         0.21         0.11           1         68732819         GPR177         5.86         0.05         0.21           1         10266754         GSTM1         6.11         0.27         0.19           1         110266754         GSTM1         6.75         0.27         0.19           1         110266774	GDPD3
12         111164237         GPN3         5.72         0.46           12         6902002         GPR162         5.49         0.36         0.46           12         6902002         GPR162         5.07         0.25         0.03           3         18860138         GPR177         6.21         0.96         0.06           1         68723819         GPR177         5.76         0.77         0.40           1         68723819         GPR177         6.50         0.79         1.43           1         68723819         GPR177         6.04         0.96         0.21           1         68723819         GPR177         6.04         0.36         0.21           1         68723819         GPR177         6.04         0.36         0.21           1         68723819         GPR177         6.50         0.21         0.21           1         101026574         GSTM1         6.11         0.24         0.25           1         110266754         GSTM1         6.11         0.27         1.14           1         11026574         GSTM1         6.36         0.25         0.48           1         11026574 <td< td=""><td>10899955 rs7577293</td></td<>	10899955 rs7577293
12         6902002         GPR162         5.49         0.36         0.46           9         655458         5.77         0.25         0.03           1         68723819         GPR177         5.47         0.25         0.06           1         68723819         GPR177         5.47         0.25         0.06           1         68723819         GPR177         6.50         0.17         0.40           1         68723819         GPR177         6.50         0.17         0.41           1         68723819         GPR177         6.50         0.01         0.24           1         68723819         GPR177         6.50         0.01         0.24           1         168723819         GPR177         6.50         0.01         0.24           1         10266754         GSTM1         6.50         0.01         0.24           1         110266754         GSTM1         6.11         0.27         0.19           1         110266754         GSTM1         6.77         0.25         0.66           1         110266754         GSTM1         6.36         0.52         0.66           1         1532346         HBG	26084476 rs7960552
12         6902002         GPR162         5.07         0.25         0.06           3         188880113         6.21         0.25         0.06           1         08732819         GPR177         5.46         0.72         0.06           1         08732819         GPR177         5.76         0.77         0.40           1         08732819         GPR177         5.43         0.31         0.11           1         08732819         GPR177         5.43         0.31         0.11           1         08732819         GPR177         5.46         0.05         0.11           1         08732819         GPR177         5.86         0.01         0.24           1         10266274         GSTM1         6.50         0.01         0.24           1         110266754         GSTM1         6.11         0.27         0.19           1         110266754         GSTM1         6.77         0.19         0.25           2         77919015         6.36         0.52         0.66           1         58877017         6.36         0.25         0.48           1         5871671         HBG2         5.70         0.25<	
9         655458         5.47         0.25         0.06           1         1 8872819         GPR177         6.21         0.05         0.06           1         68722819         GPR177         5.76         0.77         0.40           1         68732819         GPR177         5.74         0.77         0.40           1         68732819         GPR177         5.43         0.79         1.43           1         68732819         GPR177         6.50         0.79         1.43           1         68732819         GPR177         6.50         0.21         0.21           1         68732819         GPR177         6.50         0.24         0.24           1         11026674         GSTM1         6.11         0.24         0.24           1         11026674         GSTM1         6.11         0.27         0.19           1         11026674         GSTM1         6.11         0.27         0.14           1         11026674         GSTM1         6.77         0.24           1         1252541         GSTM1         6.77         0.25         0.48           1         15271671         HBG2         5.96 <td>_</td>	_
3         18888011         G67232819         GPR177         5.45         0.96         0.06           1         68722819         GPR177         5.76         0.17         0.40           1         68722819         GPR177         6.50         0.17         0.40           1         68722819         GPR177         6.04         0.31         0.11           1         68722819         GPR177         6.50         0.01         0.24           1         68722819         GPR177         6.50         0.01         0.24           1         110266754         GSTM1         6.11         0.27         0.19           1         110266754         GSTM1         6.11         0.27         0.19           1         110266754         GSTM1         6.77         0.27         0.19           2         77919015         GSTM1         6.77         0.27         0.14           2         77919015         G.52         0.66         0.25         0.48           1         5271671         HBG2         5.94         0.05         0.64           1         5271671         HBG2         5.98         0.15         0.24           1 </td <td>GPR162</td>	GPR162
08732819 GPR177 5.45 0.77 0.67     08732819 GPR177 5.76 0.77 0.40     08732819 GPR177 5.76 0.17 0.40     08732819 GPR177 5.43 0.17 0.40     1 08732819 GPR177 5.43 0.13 0.11     1 08732819 GPR177 6.04 0.95 0.21     1 101026674 GSTM1 6.11 0.27 0.19     1 110266754 GSTM1 6.11 0.27 0.19     1 11026374 GSTM1 6.11 0.27 1.14     1 1 110254 GSTM1 6.11 0.27 0.19     1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2 GPR162
1         0.8732819         GPR177         6.76         0.17         0.04           1         0.8732819         GPR177         6.50         0.77         0.43           1         0.8732819         GPR177         6.04         0.91         0.11           1         0.8732819         GPR177         6.50         0.24         0.21           1         1         0.8732819         GPR177         6.50         0.01         0.24           1         1         10.10266754         GSTM1         6.11         0.27         0.19           1         1         10.266754         GSTM1         6.11         0.27         0.19           1         1         10.266754         GSTM1         6.77         0.27         0.19           2         77919015         GSTM1         6.77         0.27         0.14           1         1         0.52546         5.70         0.25         0.66           1         1         0.525646         5.70         0.26         0.48           1         1         0.527671         HBG2         5.98         0.15         0.24           1         1         1         1         1	
1         0.8732819         GPR177         5.43         0.14           1         0.8732819         GPR177         5.43         0.31         0.11           1         0.8732819         GPR177         5.64         0.95         0.21           1         0.8732819         GPR177         5.86         0.01         0.24           1         1.01608261         GSTM1         6.51         0.27         0.19           1         1.10266754         GSTM1         6.11         0.27         0.19           1         1.10266754         GSTM1         6.77         0.29         0.66           1         1.10266754         GSTM1         6.36         0.27         0.19           2         77919015         6.36         0.27         0.14           2         1.953244         GSTM1         6.36         0.25         0.66           1.1         5271671         HBG2         5.70         0.05         0.48           1.1         5271671         HBG2         5.98         0.15         0.24           1         21308494         LQK1         6.78         0.06         0.66           1         414533835         HBG2	_
1         0.8732819         GPR177         5.43         0.31         0.11           1         0.8732819         GPR177         6.04         0.24         0.21           1         0.8732819         GPR177         6.56         0.24         0.34           15         10.026674         GSTM1         6.11         0.27         0.20           1         110.266754         GSTM1         6.11         0.27         0.19           1         110.26574         GSTM1         6.77         0.27         1.14           1         110.2653241         GSTM1         6.77         0.27         1.14           2         77919015         6.73         0.27         0.31           2         77915015         HBC2         5.70         0.25         0.48           11         5271671         HBC2         5.77         0.00         0.66           11         5271671         HBC2         5.98         0.15         0.24           1         13088494         LQK1         6.78         0.08         0.52           4         143838322         6.42         0.01         0.41           1         1309695         HBC2         0.0	
1 08732819 GPR177	11169683 rs1206
1 68732819 GPR177 6.50 0.21 0.24     15 101508261 GSTM1 6.11 0.27 0.29     1 10266754 GSTM1 6.11 0.27 0.19     1 10266754 GSTM1 6.11 0.27 0.19     1 10263241 GSTM1 6.77 0.27 0.19     1 10253241 GSTM1 6.77 0.27 0.19     1 10253246 GSTM1 6.77 0.27 0.31     1 1 5271671 HBG2 5.70 0.25 0.48     1 1 5271671 HBG2 5.98 0.15 0.24     1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
15   101508261   5.88   0.68   0.20     1   110266754   GSTM1   6.71   0.27   0.19     1   110253241   GSTM1   6.77   0.27   0.19     2   77919015   6.36   0.27   0.31     3   58777017   6.52   0.27   0.31     1   5271671   HBG2   5.47   0.00   0.66     1   5271671   HBG2   5.98   0.15   0.24     1   13088494   LQK1   6.78   0.01   0.46     1   5309695   HBG2   6.06   0.01   0.41     1   5309695   5309695   1.00   0.00   0.00     1   5309695   5309695   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5309695   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00     1   5305605   0.00   0.00   0.00   0	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	38028634 GSDMB rs4965745
110266754 GSTMI 6.77 1.14   1102263741 GSTMI 6.77 0.27 1.14   177919015 6.36 0.52 0.27 0.31   15 8877017 6.52 0.25 0.48   11 5271671 HBG2 5.47 0.00 0.66   11 5271671 HBG2 5.98 0.15 0.24   1 13088494 LQKI 6.78 0.08 0.52   1 141333832 HBG2 6.06 0.01 0.46	53192833 rs11101992
1 110253241 GSTM1 6.77 0.66 15 8771017 6.52 0.27 0.31 21 19522546 5.70 0.25 0.48 11 5271671 HBG2 5.47 0.00 0.66 11 5271671 HBG2 5.98 0.15 0.24 1 121308849 LQK1 6.78 0.08 0.52 1 5309695 HBG2 6.06 0.01 0.46	85344527 rs11101992
2         77919015         6.36         0.52         0.66           15         5887707         6.52         0.27         0.31           21         19532546         5.70         0.25         0.48           11         5271671         HBG2         5.47         0.00         0.66           11         5271671         HBG2         5.98         0.15         0.24           1         213088494         LQK1         6.78         0.08         0.52           4         141533835         HBG2         6.78         0.01         0.41           11         5306955         HBG2         6.06         0.01         0.41	96159560 rs3754446
15         85877017         6.52         0.27         0.31           21         1953246         6.52         0.27         0.31           11         5271671         HBG2         5.47         0.06         0.66           11         5271671         HBG2         5.98         0.15         0.24           1         213088494         LQK1         6.78         0.08         0.52           4         1415383322         6.42         0.01         0.46           11         5309695         HBG2         6.06         0.01         0.41	38399979 rs4853333
21         1952246         5.70         0.25         0.48           11         5271671         HBG2         5.47         0.00         0.66           11         5271671         HBG2         5.98         0.15         0.24           1         21308849         LQK1         6.78         0.08         0.52           4         1415383832         6.42         0.01         0.46           11         5309695         HBG2         6.06         0.01         0.41	38399979 rs6497007
11         5271671         HBG2         5.47         0.00         0.66           11         5271671         HBG2         5.98         0.15         0.24           1         21308849         LQK1         6.78         0.08         0.52           4         141538342         6.42         0.01         0.46           11         5309695         HBG2         6.06         0.01         0.41	38399979 rs9983949
11         5271671         HBG2         5.98         0.15         0.24           1         1213088494         LQK1         6.78         0.05         0.52           4         1415383323         6.42         0.01         0.46           11         5309695         HBG2         6.06         0.01         0.41	4523167 rs2855039
1 213088494 LQK1 6.78 0.08 0.52 4 141533832 6.42 0.01 0.46 11 5309695 HBG2 6.06 0.01 0.41	35723501 rs2855039
4 141533832 6.42 0.01 0.46 11 5309695 HBG2 6.06 0.01 0.41	5271671 HBG2   rs1204218;
11 5309695 HBG2 $6.06$ 0.01 $0.41$	HBG2
	4523167 rs169

Expression trait Probe ID <sup>b</sup> Chr.	Chr.	$\vdash$	rs ID	Chr.	SNP 1 Pos/Mb <sup>c</sup>	Associationd	rs ID	Chr.	SNP 2 Pos/Mb <sup>c</sup>	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	r Os/ 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	O L	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	
rs12435486 14	rs12435486 14	0 4		98670849			rs2525404	οœ	28876221	HMBOX1	6.54	0.92	1.11	1.34	
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
8 rs8180944 8 28904086	8 28904086	8 28904086	28904086		Ц;	HMBOXI	rs4553956	1 m	189533772				0.03	2.20	
28904086 13 110897444	28904086 13 110897444	28904086 13 110897444	110897444		-	HMBOAL	rs/810884	~ oc	28904086	HMBOX1	5.45	0.67	0.26	0.52	
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				
ILMN_3394087 1 rs7088558 10 101884937 C	10 101884937	10 101884937	101884937		ב כ	CWF19L1	rs4654783	1.5	22439520	HSPC157	6.48	01.0	0	000	
16 rs765044 19 2560423	rs765044 19 2560423	19 2560423	2560423		3	4	rs1554999	1 1 1	3115628	11.32	. r. . r. . r. . r.	0.69	0.23	0.43	
9 rs8044524 16 8	rs8044524 16 8	4 16 8	œ	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
TEMN 9419914 17 "=1945052 19 989/1059	120	120		2897 T022			rs000/003	чĸ	170608360	LULUALI	6.00	и 6	0.40	0 37	
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	
ILMN_1815205 12 rs2168029 12 69734641	rs2168029 12 69734641	12 69734641	69734641			LYZ	rs11981725	٠.	154137150	1377	5.95	0.15	0.03	0.03	
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

Ex	Expression trait				SNP 1				SNP 2		Interact	Interaction statistic /	$-\log_{10} p$ -values	alues	
Gene ID <sup>a</sup>	Probe ID <sup>b</sup>	Chr.	rs ID	Chr.	$Pos/Mb^{c}$	Associationd	rs ID	Chr.	$Pos/Mb^{c}$	Associationd	BSGSe	Fehrmann <sup>f</sup>	$\mathtt{EGCUT}^{\mathrm{f}}$	Metag	Distance / Mbh
MBNL1	ILMN_2313158	3	rs4392535	4	41513423		rs13069559	3	152187431	MBNL1	8.39	0.02	4.33	3.02	
MBNL1	ILMN_2313158	33	rs4735830	œ	895841		rs13069559	3	152187431	MBNL1	6.74	0.32	4.21	3.38	
MBNL1	ILMN_2313158	က	rs4939558	18	46278591		rs1522374	က	152235530		7.72	0.03	0.27	0.07	
MBNL1	ILMN_2313158	က	rs6128397	20	57253132		rs16864367	က	152234166		7.22	1.34	1.15	1.73	
MBNL1	ILMN_2313158	က	rs7710738	IJ	22101322		rs13069559	33	152187431	MBNL1	7.92	2.55	7.89	9.28	
MBP	ILMN_2331544	18	rs6079849	20	15462611		rs2051344	18	74715653	MBP	6.26	0.10	0.03	0.02	
MBP	ILMN_2398939	18	rs139568	22	42210985		rs2051344	18	74715653	MBP	5.56	0.03	0.23	0.02	
MBP	ILMN_2398939	18	rs2051344	18	74715653	MBP	rs1125539	n	155204939		5.79	0.05	0.76	0.27	
MBP	ILMN_2398939	18	rs2051344	18	74715653	MBP	rs2619046	្ន	55097534		6.03	0.15	0.50	0.26	
MBP	ILMN_2398939	18	rs4805021	19	33436367		rs2051344	18	74715653	MBP	5.82	0.03	0.47	0.14	
MBP	ILMN_2398939	18	rs8092433	18	74747424		rs4890876	18	74732087		5.40	2.06	21.91	28.73	0.015
MEGF9	ILMN_2290118	6	rs13039689	20	51922071		rs966396	6	123453281	MEGF9	4.63	1.13	1.33	1.71	
MFN2	ILMN_1651385		rs7989895	13	109401737		rs4846085		12050634	MFN2	5.76	0.61	0.25	0.41	
MGC13057	ILMN_1787526	61	rs12718598	-1	50428445	MGC13057	rs11725347	4	171860973		5.81	0.13	0:30	0.14	
MGC13057	ILMN_1787526	61	rs674608	18	69070772		rs12718598	-1	50428445	MGC13057	5.57	0.02	1.03	0.20	
MGC13057	ILMN_1787526	61	rs8058318	16	82628245		rs12718598	-	50428445	MGC13057	7.05	0.11	0.12	0.02	
MGC72104	ILMN_1688318	20	rs845787	20	26197931	MGC72104	rs2660665	œ	137526799		4.17	0.02	80.0	0.05	
MGST3	ILMN_1751956	-	rs740441	17	55779644		rs4147592	-	165600146	MGST3	5.45	0.57	0.27	0.40	
MPZL2	ILMN_1752932	11	rs1805	11	118076069	MPZL2	rs11771552	7	154708716		5.90	0.01	0.23	0.04	
MPZL2	ILMN_1752932	11	rs7316716	12	19953193		rs1805	11	118076069	MPZL2	5.64	0.97	1.08	1.35	
MRPL36	ILMN_1800197	rO	rs17469061	10	8436432		rs750495	IJ	1782046	MRPL36	68.9	0.34	0.18	0.19	
MRPL43	ILMN_2258774	10	rs6564769	16	80641040		rs2863095	10	102746503	MRPL43	5.71	0.26			
MRPL52	ILMN_1713966	14	rs1950857	14	26710271		rs3811188	14		MRPL52	6.56	0.14	0.44	0.22	
MRPS10	ILMN_1663664	9	rs10955512	œ	110202230		rs722269	9	42194916	MRPS10	7.48	0.46	0.70	0.64	
MRPS10	ILMN_1663664	9	rs11698155	20	15063214		rs2395803	9	42158596	MRPS10	6.85	0.31	0.63	0.46	
MRPS10	ILMN_1663664	9	rs1420537	16	52453567		rs13217993	9	42164401	MRPS10	6.21	0.41	0.25	0.28	
MTMR15	ILMN_2152178	12	rs7178375	15	31215935	MTMR10	rs12431444	14	42068689		5.18	1.87	1.87	2.86	
MX1	ILMN_1662358	21	rs459498	21	42795027		rs11160227	14	95514596		6.31	0.46	0.52	0.50	
MX1	ILMN_1662358	21	rs459498	21	42795027		rs4973801	3	26706382		5.83	0.11	0.50	0.23	
MX1	ILMN_1662358	21	rs459498	21	42795027		rs8130120	21	29363604		6.78	0.29	0.92	0.65	13.431
MYBPC3	ILMN_1781184	11	rs10134030	14	61593110		rs1317149	11	47486885	MYBPC3	5.56	0.13	0.46	0.23	
MYBPC3	ILMN_1781184	11	rs7322768	13	109550561		rs7124681	11	47529947	MYBPC3	5.70	0.04	0.08	0.02	
MYOM1	ILMN_1680344	18	rs4798075	18	3247256	MYOM1	rs2737422	œ	134485237		6.02	0.74	0.15	0.40	
N4BP1	ILMN_2201966	16	rs12444224	16	87580855		rs11649236	16	48632478	N4BP1	5.54	2.00	0.59	1.77	38.948
NAAA	ILMIN_1668605	4 -	rs2/0/5/5	- 0	14/038/23		rs0820085	4 -	108/0229	NAAA	0.00	0.20	0.03	0.04	
NAAA	ILMIN_2391512	4 ox	rs20/1856	N 00	144663661	NAPRT1	rs0826085	4 -	78870229	NAAA	5.40	0.27	0.43	0.00	
NAPRTI	II.MN 1710752	0 00	rs2123758	o oc	144663661	NAPRTI	rs3889129	+ ox	144613680		0.00	15.12	16.08	30.10	0.050
NAPRT1	ILMN_1710752	000	rs2123758	000	144663661	NAPRTI	rs4862705	4	187445552		5.62	1.27	0.19	0.81	
NAPRT1	ILMN_1710752	00	rs2123758	00	144663661	NAPRT1	rs6455553	9	167811764		6.12	0.87	0.76	1.01	
NAPRT1	ILMN_1710752	00	rs2123758	œ	144663661	NAPRT1	rs700276	7	146189057		6.86	1.10	2.58	2.77	
NAPRT1	ILMN_1710752	œ	rs2123758	œ	144663661	NAPRT1	rs7571561	2	213386267		6.03	0.13	0.47	0.23	
NAPRT1	ILMN_1710752	œ	rs2208123	22	48214812		rs2123758	œ	144663661	NAPRT1	6.60	0.29	0.88	0.63	
NAPRT1	ILMN_1710752	œ	rs4743420	6	103488089		rs2123758	œ	144663661	NAPRT1	5.50	0.12	0.17	80.0	
NAPSA	ILMN_1784040	19	rs1405655	19	50882619	NAPSB	rs930280	6	98391111		5.58	0.82	0.10	0.40	
NAPSB	ILMN_2109416	61	rs1405655	61	50882619	NAPSB	rs10882406	10	95976932		10.1 10.1 10.1	0.67	1.10	1.12	
NAPSB	ILMIN_2109416	61	rs1405655	61	50882619	NAPSB	rs7577137	201.0	234721287		0.08	1.2.1	0.44	17.1	0
NCL	ILMIN-2121437	201.5	rs7563453	21 6	232301670		11102012	71 7	232291471	0.4011016	7.31	7.51	6.33	12.70	0.010
NDOFAIZ	TIMIN_1737738	7 5	rs2/469/1	77 -	37101890	NIMETO	rs11107847	21 0	163114006	NDOFAIZ	50 50 50 50 50 50 50 50 50 50 50 50 50 5	0.39	0.18	0.77	
NMIZ	ILMIN-1030378	1 91	rs10906557	0,0	10259490	Z I IVI VI	1S12490976	٥ ۾	50710109	SCON	0.04 0.04	24.0	40.0	0.55	
NRRES	ILMN 3237385	10	re11063498	1.0	5200078		20120261	2 0	65133800	NBBE	0. v	# 4	<b>*</b> 0.0	00.0	
NEBF2	ILMN_3237385	10	rs2375269	1 :	69876894		rs7923609	10	65133822	NRBF2	5.53				
											11111				4

Ex	Expression trait				SNP 1				SNP 2		Interacti	Interaction statistic /	- log10 p-values	values	
Gene IDa	Probe ID <sup>b</sup>	Chr.	rs ID	Chr.	Pos/Mb <sup>c</sup>	Associationd	rs ID	Chr.	Pos/Mb <sup>c</sup>	Associationd	BSGS <sub>e</sub>	Fehrmann <sup>f</sup>	$EGCUT^{f}$	Metag	Distance / Mb <sup>h</sup>
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	<b>⊣</b> 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	. <del>.</del>	7559930	PDFIRDS	0.10	0.01	0.70	0.00	
PPP9R3C	II.MN 1662617	17	re12914603	4 <del>-</del>	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	2.00	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	80.0	
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				:									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 <sup>a</sup>	Probe ID <sup>b</sup>	Chr.	rs ID	Chr.	$Pos/Mb^{c}$	Associationd	rs ID	Chr.	$Pos/Mb^{c}$	Associationd	BSGSe	Fehrmann <sup>f</sup>	$\mathtt{EGCUT}^{\mathrm{f}}$	Metag	Distance / Mb <sup>h</sup>
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 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	0.08	0.20	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-LITTOOL	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 7.0	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	- 60	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	00.00	
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 <sup>II</sup>					0.122																				0	0.031	12.131				1	5.389														45.345		
8	Meta <sup>8</sup> 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 <sup>1</sup>	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	0.90	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	00.9	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	<b>⊳</b> 1	- 1-	1 [	10	œ	9	- !	19	12	4	-	14	19	S 1 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	51 51	13	19	19	19	 61 C	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 <sup>a</sup>	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 <sub>p</sub>			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 <sup>d</sup>	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 <sup>b</sup>	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<sup>-11</sup>)
Interaction - log<sub>10</sub> p-value from discovery dataset
Interaction - log<sub>10</sub> 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 <sup>a</sup>	Dataset	$n^{\mathrm{b}}$	Expected <sup>c</sup>	Observed <sup>d</sup>	<i>p</i> -value
$1^{\mathrm{e}}$	All	EGCUT	434	217.00	306	$6.69 \times 10^{-18}$
		Fehrmann	434	217.00	278	$5.04 \times 10^{-9}$
		Both	434	108.50	221	$5.56 \times 10^{-31}$
	Significant	EGCUT	30	15.00	25	$3.25\times10^{-4}$
		Fehrmann	30	15.00	24	$1.43\times10^{-3}$
		Both	30	7.50	22	$3.76 \times 10^{-8}$
$2^{\mathrm{f}}$	All	EGCUT	434	54.25	92	$4.22 \times 10^{-7}$
		Fehrmann	434	54.25	79	$6.18 \times 10^{-4}$
		Both	434	6.78	30	$2.55 \times 10^{-11}$
	Significant	EGCUT	30	3.75	19	$9.46 \times 10^{-11}$
		Fehrmann	30	3.75	19	$9.46 \times 10^{-11}$
		Both	30	0.47	18	$2.23 \times 10^{-25}$
$\overline{3^{\mathrm{g}}}$	All	EGCUT	1133	566.50	775	$7.10 \times 10^{-36}$
		Fehrmann	1133	566.50	726	$1.90 \times 10^{-21}$
		$\operatorname{Both}$	1133	283.25	562	$1.39 \times 10^{-70}$
	Significant	EGCUT	73	36.50	55	$1.69\times10^{-5}$
		Fehrmann	73	36.50	55	$1.69\times10^{-5}$
		Both	73	18.25	46	$7.86 \times 10^{-12}$

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

<sup>&</sup>lt;sup>b</sup> Number of tests for concordance

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

<sup>&</sup>lt;sup>d</sup> Observed number of concordant cases

<sup>&</sup>lt;sup>e</sup> 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.

<sup>&</sup>lt;sup>g</sup> 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 <sup>a</sup>	Dataset	$n^{ m b}$	$0_{\rm c}$	$1^{c}$	$2^{c}$	$3^{c}$	$4^{c}$	p
Expected <sup>d</sup>	-	-	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	$4.72\times10^{-4}$
Significant	Fehrmann	30	0.03	0.07	0.33	0.27	0.30	$6.69 \times 10^{-4}$
Significant	Combined	60	0.05	0.05	0.32	0.30	0.28	$5.49 \times 10^{-8}$

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

<sup>&</sup>lt;sup>b</sup> Number of tests for concordance.

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

<sup>&</sup>lt;sup>d</sup> 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