Detection and replication of epistasis influencing transcription in humans

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Abstract

Epistasis is the phenomenon whereby one polymorphism's effect on a trait depends on other polymorphisms present in the genome. The extent to which epistasis influences complex traits and contributes to their variation^{2,3} is a fundamental question in evolution and human genetics. Though epistasis has been demonstrated in artificial gene manipulation studies in model organisms, 4,5 and examples have been reported in other species, 6 few convincing examples with independent replication exist for epistasis amongst natural polymorphisms in human traits.^{7,8} Its absence from empirical findings may simply be due to its low incidence in the genetic control of complex traits, ^{2,3} but an alternative view is that it has previously been too technically challenging to detect due to statistical power and computational issues.⁹ Here we show that, using advanced computation techniques¹⁰ and a gene expression study design, many instances of epistasis are found between common single nucleotide polymorphisms (SNPs). In a cohort of 846 individuals with data on 7339 gene expression levels in peripheral blood, we found 501 significant pairwise epistatic interactions between common SNPs acting on the expression levels of 238 genes $(p < 2.91 \times 10^{-16})$. Replication of these signals in two independent data sets^{11,12} showed both concordance of direction of epistatic effects $(p = 5.56 \times 10^{-31})$ and enrichment of interaction p-values, with 30 being significant at a conservative threshold of p < 0.05/434. There was evidence of functional enrichment for the interacting SNPs, for instance 44 of the genetic interactions are located within 5Mb of regions of known physical chromosome interactions¹³ ($p = 1.8 \times 10^{-10}$). Epistatic networks of three SNPs or more influence the expression levels of 129 genes, whereby one cis-acting SNP is modulated by several trans-acting SNPs. For example MBNL1 is influenced by an additive effect at rs13069559 which itself is masked by trans-SNPs on 14 different chromosomes, with nearly identical genotype-phenotype (GP) maps for each *cis-trans* interaction. This study presents the first evidence for multiple instances of natural genetic polymorphisms interacting to influence human traits.

Main text

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

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

In our discovery dataset (Brisbane Systems Genetics Study, BSGS²²) of 846 individuals genotyped at 528,509 SNPs, we 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 (5% significance threshold $p < 2.91 \times 10^{-16}$, 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 $\alpha \approx 0.07$, Methods, Supplementary Figure S1). Using this design we identified 501 putative genetic interactions influencing the expression levels of 238 genes (Supplementary Table S1). Of the 501 discovery interactions, 434 had available data and passed filtering (Methods) in two independent replication datasets, Fehrmann¹² and the Estonian Genomics Centre University of Tartu (EGCUT), ¹¹ in which we saw convincing evidence for replication. We used the summary statistics from the replication datasets to perform a meta analysis to obtain an independent p-value for the putative interactions, and 30 were significant after applying a Bonferroni correction for multiple testing (5\% significance threshold p < 0.05/434, Table 1). These significant interactions exhibited remarkable similarity in GP maps between all three datasets (Figure 1). We decomposed the genetic effects of each of the SNP pairs into orthogonal additive, dominance and epistatic effects $(A1, A2, D1, D2, A \times A, A \times D, D \times A, D \times D)$ and tested for concordance of the sign of the most signicant effect in the independent datasets (Methods). The most significant epistatic effect in the discovery sample was in the same direction in both replication datasets in 22 out of the 30 significantly replicated interactions ($p = 3.76 \times 10^{-8}$, Supplementary Table S3).

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 ($p << 1.0 \times 10^{-16}$, Figure 2 and Supplementary Figure S2). Concordance of the directions

tion of the effect of the largest variance component was also highly significant $(p=5.71\times 10^{-31}, \, \mathrm{Supplementary \, Table \, S3})$. 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, ²³ 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 signals from the discovery set, replication of epistasis is difficult in practice because the dependence on LD between observed SNPs and causal variants is up to three orders of magnitude higher than it is for independent additive effects. ^{17,18} Therefore these results are encouraging with regards to the detection and replication of epistasis.

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

Of the discovery interactions, 47 were cis-cis acting (both SNPs were on the same chromosome as the expression gene), 441 were cis-trans-acting, and 13 were trans-trans-acting. We observed a wide range of significant GP maps (Figure 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 splicing²⁵) has a *cis* effect at rs13069559 which in turn is controlled by 13 trans-SNPs and one cis-SNP that each exhibit a masking pattern, such that when the trans-SNP is homozygous for the masking allele the decreasing allele of the cis-SNP no longer has an effect (Supplementary Figure S7). 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 S8), NAPRT1 (Supplementary Figure S9), TRAPPC5 (Supplementary Figure S10), and CAST (Supplementary Figure S11). 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 previously²¹ (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 types²⁶ (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 states²⁷ (Supplementary Figure S4).

We also demonstrate physical organisation of interacting loci within the cell, suggesting a mechanism by which biological function can lead to epistatic genetic variance. It has been shown that different chromosomal regions spatially colocalise in the cell through chromatin interactions. We cross-referenced our epistatic SNPs with a map of chromosome interacting regions (n=96,139) in K562 blood cell lines (Methods) and found that 44 epistatic interactions mapped to within 5Mb ($p<1.8\times10^{-10}$), (Supplementary Figure S12). Interaction of distant loci may occur through physical proximity in transcriptional factories that organise across different chromosome regions and can regulate transcription of related genes. (29,30)

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

However in terms of their contribution to complex traits a more important metric might be the proportion of the variance that the epistatic loci explain.² Ideally one would approach this question from a whole genome perspective³¹ but this is intractable for non-additive variance components. Nevertheless, some inference can be made from the ascertained effects in these analyses and it is evident that additive variance is overall a larger component than epistatic variance, as has been argued previously.^{2,3} Taking the additive effects detected in Powell et al (2012) at the $p < 2.91 \times 10^{-16}$ threshold, we calculate that on average they explain 1.73% of the phenotypic variance of each of the 7339 probes. By contrast, the epistatic variance from the interacting SNPs detected in this study on average explain 0.25% of phenotypic variance, approximately

seven times lower than the additive variance. There are several caveats to this comparison. Firstly, the ratio of additive to epistatic variance may differ at different effect sizes, and our estimate is determined by the threshold used. Secondly, the power of a 1 d.f. test exceeds that of an 8 d.f. test. And thirdly, the non-additive variance at causal variants is expected to be underestimated by observed SNPs in comparison to estimates for additive variance, due to differences in the rate of decay of the estimate of the genetic variance of the causal SNPs as LD decreases with the observed SNPs.

Overall, we have demonstrated that it is possible to identify and replicate epistasis in complex traits amongst common human variants, despite the relative 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 to understanding molecular mechanisms and complex trait variation in greater detail. With computational techniques and data now widely available the search for epistasis in larger datasets for traits of broader interest is warranted.

Methods Summary

We searched for pairwise epistasis exhaustively in the BSGS discovery dataset, ²² which comprises 846 individuals who are genotyped at 528,509 autosomal SNPs. Each individual had gene expression levels measured in peripheral blood at 47,323 probes. Only the probes that passed quality control and had significant expression in $\geq 90\%$ of individuals were used in the analysis (7,339 probes representing 6,158 RefSeq genes). Recent hardware and software 10 advances that use graphics processing units (GPUs) made it possible to perform the 1.03×10^{15} statistical tests to complete this analysis. We used permutation analysis³² to calculate an experiment-wide significance threshold of $T_e = 2.91 \times$ 10^{-16} at the 5% family-wise error rate (FWER). SNP pairs were modelled for full genetic effects, including marginal additive and dominance at both SNPs plus four interaction terms. Though we could have used a less complex model to improve statistical efficiency, we deemed it important to be agnostic about the type of epistasis that might exist, and therefore chose not to over-parameterise the test. ^{18, 19} Because there are many large marginal effects present in these data it was necessary to perform several filtering steps to exclude SNP pairs that were significant due to marginal effects alone. All SNP pairs with LD $r^2 > 0.1$ and $D'^2 > 0.1$ were removed to minimise the possibility of haplotype effects. All SNP pairs were required to have at least five data points in all nine genotype classes. If multiple SNP pairs were present on the same chromosomes for a particular expression trait then only the sentinel SNP pair was retained. Finally, a nested test contrasting the full genetic model against the marginal additive and dominance model was performed for each remaining SNP pair (Methods), resulting in 501 significant interactions after Bonferroni correction for multiple testing of the filtered SNPs. The significant SNP pairs were carried forward for replication in two independent datasets that used the same expression assays for analysing transcription in peripheral blood, the Fehrmann dataset 12 (n=1240) and the Estonian Genome Centre University of the University of Tartu (EGCUT) dataset 11 (n=891). Of these, 434 passed filtering in both replication datasets. A meta analysis on the interaction p-values from each replication dataset was performed to provide an overall replication statistic for each putative interaction.

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Tables

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

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

 $^{^{1}}$ – $\log_{10} p$ -values for 4 d.f. interaction tests 2 Discovery dataset

 ³ Independent replication dataset
 ⁴ Meta analysis of interaction terms between replication datasets only

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

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.

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Supplementary Figures

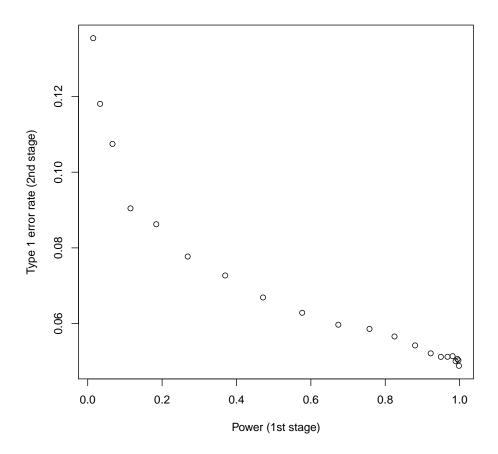


Figure S1: Type 1 error rate of two stage design In stage 1 SNPs are tested for full genetic effects (8 d.f.) and those that surpass a threshold for multiple testing are then tested for significant interaction terms in stage 2. These interaction p-values are then adjusted (Bonferroni) for the total number 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.

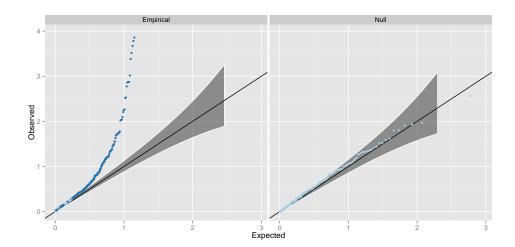


Figure S2: Q-Q plots of interaction p-values from replication datasets, excluding the 30 points significant at the Bonferroni level The right panel (Null) shows the interaction p-values from a meta analysis across two independent datasets on 434 randomly drawn SNP pairs. The left panel (Empirical) shows the interaction p-values from the 404 putative interactions that were not significant at the Bonferroni correction threshold. Dark blue points represent p-values that surpass the 2.5% FDR level, as in Figure 2.

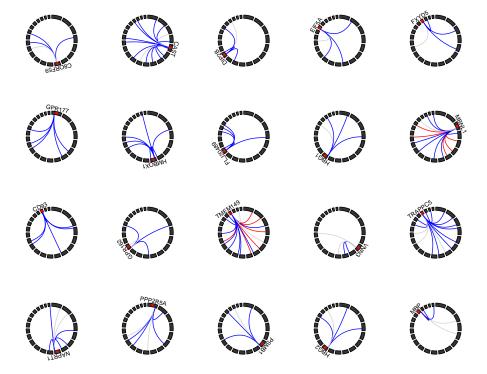


Figure S3: Gene expression traits with four or more genetic interactions Circle plots represent the genomic positions for SNPs (linking lines) and expression probes (red points). Chromosomes are represented by black blocks and ordered from 1 to 22 clockwise, starting from the top. Grey lines represent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



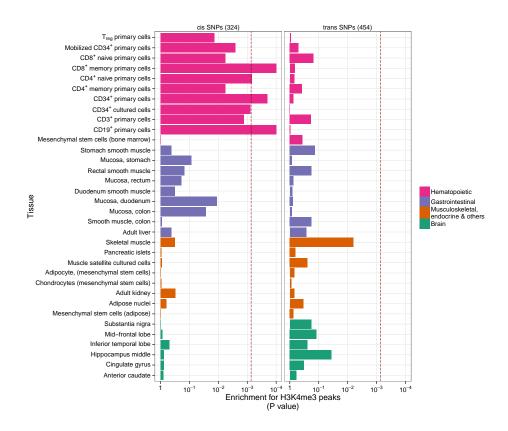


Figure S5: Tissue specific enrichment of SNPs in transcriptionally active regions The locations of transcriptional activity can be predicted by chromatin marks, assayed by H3K4me3. Enrichment p-values are calculated using permutation analysis for 34 different cell types (y-axis) in four tissue types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

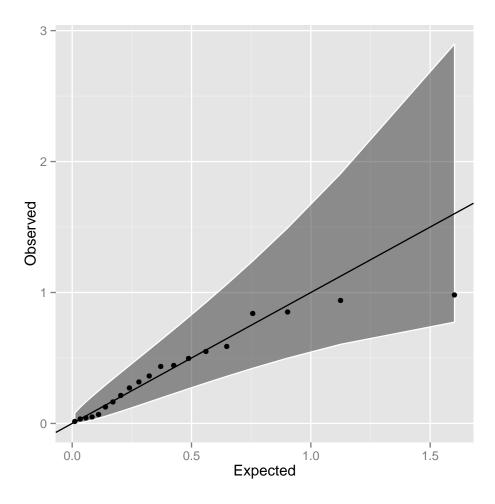


Figure S6: Q-Q plot of interaction p-values in the CDHWB dataset Twenty of the 501 discovery SNP pairs passed filtering in the CDHWB dataset (mainly due to small sample size). There is no evidence for enrichment of interaction terms, most likely due to insufficient power given the limited sample size.

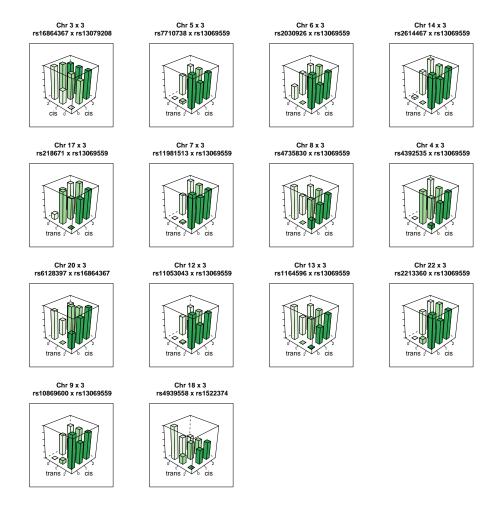


Figure S7: Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1 Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions the *cis* effect is masked when the *trans* SNP is homozygous for the masking allele.



Figure S8: 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.

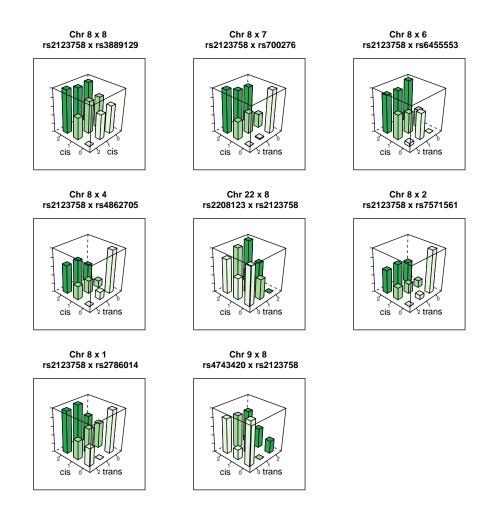


Figure S9: Genotype-phenotype maps for 8 interactions influencing the expression of NAPRT1 Each bar represents the mean phenotypic value for individuals in that genotype class.



Figure S10: Genotype-phenotype maps for 16 interactions influencing the expression of TRAPPC5 Each bar represents the mean phenotypic value for individuals in that genotype class.

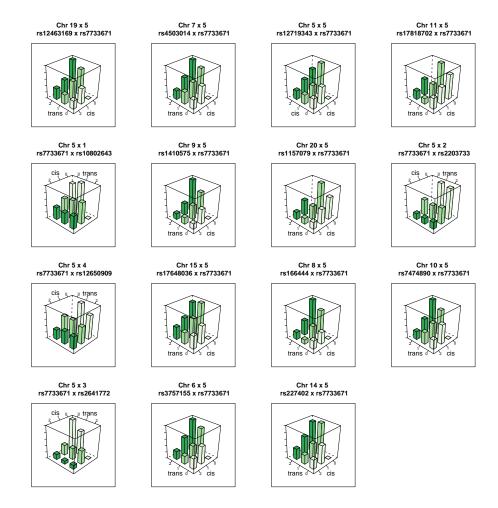


Figure S11: Genotype-phenotype maps for 15 interactions influencing the expression of CAST Each bar represents the mean phenotypic value for individuals in that genotype class.

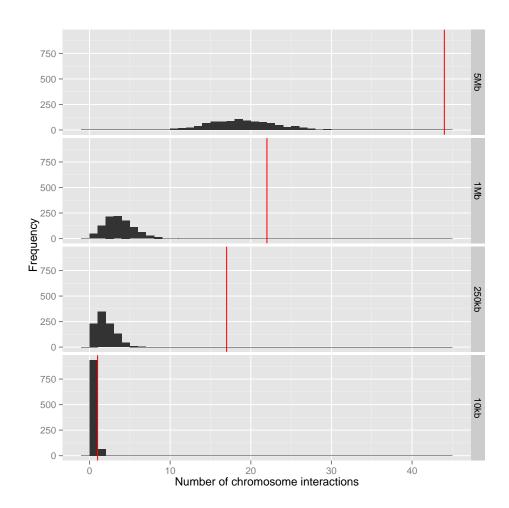


Figure S12: Number of overlaps between chromosome interactions and epistatic interactions Interacting chromosome regions may be a possible mechanism underlying epistatic interactions. The number of epistatic interactions within 20kb, 500kb, 2Mb and 10Mb of known chromosome interacting regions are shown by red vertical lines. The histograms represent the null distribution based on random sampling of 1,000 datasets for each window size.

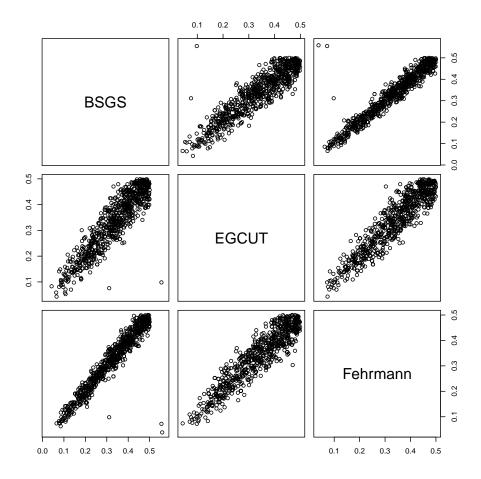


Figure S13: Comparison of allele frequencies for 781 SNPs involved in genetic interactions across independent populations Outliers were removed from the analysis as part of the filtering stage during replication.

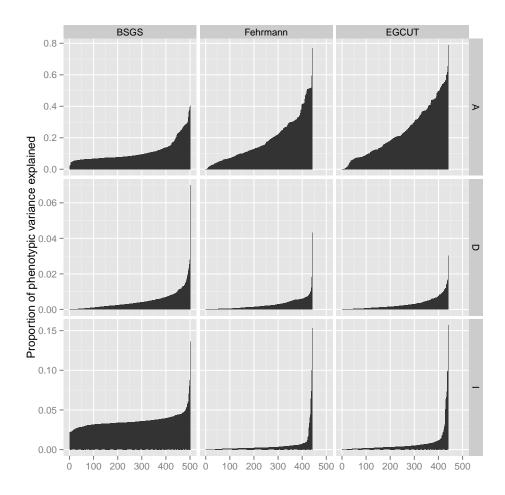


Figure S14: Comparison of variance explained by additive, dominant and epistatic effects from different cohorts How does the estimated variance decomposition change in different cohorts? The proportion of the phenotypic variance that is additive (A), dominant (D), or epistatic (I) for each putative interaction 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 rs227064 rs12431896 rs8058066 rs8058066 rs2395095 rs23151512 rs10881585	Chr. 19	Pos/Mbc	Association		,		-					
		19		******	rs ID	CITY:	Pos/Mbc	Association	BSGSe	Fehrmann ¹	EGCUT.	Metag	Distance / Mb
			1047161	ABCA7	rs596183	9	158100199		5.82	0.38^{1}	0.02^{1}	0.09j	
		1 5	1047161	ABCA7	rs914737	10	139522101		5.50	0		1	
		11	108207303	A D C C S	rs4/32202	- 0	72001517		6.10	1.02	1.01	0.83	
		14	78088813	ADCK1	rs4833241	0 4	122933691		2.20	0.36	1.14	0.87	
		16	88462550		rs12431896	14	78088813	ADCK1	6.58	2.04	0.83	2.05	
		10	76446305	ADK	rs10824092	10	75929517		69.9	18.33	21.21	39.82	0.517
		10	51515534	AGAP8	rs2547996	Ю	95174319		6.22				
	_	6	137112421		rs842647	2	61119471		7.15	1.83	1.93	2.88	
		9	29938258	HLA-G	rs1177303	2	61388355	AHSA2	5.45	0.92	0.64	0.94	
		16	57721127		rs13332406	16	53489705	AKTIP	6.91	0.16	0.99	0.57	4.231
	_	16	53536345	AKTIP	rs1362032	7	125543391		5.93	0.71	0.20	0.42	
		16	53536345	AKTIP	rs1473017	4	179323762		6.18	0.27	0.30	0.23	
	rs3760489	17	19581009	ALDH3A2	rs11720112	က	161996349		6.26	0.33	1.37	1.01	
	rs9322855	14	21153299	ANG	rs4866516	IJ	3032625		5.75	0.02	0.20	0.04	
	rs11073891	15	90363995	ANPEP	rs3823523	-	154511163		5.85	0.44	1.09	06.0	
ILMN_1763837 15	rs11073891	15	90363995	ANPEP	rs6846031	4	178019148		6.31	0.47	0.17	0.26	
ILMN_1768867 5	rs6453374	ю	77508159	AP3B1	rs4684443	က	4818792		5.94	0.05			
_		12	105580918	APPL2	rs2769594	6	87918528		5.60	0.80	1.02	1.16	
ILMN_3231952 17	rs12947580	17	75768225		rs8079215	17	44064851	ARL17B	5.96				31.703
ILMN_3231952 17	rs2834541	21	35932619		rs8079215	17	44064851	ARL17B	6.65				
ILMN_3231952 17	_	17	44064851	ARL17B	rs1950646	14	94722497		7.64				
ILMN_3231952 17	rs8079215	17	44064851	ARL17B	rs2197777	12	125831219		6.26				
ILMN_3231952 17	rs8079215	17	44064851	ARL17B	rs2684789	15	99492045		5.98				
	_	17	44064851	ARL17B	rs9834627	က	191203546		5.72				
	_	19	19810050		rs873870	19	19738554		5.30	12.18	3.25	14.23	0.071
	_	22	18213057	BID	rs9804943	12	129906275		5.84	90.0	0.40	0.14	
•••	_	22	18233000		rs10888267	-	248059423		09.9	0.87	0.16	0.20	
	_	11	8886260	C11ORF17	rs6553184	4	189150656		5.66	1.15	0.04	0.54	
	_	16	6259852	0	rs674754	13	46913416	C13ORF18	6.66	0.28	0.28	0.22	
	_	13	46913416	C13ORF18	rs6857876	4 ;	153610164		3.80	0.38	0.50	0.43	
	_	55	37575398		rs4983382	14	105189504	C140RF173	6.02	09.0	0.84	0.85	
	_	15	92276674	0.10	rs4983382	14	105189504	C14ORF173	10.08	0.31	0.28	0.24	
ILMIN_2393450 14	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	

	цq							6																							۲-					-												-
	Distance / Mb ^h							29.369																							14.697					15.781												
values	Metag	0.87	0.34		0.42	1 75	-	1.20	0.78	0.37	0.41	1.09	0.01		0.12	1.72	0.23	0.03	0.50	0.54	0.15	0.22	0.31	0.02	0.02	1.20	0.42	80.0	1.16	0.45	0.81				0.11	0.45	0.48	1.44	0.12	0.0	0.44	0.36	0.67	0.73		0.02	1.39	
$-\log_{10} p$ -values	\mathtt{EGCUT}^{f}	0.18	0.00		0.86	0.96		1.57	1.34	0.52	0.03	0.59	0.01		0.33	1.56	0.12	0.78	0.78	0.87	0.26	0.30	0.57	0.10	0.03	0.24	0.80	0.27	1.67	0.22	0.75				0.14	0.07	0.12	0.16	0.24	0.10	0.20	0.02	1.28	0.36	0.27	0.07	0.28	
Interaction statistic /	$Fehrmann^{f}$	1.39	0.94		0.09	0.23		0.36	0.13	0.27	0.97	1.15	0.11		0.07	0.92	0.49	0.75	0.23	0.22	0.19	0.26	0.00	0.23	0.08	1.74	0.13	0.04	0.24	0.71	0.64				0.21	0.95	0.90	2.16	0.15	07:0	0.72	0.92	0.07	0.95		0.07	1.92	0.0
Interactic	BSGS ^e F	5.79	6.36	5.81	6.61	7.07	7.00	7.68	6.55	7.01	7.81	6.62	6.12	6.87	7.24	5.88	6.74	7.42	7.42	6.07	6.93	0.4I	00.00	0.00	5.09	6.06	5.71	5.56	6.31	7.88	5.71	7.43	6.13	6.08	5.46	5.47	6.15	6.67	5.75	0 .0 0 .0 0 .0	5.74	4.75	5.55	7.54	5.55	7.56	6.33	
	Associationd	C8ORF59	CABCI		INPPSE	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST				E	CAT	CCDCssb	VAMPS	CD55						CD93				CDC16	CDK5R1	CEACAM21		0120474	ANALCIO	CHPT1		CLEC12A		CLTB			
SNP 2	Pos/Mb ^c	86102223	227174210	82128660	139266496	96000269	_	_	_	96000269		96000269	_			_	_	238120177	170192890	224093101		34447586	04125142	85816334	207502534	157182040	7992632	196721395	125145394		_	238899903	74439542	77264482	115008038		42066556	158943044	180265266	13424//00	102087844	81937002	10132283	134236688	175595960	63121080	67713633	1000001
SIS	Chr.	∞ -		1	6	υĸ	ı.c	10	ю	ю	ю	ю	ю	ю	ю	ю	ıo.	.,,	4.0	. 7 .	n -	1:	110	70	- 1	. 1	4	3		13	50	- · ·	, , ,	17		1.7	19	0.4	4.0	00	10		12	10 1		16	13	,
	rs ID	rs2896452	rs3738725	rs684040	rs4077515	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs7733671	rs10802643	rs12650909	rs2203733	rs2641772	rs11032695	rs541207	rs1254900	rs6700168	rs10255470	rs4696726	rs7622580	rs838875	rs9576388	rs1884655	rs10925747	rs4328531	rs4789981	rs7324744	rs11655031	rs4803481	rs2421050	rs13132719	rs15079012	rs2695290	rs867578	rs7313235	rs3903088	rs6863172	rs169130	rs7336017	0000111
	Associationd	COORE72		INPP5E														CAST	CAST	CAST	CAST		0000000	T C C C C C C C C C C C C C C C C C C C		CD93	CD93	CD93	CD93	CD93		CD93	CD93	CD93		HOXB2		CEACAM21	CEFISZ	CES1	CEST					ABCA7	ABCA7	
SNP 1	Pos/Mb^{C}	7188323	4353908	139289825	6026661	17321669	81840122	125369113	78255630	78392770	27311111	86107920	70496867	15166804	136458593	31149140	59590078	96000269	96000269	96000269	96000269	1700000	64007333	80280117	76033374	23074375	23074375	23074375	23074375	23074375	37771578	23076914	23076914	23076914	104162263	46614102	51956250	42066556	13069782			102277782	84471642	10156646	96929337	1047161	1047161	1010011
S	Chr.	16	10	6	Ξ:	07-	16	10	6	œ	12	11	14	21	9	-	10	ı, n	ı, n	ລາ	0 0	0 0	S -	11	11	20	20	20	20	20	20	0.70	20	20	14	17	20	5.	× -	14	13	173	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 ^b	ILMN_1653205	ILMN_1731064	ILMN_1712532	ILMN_1712532	ILMN-1717234 II.MN 1717234	ILMN_1717234	ILMN-1717234	ILMN_1717234	ILMN-1717234	ILMN-1717234	ILMN-1717234	ILMIN-1717234	ILMIN_1651705	ILMIN_1772208	II.MN 1784863	ILMN_1800540	ILMN_1704730	ILMN_1704730	ILMN_1704730	ILMN_1704730	ILMN_1704730	ILMN-1704730	ILMN-1704730	II.MN 1704730	ILMN_1704730	ILMN_2339796	ILMN_1730928	ILMN_1745949	ILMIN_1745949	ILMIN_1703754	ILMN-1787808	II.MN 2202940	ILMN_2202940	ILMN_1663142	ILMN_2403228	ILMN_1674609	ILMN_1770290	ILMN_1770290	TINGS TOTAL								
Exp	Gene ID ^a	CSORF59	CABC1	CARD9	CARD9	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CAST	CASI	CAI	10000000000000000000000000000000000000	CD36	CD55	CD93	CD93	CDC16	CDK5R1	CEACAM21	CEACAM21	CEFISZ	CEFES	CHPT1	CHPT1	CLEC12A	CLEC12A	CLTB	CNN2	CNNZ	ינוכנכ							

Ex	Expression trait				SNP 1				SNP 2		Interacti	Interaction statistic /	- log10 p-values	ralues	
Gene IDa	Probe ID ^b	Chr.	rs ID	Chr.	Pos/Mb ^c	Associationd	rs ID	Chr.	Pos/Mb ^c	Associationd	BSGS _e I	Fehrmann ^f	EGCUT	Metag	Distance / Mbh
FEZ2	ILMN_1739586	61.6	rs2356400	19	44321776		rs13406184	61.6	36791226	FEZ2	5.78	0.14	0.33	0.16	
FE22	ILMN-1739586 ILMN-2115005	71 92	rs969010	4 6	159963132		rs11691600 rs831486	7 9	37001267	FE22	0.00	0.14	0.25	0.14	
FGD2	ILMN_2115005	9	rs902634	10	133943951		rs831489	9	36999682	FGD2	5.49	1.20	0.11	99.0	
FLJ20489	ILMN_1778144	12	rs17615703	12	117036766		rs3782908	12	48169526	FLJ20489	5.81	0.06	0.70	0.29	68.867
FLJ20489	ILMN-1778144	7 7	rs3782908	1 5	48169526	FLJ20489	rs897511	4 6	167695661	ET. 120.480	5.53	0.03	0.11	0.00	
FLJ20489	ILMN_1778144	12	rs4984440	12	97033129		rs3782908	121	48169526	FLJ20489	6.49	0.31	0.47	0.36	
FLJ20489	ILMN_1778144	12	rs7204135	16	50626195		rs3782908	12	48169526	FLJ20489	6.90	0.38	0.17	0.21	
FLJ20718	ILMN_1763663	16	rs9325634	21	43818790		rs2287197	16	50106594	FLJ20718	6.04	0.14	0.95	0.53	
FLJ43093	ILMN_2123450	9	rs17112712	14	107276627		rs6906101	9	36667610	FLJ43093	5.48	0.39	90.0	0.13	
FLJ43093	ILMN_2123450	9	rs6906101	9	36667610	FLJ43093	rs13214069	9	32705248		5.44	0.00	0.64	0.18	3.962
FN3KRP	ILMN_1652333	17	rs898095	17	80890638		rs9892064	17	80827903		16.16	28.24	29.39	59.95	0.063
FUCAL	ILMN_1752728	- o	rs4971478	24 6	1346063		rs12744386	- č	24168019	FUCAL	6.41	0.01	0.30	0.06	
FXYD5	ILMN_2309848	19	rs17398183	20	55609148		rs2285515	1.0	35660450	FXYD5	6.58	0.03	0.48	0.15	
FXYD5	ILMN_2309848	19	rs2285515	19	35660450	FXYD5	rs11739594	10	141709563		5.70	0.07	0.17	0.02	
FXYD5	ILMN_2309848	19	rs2285515	19	35660450	FXYD5	rs13067700	က	95331048		6.00	0.09	0.51	0.22	
FXYD5	ILMN_2309848	19	rs2285515	19	35660450	FXYD5	rs17036504	5	47567329		6.10	0.28			
G3BP2	ILMN_2381758	4	rs10230232	4	29390239		rs1553985	4	76554604		5.19	0.08	0.37	0.14	
GAA	ILMN_2410783	17	rs11150847	17	78153130		rs12602462	17	78146016		13.91	19.98	12.99	32.60	0.007
GAA	ILMN_2410783	17	rs8068856	17	78100731	GAA	rs10902506	12	132678089		5.65	0.11	0.39	0.17	
GAPT	ILMN_1675191	ı, ı	rs10070522	ıo ,	57786110	GAPT	rs7605821	71	235695228		10.18 10.00	0.01	0.78	0.28	
GAPT	ILMN_1675191	ıo ı	rs7082031	10	128038717		rs10070522	ıo ı	57786110	GAPT	5.72	0.26	0.11	0.11	
GATS	ILMN_1699631	- 1	rs1147447	14	66460742		rs2950520	1 ~	99827148	GAIS	5.47	0.83	0.63	0.87	
GAIS	ILMIN-1099051	7 -	rs2425256	071	201026012	, רם ר	rs2950520		9902/140	GAIS	0.72	000	0.42	000	
GDFDS	ILMIN_1774901	16	rs3809624	16	30102802	GULUS STATUS	rsz197405	41	485/2052		0.07	0.0	0.33	0.00	
GULDS	ILMN 1790692	01	rs4145072	13 1	11089955	50105	rs7577293	4 0	85935282	CINIC	20.00	0.00	0.03	4 6 6	
GPN3	ILMN_3239426	175	rs7198646	16	26084476		rs7960552	12	111164237	GPN3	5.72)	
GPR162	ILMN_1730816	12	rs1860563	16	6478898		rs2707210	12	6902002	GPR162	5.49	0.36	0.46	0.39	
GPR162	ILMN_1730816	12	rs2272500	12	79685913		rs2707210	12	6902002	GPR162	5.07	0.25	0.03	90.0	72.784
GPR162	ILMN_1730816	12	rs2707210	12	6902002	GPR162	rs4740848	6	6554558		5.47	0.25	90.0	0.07	
GPR162	ILMN-1730816	12	rs2707210	12	6902002	GPR162	rs9827054	က	188880113		6.21	0.96	0.06	0.44	
GPR177	ILMN_1660549		rs11057383	12	124369421		rs12065581		68732819	GPR177	5.45	0.72	0.67	0.81	
GPR177	ILMN_1660549		rs12527241	: O	120468039		rs12065581		68732819	GPR177	5.76	0.17	0.40	0.22	
GFR177	ILMIN-1660549		rs12032999	- 9	11160699		rs12005551		66793619	GFR177	0.00 4.0	0.70	L.43	1.30	
GPR177	ILMN 1660549		rs9575097	2 5	82986268		rs12065581		68732819	GPR177	6.04	10.0	0.21	09.0	
GPR177	ILMN_2283325	-	rs6566669	18	70506011		rs12065581	-	68732819	GPR177	5.86	0.24	0.34	0.23	
GPR177	ILMN_2283325	1	rs9290426	ო	171399321		rs12065581	1	68732819	GPR177	6.50	0.01	0.24	0.04	
GSDMB	ILMN_2347193	17	rs11557467	17	38028634	GSDMB	rs4965745	15	101508261		5.88	89.0	0.20	0.41	
GSTM1	ILMN_2391861	1	rs12248673	10	53192833		rs11101992	1	110266754	GSTM1	6.11	0.27	0.19	0.16	
GSTM1	ILMN_2391861	1	rs1547574	13	85344527		rs11101992	-	110266754	GSTM1	5.91	0.27	1.14	0.79	
GSTM2	ILMN_2201580	1	rs6492807	13	96159560		rs3754446		110253241	GSTM1	6.77				
HIFO	ILMN_1757467	5 5	rs139898	5 5	38399979		rs4853333	C1 ±	77919015		6.36	0.52	0.66	0.65	
11150	ILMIN-11/5/46/	7 0	1S159090	7 0	000000000		rso497007	0 -	00001011		100	7 0 0	0.51	0.23	
HBC1	ILMIN_1796678	77 -	rs159696	1 17	4598167		159905949	7 -	5971671	HBG9	0.70 74	0.23	0.40	0.02	
HBG1	II.MN 1796678	: =	rs12975066	- 61	35723501		rs2855039	: :	5271671	HBG2	00 00 10	0.00	0.24	21.0	
HBG1	ILMN_1796678	11	rs2855039	11	5271671	HBG2	rs12042181	-	213088494	LQK1	6.78	0.08	0.52	0.21	
HBG1	ILMN_1796678	11	rs2855039	11	5271671	HBG2	rs12503379	4	141533832	,	6.42	0.01	0.46	0.11	
HBG2	ILMN_2084825	11	rs11078523	17	4523167		rs16912979	11	5309695	HBG2	90.9	0.01	0.41	0.10	
														Continu	Continued on next page

Table S1 - continued from previous page

at DD OFA. Pos/Albe Association of As	Probe ID ^b ILMN_2084825 ILMN_2084825 ILMN_2084825 ILMN_3086186 ILMN_3266186			2	SNF I				SNF 2		Interac	Interaction statistic	$-\log_{10} p$ -values	values	•
11 1757/2009 19 3721/271 18022 10008248 11 17508648 11 17508648 11 17508648 11 17508648 11 17508648 11 17508648 11 17508648 12 1750848 12	ILMN_2084825 ILMN_2084825 ILMN_2084825 ILMN_3266186 ILMN_1802557	Chr.	rs ID	Chr.	Pos/Mb^{c}	Associationd	rs ID	Chr.	$_{ m Pos/Mb^c}$	Associationd	$BSGS_{e}$	$Fehrmann^{f}$	$\mathtt{EGCUT}^{\mathrm{f}}$	Metag	Distance / Mb ^h
11 17.266.009 11 27.71 11 11 11 11 11 11 11	LMN_2084825 LMN_3266186 LMN_3266186	11	rs12975066	19	35723501	HBG3	rs2855039	11	5271671	HBG2	5.77	0.08	0.13	0.05	
12 1775 17	LMN_3266186 LMN_1802557	11	rs2855039	11	5271671	HBG2	rs12503379	4	141533832	13170	5.98	0.00	0.46	0.10	
12 11 12 12 13 13 13 13	1.MN 1802557	12	rs2109029	16	6036851		rs4760636	12	48173352	HDAC7	5.75				
Transference 1.5 Transferenc	-000	12	rs3782567	12	13145613	HEBP1	rs17686635	οο <u>ι</u>	135220622		5.98	0.15	0.59	0.32	
6 milliones 18 Trackfortish minestages 18 Trackfortish 18 <	LMN 2157441 LMN 2157441	77	rs1942/19	8 7	77532672		rs719057	- 1	32411646	HI.A-DBB6	0.01 0.01	19.1	0.34	1.22	
8 mi230468 14 42117794 48 mi230468 14 42117794 11 134 8 mi220468 14 421177746 mi230404 8 28877881 MINDOXI 14 11 134 8 mi20044 8 28040486 HMBOXI mi200446 8 28040486 MINDOXI mi200448 8 28040486 MINDOXI 14 15 26 0.05 0.11 1.34 8 mi200444 8 28040486 HMBOXI mi2004448 8 28040486 MINDOXI 14 16 26 0.05 0.04 0.05 0.04 0.05 0.05 0.04 0.05 <th< td=""><td>LMN_1762861</td><td>9</td><td>rs11660982</td><td>18</td><td>75467313</td><td></td><td>rs2523404</td><td>9</td><td>29695713</td><td>HLA-H</td><td>5.69</td><td>1.00</td><td>0.47</td><td>0.86</td><td></td></th<>	LMN_1762861	9	rs11660982	18	75467313		rs2523404	9	29695713	HLA-H	5.69	1.00	0.47	0.86	
8 misSPATEM 2.1 1.1 1.0 0.46 0.46 0.0 0.46 0.46 0.0 0.46 0.46 0.0 0.46 0.46 0.0 0.46 0.46 0.46 0.0 0.46 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.0 0.46 0.46 0.0 0.0 0.46 0.0 0.0 0.46 0.0	LMN_1720059	œ	rs12435486	14	98670849		rs7837237	œ	28876221	HMBOX1	6.54	0.92	1.11	1.34	
8 mark 500-44 18 13272/3744 mark 100-44 8 28004086 HAIRDOXI 6.58 0.53 0.313 2.52 8 mark 703-1044 8 13272/37444 mark 100-1044 8 28004086 HAIRDOXI 6.58 0.53 0.34 0.44 8 mark 200-1044 8 110-1047 6.00 0.33 0.34 0.44 8 mark 200-1044 8 110-1047 6.00 0.33 0.04 0.04 1 mark 200-104 1 24240802 HSPC157 6.51 0.00 0.20 0.04 1 mark 200-104 1 12240802 1 22440922 HSPC157 6.01 0.00 0.02 0.02 1 mark 200-104 1 12440000 1 1244000 1 0.00 0.03 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.	LMN_1720059	00	rs2837803	21	42112794		rs4732890	œ	28751381	HMBOX1	6.62	0.05	1.01	0.46	
8 18257739 18 MBOX 18757259 18 MBOX 187572461 18 MBOX 187572461 18 MBOX 187572461 18 MBOX	LMN_1720059	00	rs4765451	12	127237464		rs8180944	œ	28904086	HMBOX1	5.80	0.39	3.13	2.52	
8 PRESIDENTAL 8 20040468 HAIRDOX 180267924 180267024 HAIRDOX 18026702 180267	MN_1720059	00	rs587639	00	132725731		rs7837237	00	28876221	HMBOX1	6.58	0.55	0.34	0.44	103.850
8 FINALIZADIA 1.000000000000000000000000000000000000	MN_1720059	x 0 0	rs8180944	20 0	28904086	HMBOXI	rs4553956	ကျေး	189533772		88.9	3.38	0.03	2.20	
1 refectors 5 1 (2002) 488 6 1 (2002) 10 (2002) 1	LMIN_1720059	x 0 0	rssisus44	× -	110807444	HMBOAI	rs/810884	- 0	158275926	TADOAL	0.12 7.7	0.34	0.00	0.02	
1 rie5558 1 1 rie5568 2 16 S888207 3 rie456478 3 1 2439920 20 HSPCIST 641 5.5 1 rie5563 4 16 46486900 rie454783 1 2439920 1 HSPCIST 641 6.5 1 rie558 5 12 131228983 CWP10L1 rie454783 1 2439920 1 6.5 0.0	LMN 2101920	0 10	rs6894268	3 10	179032488		rs4700810	0 10	178991794	IMBOAI	20.50	0.00	3.01	10.37	0.041
1 red003164 2.0 red646800 red646800 <td>LMN_3194087</td> <td></td> <td>rs555812</td> <td>16</td> <td>88882257</td> <td></td> <td>rs4654783</td> <td>·</td> <td>22439520</td> <td>HSPC157</td> <td>5,51</td> <td></td> <td>i)</td> <td></td> <td></td>	LMN_3194087		rs555812	16	88882257		rs4654783	·	22439520	HSPC157	5,51		i)		
1 raf062789 12 12129883 1 2143870 RSPC157 6.61 16 raf064789 1 2243870 RSPC157 6.61 0.02 0.29 16 raf05499 1 1316249 1 243876 0 0 0 0 0 0 0 16 raf05492 16 11623 IL32 RSPC1473 6.64 0 <t< td=""><td>LMN_3194087</td><td>-</td><td>rs6063164</td><td>20</td><td>46486900</td><td></td><td>rs4654783</td><td>-</td><td>22439520</td><td>HSPC157</td><td>6,51</td><td></td><td></td><td></td><td></td></t<>	LMN_3194087	-	rs6063164	20	46486900		rs4654783	-	22439520	HSPC157	6,51				
1 raf764969 16 0.0846648 CWP 191.1 raf4664783 1 24749650 G 48 O.09 O.29 16 raf56494 16 3116628 L.22 raf56499 16 3116628 L.25 0.09 0.09 0.02 0.04 16 raf56444 19 2266423 L.82 raf157499 16 3116628 L.25 0.09 0.02 0.04 0.02 27 raf56444 11 254644 0.0 <th< td=""><td>LMN_3194087</td><td>-</td><td>rs662739</td><td>12</td><td>121229893</td><td></td><td>rs4654783</td><td></td><td>22439520</td><td>HSPC157</td><td>6.61</td><td></td><td></td><td></td><td></td></th<>	LMN_3194087	-	rs662739	12	121229893		rs4654783		22439520	HSPC157	6.61				
16 rand/1949 16 3115028 IL32 rand/1999 12 3115078 IL32 6.90 0.19 0.50 0.29 7 rand/1954 16 81604771 rand/1990 16 3116028 IL32 6.50 0.019 0.29 0.29 7 rand/1954 16 81603771 rand/1959 rand/1959 17 7 28288174 17 6.64 0.02 0.26 0.02 0.20 2 rand/1958 12 3806773 7 28288174 1 6.64 0.02 0.26 0.02 0.02 0.02 0.02 0.03 <	LMN_3194087	1	rs7088558	10	101884937	CWF19L1	rs4654783	1	22439520	HSPC157	6.48				
16 rsv60404 19 25600423 rsv165094 19 25600423 rsv16549 16 11662499 16 11662499 17 288174 0.69 0.69 0.23 0.44 21 rsv57555 12 47970693 RCN115 rs442199 11 5532465 1.66 0.69 0.02 0.05	LMN_1778010	16	rs1554999	16	3115628	IL32	rs4759890	12	131757163		6.90	0.19	0.50	0.29	
9 resolvation 10 resolvation 10 <td>LMN_2368530</td> <td>16</td> <td>rs765044</td> <td>19</td> <td>2560423</td> <td></td> <td>rs1554999</td> <td>16</td> <td>3115628</td> <td>IL32</td> <td>5.53</td> <td>0.69</td> <td>0.23</td> <td>0.44</td> <td></td>	LMN_2368530	16	rs765044	19	2560423		rs1554999	16	3115628	IL32	5.53	0.69	0.23	0.44	
7 9 1 9 9 6 6 0	LMN_1811301	6	rs8044524	16	81603771		rs1127152	6	139335599	INPP5E	5.58	1.46	0.84	1.55	
21 re2186344 21 350405676 MCNALIS re424299 11 5570771 5.54 0.65 0.93 0.73 21 re4242004 13 84540713 KRRDLI re424206 3 101919433 KFELCI 5.53 0.08 0.89 0.37 22 re4242006 2 45100012 re444288 1 101919433 KFELCI 5.53 0.08 0.89 0.37 4 re8815053 4 10000220 1 20384502 A.74 0.06 0.09 0.08 0.37 4 re1552056 1 1000520 1 20384502 A.74 0.04 0.05 0.09 0.03 0.04 0.03 0.04 0.05 0.03 0.04 0.05 <td>LMN_1682727</td> <td>-</td> <td>rs757355</td> <td>12</td> <td>47970693</td> <td></td> <td>rs849341</td> <td>-1</td> <td>28288174</td> <td></td> <td>8.16</td> <td>0.02</td> <td>0.26</td> <td>0.02</td> <td></td>	LMN_1682727	-	rs757355	12	47970693		rs849341	-1	28288174		8.16	0.02	0.26	0.02	
3 Free49016 1 S5324655 KHK2DL1 Free41959 4 74 0.46 0.89 0.77 2 Free42916 1 9.5324655 KHK2DL1 Free421965 4 183109012 0.88 0.28 0.77 2 Free421067 2 4 183109012 Free421065 3 119119591 KFELC1 5.53 0.08 0.28 2 Free421067 3 12602688 Free1240022 1 207880501 LAPS 0.024 0.04 0.09 0.37 1 Free180102 15 56971685 Free170002 1 207880501 LAPS 1 2.2 0.04 0.09 0.77 1 Free180102 15 56973681 Free170002 1 207880501 LAPS 1 0.04 0.09 0.77 1 Free18002 15 56973681 Free17700 1 2.24 0.04 0.09 0.07 0.01 0.03 0.05	LMN_1675756	21	rs2186344	21	39606769	KCN315	rs424299	11	5570771		5.64	0.65	0.13	0.33	
3 Fig3419034 1 S4591119 Fig44283 3 19918433 M.ELLO1 5.53 0.00 0.08 0.33 4 Fig4819036 2 41519362 L3MBTL2 7524903 KFELO1 5.53 0.04 0.08 0.33 4 Fig481906 2 41519362 L3MBTL2 7508200 1.03834862 0.34 0.09 0.09 0.08 0.09 1 Fig52014 1 20387662 1 203880821 LDLRAPI 6.00 0.03 0.04 0.09 1 Fig52042 1 20388082 LDLRAPI 6.00 0.35 0.04 0.03 1 Fig52042 1 20388082 LDLRAPI 6.00 0.35 0.04 0.03 1 Fig1245032 1 2038802 LDLRAPI 6.00 0.35 0.04 0.03 1 Fig124330 Fig14407 1 2 1 2 0.04 0.03 0.03	LMN_1691803	19	rs649216	19	55324635	KIR2DL1	rs6419960	4 (189055298		4.74	0.46	0.89	0.77	
2 FEROLISCO 24 LASHORICAL FEROLISCO A. F. L. L. L. CO. C. L. A. CO. C. C. L. A. CO. C.	LMN_1811104	ကင	rs4349034	13	84597119		rs727905	n 0	119119433	KTELC1	5.53	0.08	0.80	0.37	
4 F87042087 9 132602868 CALL 1 T7568240 4 T7588900 LAP3 5.72 0.24 0.47 0.31 1 F81562032 1 208877662 1 208877662 1 208877662 1 208877662 1 208877662 1 208877662 1 208877662 1 208877662 1 208877662 1 208877662 1 20887768 1 20887863 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878683 1 208878883 1 208878883 1 208878883 1 208878883 1 208878883 1 208878883 1 208878883 1 208878883 1 208878883 1 208878883 2 20888883 2 20888883	LMN 2336109	o cc	rs0813933	* 66	41510362	LaMBTL9	rs0414263	o -	033438050	PIEDO	. r.	0.04	0.00	00.00	
1 rs1891432 1 203877662 rs10900520 1 203780591 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 203877662 1 20378052 LDLRAP 1 20889622 LDLRAPP 6.00 3.5 0.40 0.35 0.03 <th< td=""><td>LMN 1683792</td><td>4</td><td>rs7042087</td><td>10</td><td>132602868</td><td>- Towns</td><td>rs7658240</td><td>4 4</td><td>17588950</td><td>LAP3</td><td>7.72</td><td>0.24</td><td>0.0</td><td>0.0</td><td></td></th<>	LMN 1683792	4	rs7042087	10	132602868	- Towns	rs7658240	4 4	17588950	LAP3	7.72	0.24	0.0	0.0	
1 rsi255032 15 59071635 re6887605 1 25889622 LDLRAP1 6.00 3.5 6.03 6.03 6.03 6.03 6.03 6.03 6.03 6.03 6.03 6.04 0.03 6.03 6.04 0.03 6.04 0.03 6.04 0.03 6.04 0.03 6.04 0.03 6.04 0.03 0.03 0.03 0.04 0.03	LMN-1769782	٠.	rs1891432		203877662		rs10900520	٠	203780591		19.16	18.60	11.22	29.24	0.097
17 F12450521 17 20083392 F11149777 5 170608360 5.16 0.35 0.40 0.34 19 F18450521 19 26820322 19 7161437 7.16 0.23 0.03 0.05 15 F18124726 15 101120963 LINS1 rs210849 18 7.16 1.2780431 6.89 0.13 0.03 0.05 16 rs977786 15 101120963 LINS1 rs2108409 0.13 0.13 0.13 0.05 0.13 0.05 0.13 0.05 0.13 0.05 0.13 0.05	LMN_1809040	1	rs1552032	15	59971635		rs6687605	-	25889632	LDLRAP1	6.00				
19 res8269582 19 54827248 LILRAD re714789 18 71501497 6.13 0.23 0.05 0.05 15 re91247226 15 101120963 LILRAD re3177857 10 127804431 10 10 0.03 0.05 0.03 0.05 <	LMN_2412214	17	rs12450521	17	26083392		rs11749727	ю	179608360		5.16	0.35	0.40	0.34	
15 res1024726 15 101120963 LINN1 res107804 1 778046451 5.89 0.13 0.13 0.13 0.13 0.15 0.015 <t< td=""><td>LMN_2357419</td><td>19</td><td>rs3859532</td><td>19</td><td>54827248</td><td>LILRA5</td><td>rs714789</td><td>18</td><td>71561497</td><td></td><td>6.13</td><td>0.23</td><td>0.03</td><td>0.02</td><td></td></t<>	LMN_2357419	19	rs3859532	19	54827248	LILRA5	rs714789	18	71561497		6.13	0.23	0.03	0.02	
19 res0009591 2 51515350 res01005 LRRC25 5.68 0.11 0.35 0.15 12 res77788 2 51515350 res04675 1 1843675 1 78946879 5.68 0.11 0.35 0.15 12 res168029 12 66734641 LYZ res168029 1 60.15 0.03 0.01 0.01 0.03 0.01 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.03 0.01 0.03 0.03 0.01 0.03 0.03 0.01 0.03 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0.01 0.03 0	LMN_2338197	15	rs11247226	15	101120963	LINS1	rs1278387	10	127804531		5.89		0.13		
6 FF97T785 6 6588881 LX86 FF8154875 1 78494879 5.61 0.13 0.15 0.07 12 FF2168029 1 6 6734641 LX86 FF3168029 0.15 0.015 0.07 12 FF2168029 1 8 77276964 TF2168029 1 6 774641 LX8 0.15 0.015 0.017 12 FF17820 1 9 774641 LX8 1 0.15 0.015 <td< td=""><td>LMN_2150196</td><td>19</td><td>rs6009951</td><td>22</td><td>51151350</td><td></td><td>rs8101804</td><td>19</td><td>18496107</td><td>LRRC25</td><td>2.68</td><td>0.11</td><td>0.35</td><td>0.15</td><td></td></td<>	LMN_2150196	19	rs6009951	22	51151350		rs8101804	19	18496107	LRRC25	2.68	0.11	0.35	0.15	
12 FEATOROGO POLITION CONTRICTOR CONT	LMN-1807825	9 5	rs977785	٥ :	6558881 60794641	LY86	rs1543675	1 1-	78946879		0.0 10.0 10.0	0.13	0.15	0.07	
12 FIGURATION FOR TAXABLE AND LINE	I MIN 2162072	1 1 2	rs2100029	7 0	77276064	717	rs11901/20	- 0	60794641	17.7	0.30	0.13	0.03	0.03	
7 rs/783715 7 1923385 MADILI rs/6414306 3 127011798 ADDLLB 5.62 0.25 0.88 0.59 20 rs/783718 13 102020346 rs/1060034 2 43531864 MAPPILC3A 5.73 0.63 1.11 1.09 20 rs/106000 9 78225815 rs/10600034 2 1.18 0.79 0.27 0.54 3 rs/1063043 12 12 1.70 MAPLC3A 7.96 0.79 0.27 0.54 3 rs/1063043 12 12 1.8 1.71 1.09 0.27 0.54 3 rs/106304 13 97100681 rs/13069559 3 152187431 MBNL1 7.71 0.43 5.36 4.158 1 rs/10630 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	LMN 2162972	12	rs2168029	12	69734641	LYZ	rs2253135	1 6	130319560		6.31	0.43	0.36	0.49	
0 re798378 1 102020346 re3006699 6 43351864 MAD1LIBP 5.93 0.63 1.11 1.09 20 re3045607 21 2943586 re30606034 20 33351864 MAP1LC3A 5.78 1.18 1.10 1.09 3 re1086900 9 7822816 re3060659 3 152187431 MBNL1 7.78 0.79 0.27 0.54 3 re1104596 1 97100681 re133069559 3 152187431 MBNL1 7.71 0.43 5.36 4.58 3 re1648456 1 7 9.4648239 re133069559 3 152187431 MBNL1 7.71 0.43 5.36 4.58 3 re16864367 3 152186431 MBNL1 7.71 0.43 5.36 4.58 4 re16864367 1 1 604708 re13069559 3 152187431 MBNL1 7.69 0.91 5.82 5.23	LMN_2358069	1	rs7783715	1	1923385	MAD1L1	rs6414306	m	127011798		5.62	0.25	0.88	0.59	
20 re9746607 21 29453869 re6006034 20 33531864 MAPLIC3A 5.78 1.18 3 re10869600 9 78225815 re13069559 3 152187431 MBNL1 7.96 0.79 0.27 0.54 3 re11053043 12 9932070 re13069559 3 152187431 MBNL1 7.36 0.79 0.27 0.27 0.53 1.34 3 re1104516 7 9 152187431 MBNL1 7.38 1.43 0.63 1.34 3 re1104516 7 9 14 0.43 5.36 4.58 3 re10864367 3 152234166 re1306759 3 152187431 MBNL1 7.10 0.43 5.80 5.53 3 re21867 7 6644708 re13069559 3 152187431 MBNL1 7.10 0.91 5.80 5.53 3 re21867 7 6644708 re13069559 <t< td=""><td>ILMN_1694711</td><td>9</td><td>rs7983718</td><td>13</td><td>103203146</td><td></td><td>rs1096699</td><td>9</td><td>43528441</td><td>MAD2L1BP</td><td>5.93</td><td>0.63</td><td>1.11</td><td>1.09</td><td></td></t<>	ILMN_1694711	9	rs7983718	13	103203146		rs1096699	9	43528441	MAD2L1BP	5.93	0.63	1.11	1.09	
3 re10656600 9 78225815 re13069559 3 152187431 MBNL1 7.96 0.79 0.27 0.54 3 re11053043 13 9932070 re13069559 3 152187431 MBNL1 7.71 0.08 2.21 0.54 3 re1104596 13 97100681 re13069559 3 152187431 MBNL1 7.71 0.43 5.36 4.58 8 re10646467 3 152187431 MBNL1 7.71 0.43 5.36 4.58 8 re2080026 6 14067127 re13069559 3 152187431 MBNL1 7.70 0.43 5.36 4.58 8 re208002 6 14067127 re13069559 3 152187431 MBNL1 7.10 0.91 5.80 5.53 8 re201867 14 6604708 re13069559 3 152187431 MBNL1 6.05 0.52 0.72 0.70 8 re2213800<	LMN_1776188	20	rs974607	21	29435869		rs6060034	20	33351864	MAP1LC3A	5.78	1.18			
3 res1045964 12 9320770 res13069559 3 152187431 MBNL1 6.70 0.08 2.21 1.37 3 res104596 3 res1045450 3 res1045430 1.34 0.68 2.21 1.37 3 res104566 3 res1069559 3 152187431 MBNL1 7.71 0.43 5.36 4.58 3 res10864367 3 res1080559 3 152116652 1.49 16.25 24.74 41.56 3 res2080266 6 114067127 res13009559 3 152187431 MBNL1 7.63 0.91 5.82 5.23 3 res213800 22 second 3 152187431 MBNL1 6.05 0.52 0.72 5.23 3 res213800 22 second 3 152187431 MBNL1 6.05 0.52 0.72 5.23 4 res213800 2 percentary res106559 3	LMN-2313158	က	rs10869600	6	78225815		rs13069559	က	152187431	MBNL1	7.96	0.79	0.27	0.54	
3 res1064566 13 97100881 res13069559 3 152187431 MBNL1 7.38 1.43 0.63 1.34 3 res1064566 3 152187431 MBNL1 7.78 1.43 0.63 1.34 3 res1664367 3 152234166 res13009559 3 152187431 MBNL1 7.10 0.43 5.80 5.80 3 res2030296 6 11467727 res13009559 3 152187431 MBNL1 7.10 0.91 5.80 5.53 3 res218671 1 604708 res13009559 3 152187431 MBNL1 6.05 0.52 0.72 0.70 3 res2035682 19 10538535 res13009559 3 152187431 MBNL1 6.05 0.72 0.70 4 res2014467 14 99770138 res13009559 3 152187431 MBNL1 6.94 1.67 2.22 5.30	LMN_2313158	n	rs11053043	12	9932070		rs13069559	n	152187431	MBNL1	6.70	0.08	2.21	1.37	
3 results resu	LMN_2313158	n	rs1164596	13	97100681		rs13069559	0	152187431	MBNL1	7.38	1.43	0.63	1.34	
3 F815025436/ F82030926 5 15223440 5 4 41.30 3 F82030926 6 144067127 rs13069559 3 152187431 MBNL1 7.63 0.91 5.80 5.53 3 rs218671 17 6604708 rs13069559 3 152187431 MBNL1 7.63 0.62 5.82 5.23 3 rs218671 17 604708 rs13069559 3 152187431 MBNL1 6.05 0.52 0.72 0.70 3 rs2201360 22 343069559 3 152187431 MBNL1 6.05 0.52 0.72 0.70 4 18 rs20136802 19 16038555 3 152187431 MBNL1 6.94 1.67 0.70 5 rs2014467 14 99770138 rs33069559 3 152187431 MBNL1 6.94 1.67 5.30	LMN_2313158	m d	rs11981513	٠- د	94648239		rs13069559	က	152187431	MBNL1	7.71	0.43	5.36	80.4	-
182013360	LMN_2313158	က	rs16864367	n	152234166		rs13079208	က	152116652		13.49	16.25	24.74	41.56	0.118
3 FF2LR071 17 0004703 FE2LR073 102187431 MBNL1 6.05 0.02 0.72 3 FF2LR075 12 FF2LR073 MBNL1 6.05 0.02 0.72 3 FF2LR073 18 FF2LR073 MBNL1 6.04 0.52 0.72 4 FF2LR073 18 FF2LR073 MBNL1 6.94 1.67 1.67 5 FF2LR073 FF2LR073 MBNL1 6.94 4.13 2.22	LMN_2313158	ကေ	rs2030926	10	114067127		rs13069559	ကင	152187431	MBNLI	7.10	0.91	5.80	5.53	
1 12215300	ILMN-2313138	0 0	rs219671) T	34291750		rs13069559	0 0	152187431	MBNL	6.05	0.02	0.07	0.70	
3 rs/201467 4 99770138 rs13069559 3 15/2187431 MBNL1 5.74 4.13 2.22	II.MN 2313158	o et	rs2305802	5 -	16038535		rs13069559	om	152187431	MBNL1	6.00	1.00			
	ILMN_2313158	n	rs2614467	14	99770138		rs13069559	n 00	152187431	MBNL1	5.74	4.13	2.22	5.30	

ļ	Distance / Mb ^h										0.015																10 401	105.01			38.948			0.050									0.010				
raines	Metag	3.02	0.00	10.01	9.28	0.02	0.02	0.27	0.26	0.14	28.73	1.71	0.41	0. I.4	0.00	0.02	0.40	0.04	1.35	0.19	0	0.22	0.46	0.28	2.86	0.50	0.23	0.03	0.03	0.40	1.77	0.04	0.30	30.10	0.81	1.01	2.77	0.23	0.63	0.08	1.12	1.71	12.70	0.22	0.35	90.0	
$-\log_{10} p$ -values	EGCUT	4.33	4.61	10. F	7.89	0.03	0.23	92.0	0.50	0.47	21.91	1.33	0.25	0.30	1.03	0.08	0.27	0.23	1.08	0.18		0.44	0.63	0.25	1.87	0.52	0.50	0.92	0.08	0.15	0.59	0.03	0.43	16.08	0.19	92.0	2.58	0.47	0.88	0.17	1.10	0.44	6.33	0.18	0.34	0.04	
Interaction statistic /	Fehrmann ^f	0.02	0.02	1.32	2.55	0.10	0.03	0.02	0.15	0.03	7.06	1.13	0.61	0.13	0.0	0.05	0.57	0.01	0.97	0.34	0.26	0.14	0.31	0.41	1.87	0.46	0.11	0.29	0.04	0.74	2.00	0.20	0.27	15.12	1.27	0.87	1.10	0.13	0.29	0.12	0.67	2.11	7.51	0.39	0.42	0.24	
meracur	BSGS ^e F	8.39	10.74	100	7.92	6.26	5.56	5.79	6.03	5.82	5.40	4.63	5.76	0.01	10.0	4.17	5.45	5.90	5.64	6.89	5.71	0.50	5.8.0	6.21	5.18	6.31	0.00	0 H	5.70	6.02	5.54	5.65	5.46	0.00 7.00	5.62	6.12	6.86	6.03	6.60	5.50 5.50	0 20 00	2.58	7.31	3.88	6.84	5.90	1
	Associationd	MBNL1	MDINEL		MBNL1	MBP	MBP			MBP		MEGF9	MFN2	MCC19087	MGC13057		MGST3		MPZL2	MRPL36	MRPL43	MRPL52	MRPS10	MRPS10				MVBDC3	MYBPC3		N4BP1	NAAA	NAAA						NAPRT1	NAPRI1				NDUFA12		NOD2	- CHOCK
2112	Pos/Mb^{c}	152187431	152210/431	15223333	152187431	74715653	74715653	155204939	55097534	74715653	74732087	123453281	12050634	1/10009/3 F043644E	50428445	137526799	165600146	154708716	118076069	1782046	102746503	49104016	42158596	42164401	42068689	95514596	26706382	47486885	47529947	134485237	48632478	76870229	76870229	144691243	187445552	167811764	146189057	213386267	144663661	144663661	95376932	234721287	232291471	95386791	183114008	50719103	00000
2	Chr.	m c	00	o 01	. m	18	18	က	D.	18	18	6		1 1	- 1-	- 00		-1	11	n	10	14	9	9	14	14	n -	7 -	: :	1 00	16	4	4 -	ı ox	4	9	7	61	00 0	χo	01	2 73	7	12	8	16	
	rs ID	rs13069559	rs15009009	re16864367	rs13069559	rs2051344	rs2051344	rs1125539	rs2619046	rs2051344	rs4890876	rs966396	rs4846085	rsii/2004/	rs12718598	rs2660665	rs4147592	rs11771552	rs1805	rs750495	rs2863095	rs3811188	rs2395803	rs13217993	rs12431444	rs11160227	rs4973801	rss130120	rs7124681	rs2737422	rs11649236	rs6826085	rs6826085	rs2880124	rs4862705	rs6455553	rs700276	rs7571561	rs2123758	rs2123758	rs930280 rs10882406	rs7577137	rs4973397	rs11107847	rs12490878	rs9302752	2000000
	Associationd							MBP	MBP				100000	MGCISOS		MGC72104		MPZL2							MTMR10					MYOM1			THOO VIV	NAPRTI	NAPRT1	NAPRT1	NAPRT1	NAPRT1		NADAR	NAPSB	NAPSB			NMT2		
* ****	Pos/Mb^{c}	41513423	46979501	40218091 57953139	22101322	15462611	42210985	74715653	74715653	33436367	74747424	51922071	109401737	600470445	82628245	26197931	55779644	118076069	19953193	8436432	80641040	11020271	15063214	52453567	31215935	42795027	42795027	61503110	109550561	3247256	87580855	147638723	37770630	144003001	144663661	144663661	144663661	144663661	48214812	103488089	50882619	50882619	232301670	37101890	15239498	7067773	30000
2	Chr.	4.0	0 2	50	, ro	20	22	18	18	19	18	20	13	- 0	9 1	20	17	11	12	10	16	4.0	20	16	15	21	5 5	77-	# C	18	16	-	7.5	0 00	000	œ	œ	oo ;	55	ء م	13	13	7	22	10	19	-
	rs ID	rs4392535	154755550 204050550	154555555	rs7710738	rs6079849	rs139568	rs2051344	rs2051344	rs4805021	rs8092433	rs13039689	rs7989895	rs12/10090	15074000	rs845787	rs740441	rs1805	rs7316716	rs17469061	rs6564769	rs1950857	rs11698155	rs1420537	rs7178375	rs459498	rs459498	rs459496	rs7322768	rs4798075	rs12444224	rs2707575	rs2071856	rs2123730	rs2123758	rs2123758	rs2123758	rs2123758	rs2208123	rs4743420 rs1405655	rs1405655	rs1405655	rs7563453	rs2746971	rs10906857	rs2967636	2017001100
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are recently	Probe ID ^b	ILMN_2313158	ILMIN_2313130	ILMIN-2313158	ILMN_2313158	ILMN_2331544	ILMN_2398939	ILMN_2398939	ILMN_2398939	ILMN_2398939	ILMN_2398939	ILMN_2290118	ILMN_1651385	ILMIN_1787526	II.MN 1787526	ILMN_1688318	ILMN_1751956	ILMN_1752932	ILMN_1752932	ILMN_1800197	ILMN_2258774	ILMN_1713966	ILMN_1663664	ILMN_1663664	ILMN_2152178	ILMN_1662358	ILMN_1662358	ILMIN_1002330	II.MN 1781184	ILMN_1680344	ILMN_2201966	ILMN_1668605	ILMN-2391512	ILMIN-1710752	ILMN_1710752	ILMN_1710752	ILMN_1710752	ILMN_1710752	ILMN_1710752	ILMN_1710752	ILMN_2109416	ILMN_2109416	ILMN_2121437	ILMN_1737738	ILMN_1656378	ILMN_1762594	1 MIN 900400E
i	Gene ID ^a	MBNL1	MENLI	MBNL1	MBNL1	MBP	MBP	MBP	MBP	MBP	MBP	MEGF9	MFN2	MGC15057	MGC13057	MGC72104	MGST3	MPZL2	MPZL2	MRPL36	MRPL43	MRFL52	MRPS10	MRPS10	MTMR15	MX1	MXI	MAI	MYBPC3	MYOM1	N4BP1	NAAA	NAAA	NAPRT1	NAPRT1	NAPRT1	NAPRT1	NAPRT1	NAPRTI	NAPKIT	NAPSB NAPSB	NAPSB	NCL	NDUFA12	NMT2	NOD2	NEEDS

	Distance / Mb ⁿ					0.039					128:140				120.688			46 389				1.137										11.228	000	0.201												
vaines	Metag		0.17	0.15	2.03	3.86	0.76	0.14	0.07	0.43	0 0	0.82	0.59	0.16	0.32	0.13	0.67	0.24	0.03	0.33	0.48	0.15	0.04	0.56	0.19	0.66	0.46	0.17	1.21	0.12	0.44	0.25	0.04	4.00	0.04	0.27	1.78	0.86	0.15	0.38	1.55	0.09	0.59	0.08	0.47	
Santa - d Olson	EGCUT		0.05	0.46	1.55	0.81	0.46	0.00	0.00	80.0	1.48	1.21	0.44	0.26	0.71	0.09	0.36	0.00	0.01	0.87	1.19	0.42	0.04	0.33	0.42	0.48	0.95	0.13	0.28	0.00	0.14	0.11	0.03	4.47	0.26	0.21	0.64	0.32	0.48	0.08	1.25	0.08	0.84	0.31	0.37	
Constant Property	Fehrmann ^I		0.47	0.03	1.27	4.12	0.87	0.42	0.30	1.20	0.13	0.25	0.66	0.19	0.09	0.34	0.87	0.03	0.20	0.02	00.00	0.05	0.16	0.31	0.12	0.72	80.0	0.36	1.69	0.37	0.81	0.53	0.19	0.03	0.00	0.44	1.95	1.18	0.03	0.80	1.03	0.25	0.28	0.03	0.58	
***************************************	e e	5.45	6.13	5.44	8.59	4.13	4.38	5.64	5.00	2.42	5.43	6.04	5.59	6.20	5.85	5.74	5.64	5 C. C.	5.60	5.23	7.11	4.12	0.35 11	5.15	5.81	5.63	5.72	5.61	5.65 0.85	7.00	6.43	7.34	5.60	4.01	5.14	5.44	4.58	5.42	.5.00 0.00	5.90 70	5.75	6.55	6.42	6.38	5.23	
	Association	NRBF2		NUDT18			OASI	OFTN	OSTEL	Colfi	OVGP1	OVGP1	HPCAL4		PEX5	PEX5	PFAAP5	PHCA				PISD	PNKU PNPI A7	PPFIRP2	PPP2B3C	PPP2R5A	PPP2R5A	PPP2R5A	PPP2R5A	PPF2R3A	PRDX5		1000	PSMB1	PSMB1	PSMB1		PSMB1	PTDSS1	PTDSSI	ODPR.				RCN1	
	Pos/Mb^{c}	65133822	52334047	21964378	163997467	113409260	00000	13169066	77755460	179590959	111992823	111969719	40139553	21395989	7364442	7364442	33126737	76708086	61728597	30398876	18236681	32097775	140467106	7559930	35619816	212447167	212447167	212447167	212447167	21244/16/	64082807	12639800	31497346	170877444	170890384	170823379	225797957	170877444	5221825	5221825	17526682	70235726	120161117	26938488	32136436	
	Chr.	10	-	00	9	12	12	0 :	10	n id	-	-	1	က	12	12	13	# -	;	14	-1	22	N C	ñ <u>-</u>	14	1	1	-			11	16	8 5	7 9	9	9	1	9	11	I [4	12	11	1.5	11	
	rs ID	rs7923609	rs6588415	rs1005901	rs1047944	rs2072133	rs3741981	rs17512962	18990039	182213110	rs1264898	rs1264894	rs784600	rs2731939	rs4329748	rs4329748	rs7328733	rs10736812	rs2065841	rs10498313	rs954627	rs6518754	rs4672884	rs928046	rs11156875	rs12120009	rs12120009	rs12120009	rs12120009	rs12120009	rs11600990	rs10492793	rs958127	rs13207114	rs6928843	rs9295415	rs2769689	rs13207114	rs11036212	rs11036212	rs10020773	rs7305307	rs7951628	rs1863464	rs4922579	
7	Association									OSTE1			PAM	PCYOX1L			1000	1951	PIK3IP1	PISD	PISD												C21ORF57				PSMB1						RABAC1	AKTIP		
4	Pos/Mb^{c}	56157341	240680022	25453482	113480510	113448652	49160255	74286646	20002343	77755469	240132968	140148107	102149795	148726162	128052636	27246462	49151303	123097386	31675185	32263131	31999127	33234931	158781604	4527109	58350896	166399467	123595064	66222691	107417238	27148475	95040482	23867776	47931653	121774705	43983954	30347832	170890384	131727816	95478823	76598123 126852438	106348246	33375704	42462788	53526551	41147155	
ı	Chr.	20		11	12	12	19	16	1 4	7 0	- 0	· 60	ю	IJ	12	15	7.7	e -	22	22	22	22	ر د م	20	2 12	7	12	13	11	0 0	14	16	5 5	7 -	18	20	9	12	14) T	9	22	19	16	12	
	rs ID	rs6025645	rs4852124	rs5017351	rs11613438	rs13311	rs2892233	rs/192613	rs2629019	rs1/100193	rs10802822	rs347331	rs28092	rs2438490	rs10444467	rs7495797	rs131969	rs12962555 rs493642	rs4141404	rs470072	rs6518752	rs715572	rsb869411	rs11639998 rs911019	rs12914603	rs10930170	rs12423255	rs1889083	rs682334	rs7871178	rs8019823	rs2188355	rs1029231	rs3862607	rs4890648	rs6060930	rs6928843	rs7299749	rs2353567	rs4969205	rs4946705	rs241730	rs1075728	rs9931702	rs10879131	
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Table Holesonder	Probe ID ^D	ILMN_3237385	II.MN 1800897	ILMN_1787885	ILMN_1658247	ILMN_1658247	ILMN_1675640	ILMN-2381899	ILMIN 1742456	II.MN 1742456	II.MN 1734542	ILMN_1734542	ILMN_2313901	ILMN_1815951	ILMN_1660232	ILMN_1660232	ILMN_1797893	II.MN 1812552	ILMN_1719986	ILMN_1793934	ILMN_1793934	ILMN_1793934	ILMIN_I774604	ILMN 1675656	ILMN_1662617	ILMN_1738784	ILMN_1738784	ILMN_1738784	ILMN_1738784	ILMN 1738784	ILMN_1711606	ILMN_1713603	ILMN_1675038	II.MN 1789176	ILMN_1789176	ILMN_1789176	ILMN_1789176	ILMN_1789176	ILMN_1743049	ILMIN_1743049	ILMN-1672443	ILMN_1803197	ILMN_2207363	ILMN_1756999	ILMN_1800276	
1	Gene ID ^a	NRBF2	NRD1	NUDT18	OAS1	OAS1	OASI	OFTN	OSEFES OSEFES	OSTEI	OVGP1	OVGP1	PAM	PCYOX1L	PEX5	PEX5	PFAAP5	PHCA	PIK3IP1	PISD	PISD	PISD	PNKU	PDFIRP2	PPP2R3C	PPP2R5A	PPP2R5A	PPP2R5A	PPP2R5A	PPP2R5A	PRDX5	PRKCB1	PRMT2	PSMB1	PSMB1	PSMB1	PSMB1	PSMB1	PWP1	PWFI	ODPR	RAB3IP	RABACI	RBL2	RCN1	

- 1	Distance / Mb ⁿ										0.135																								0.324	14.040												
alues	Metag	1.17	0.06	0.21	0.26	0.70	0.0	0.64	0.13	1.28	17.24	0.38	0.02	0.19	0.15	0.22		1.17	0.15	0.10	0.31	0.35	0.30	0.0	0.17	0.09	90.0	0.19	1.24	0.40	0.26	0.00	1	0.72	23.22			0.83	90.0		0.33	0.31	0.30		0.14	0.24	0.03	C 10
$-\log_{10} p$ -values	$EGCUT^{t}$	1.23	0.10	0.33	0.60	0.21	0.44	0.46	0.30	0.52	14.41	0.73	90.0	0.20	0.37	0.45		1.73	0.51	0.06	0.51	0.12	0.51	0.18	0.18	0.24	0.10	0.13	0.82	0.07	0.58	0.03	1	1.03	10.96			1.41	0.00		0.12	0.17	0.24	0.00	0.16	0.31	0.15	0.76
Interaction statistic /	$Fehrmann^{I}$	0.61	0.14	0.21	0.08	0.42	60.0	0.71	0.11	1.48	3.79	0.13	0.09	0.32	0.10	0.13		0.22	0.02	0.31	0.21	0.70	0.20	0.32	0.29	0.00	0.15	0.39	1.10	0.86	0.09	0.39		0.29	13.11			0.13	0.34		0.67	0.57	0.40	0.01	0.26	0.28	0.03	16.0
Interacti	BSGS ^e I	5.66	5.74	5.12	5.71	0.48 8 - 1	0.11	- 62.53	6.27	4.32	86.4	5.55	5.46	5.86	4.59	4.33	6.48	5.70	5.50	5.67	5.60	5.52	5.97	7.40	5.74	5.47	5.70	6.15	88.0	5.95	5.52	0.10	6.11	09.9	7.31	6.08	0.00	6.45	5.59	5.44	5.65	00 i	0.01	0.00	6.14	5.47	5.55	E 0
-	Association	RERE	KEKE	REKE	KEKE	DNACEG	DIN ASEO					RPL23AP7				RPL8	SEC13	SEMA4A	SESN3	SESN3		PPBP	PFBF	SH3GLB2		SLC22A18			SLC41A3	0	SLC46A3	SMC	SNHG8	SNORD14A		SNOKD89	SNORDS9			SPATA5L1		STYXL1	TITEM	TUFM	SURF6	SYTL2	THBS3	COULTE
SNF 2	Pos/Mb^{c}	8501786	82.1008	8501786	820T.V86	21182800	54668512	36348968	201983242	201983242	89513234	114450028	138038093	66137260	234585790	145984615	10342876	156147326	94906111	94906111	134606425	56849749	56849749	131785369	60489510	2923826	153224179	241678528	125801067	174598073	29259349	65800982	119225940	17291499	17015557	101889306	101889306	81888905	193706323	45652086	72509713	75616105	180439235	28550667	136281753	85495269	155162067	000000
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	rs ID	rs301819	rs301819	rs301819	rs301819	rs/324305	rs4884857	rs11706900	rs2819365	rs2819365	rs2965817	rs4849261	rs17495030	rs1502991	rs1619856	rs2958482	rs696221	rs7695	rs684856	rs684856	rs7004947	rs1354034	rs1354034	rs17455517	rs6842739	rs367035	rs3110874	rs3772054	rs6771703	rs7701916	rs7981190	rs11677815	rs705837	rs214097	rs6486334	rs750783	rs/50/83	rs7185362	rs1472075	rs4774580	rs1000620	rs17685	18939294 100707084	rs3785354	rs3118663	rs485485	rs4072037	2000100
	Association					KNASEO		RNF167					RPL36AL	RPL36AL	RPL8						NEW NS				SIRPG		SLC22A18	SLC22A18		SLC45A4		SMOX						SNUPN	SNUPN			-	SOLFZ					
SNF I	Pos/Mb^{c}	24987865	135248366	13174312	112844086	8106591	487556	4839930	46127549	67153386	89648580	80320056	50103816	50020817	145984615	4741304	80913946	95388015	104412137	46591793	94906111	43893658	00383979	18196922	1612819	52181798	2923826	2923826	24616743	142337734	55602091	4161500	133050233	46259108	17339127	115929241	26778066	46376528	46376528	41117869	90174526	104947517	40153148 74999054	40119768	56013994	103410782	95422867	00000000
	Chr.	14	4	19	n ;	101	12	17	21	17	16	16	14	14	œ	20	16	ທ	14	15	11	11,	o 4	2.1	50	19	11	11	11	ω į	17	20	6	15	11	Ν,	1 10	21	21	19	13	14	07.	210	20	13	11	,
	rs ID	rs4982958	rs/69/290	rs11085829	rs3852011	rs11628398	re238230	rs400688	rs1107121	rs8071611	rs352935	rs1401202	rs3007033	rs4900928	rs2958482	rs4143674	rs4889214	rs17085428	rs12147460	rs355391	rs684856	rs10838191	rs2545385	rs1034120	rs1535883	rs11673260	rs367035	rs367035	rs1912136	rs6985508	rs949805	rs8118315	rs1105621	rs1520429	rs2634462	rs10445863	rs1150522 rs2135064	rs8134646	rs8134646	rs1131620	rs2221406	rs4073164	rs11700065	rs2836657	rs6099626	rs1375719	rs1939875	02014080
	Chr.		_	н,	7;	4 -	1 1	17	-	-	16	61	14	14	œ	œ	n	-	11	Ξ;	11	9 (و و	0 0	20	11	11	11	က	oo (13	30	4	11	11	20 0	71 (7)	15	15	15	= '		07.	91	6	11	1	-
Expression trait	Probe ID ^b	ILMN_1802380	ILMN-1802380	ILMN_2327795	ILMIN_2327795	ILMIN-1780533	II.MN 1794726	ILMN_1794726	ILMN 1738347	II.MN 1738347	ILMN_2413278	ILMN_2222750	ILMN_2189933	ILMN_2189936	ILMN_1764721	ILMN_1764721	ILMN-3297880	ILMN_1702787	ILMN_1694027	ILMN_1694027	ILMN_1694027	ILMN_1762764	ILMIN-1762764	ILMN 2158336	ILMN_1771801	ILMN_2382505	ILMN_2382505	ILMN_2382505	ILMN_2356111	ILMN_1745778	ILMN_1658639	II.MN 1775380	ILMN_3309349	ILMN_1799381	ILMN_1799381	ILMIN-3238662	ILMN 3238662	ILMN_1733932	ILMN_2364535	ILMN_1729179	ILMN_1717052	ILMN_2210729	ILMIN_2345142	ILMN 2336133	ILMN_1778032	ILMN_2336609	ILMN_1804663	11 MAN 100 4009
	Gene ID ^a	RERE	KEKE	KEKE	KEKE	KNASEO	RNF167	RNF167	RNPEP	RNPEP	RPL13	RPL23AP7	RPL36AL	RPL36AL	RPL8	RPL8	SEC13	SEMA4A	SESN3	SESN3	SESN3	SH3BGRL2	SH3BGRLZ	SH3GLB2	SIRPG	SLC22A18	SLC22A18	SLC22A18	SLC41A3	SLC45A4	SLC46A3	SMOX	SNHG8	SNORD14A	SNORD14A	SNOKD89	SNORD89	SNUPN	SNUPN	SPATA5L1	STARD10	STYXL1	SULFZ	SULTIA4	SURF6	SYTL2	THBS3	TIDES

- 1	Distance / Mb ^h				0.122																			0.031	10101	161.21				5.389														45.345		
values	Metag	0.70	0.70		145.78	3.67	0.80	0 00	0.03	2.87	00.9	8.00	2.27	0.19	3.51	7.30	10.72	9.20	4.47	;	0.32	0.07	0.62	4.09	0.29	1.07	0.68	0.08	0.59	0.16	0.25	0.22	0.16	0.08	1.01	0.56	0.02	0.13	0.40	0.69	1.69	0.39	90.0			
$-\log_{10} p$ -values	$EGCUT^{f}$	1.34	0.40		45.78	3.09	0.99	1.10	0.07	0.77	3.33	9.61	1.52	0.33	3.62	0.15	08.80	6.96	5.75		0.12	0.15	0.17	1.89	0.40	1.60	0.87	0.18	0.47	0.24	0.65	0.36	0.33	0.07	0.78	0.55	0.02	0.26	98.0	0.90	1.23	0.91	0.18			
Interaction statistic /	Fehrmann ^f	0.06	0.10	0.76	81.55	1.55	0.40	2.41	80.0	3.06	3.72	0.04	1.57	0.19	0.90	3.31	3.00	3.36	0.10		0.64	0.11	1.03	3.19	0.28	0.23	0.37	0.12	0.63	0.21	0.04	0.20	0.15	0.24	0.85	0.51	0.14	0.14	80.0	0.36	1.20	0.04	0.07			
Interactio	BSGS _e F	5.70	6.79	11.09	12.16	8.12	8.02	7.37	6.95	6,93	6.21	7.30	6.70	5.92	00 i	00.00	0.80	6.22	9.44	5.60	5.79	5.61	5.52	80 i	5.61	5.07	6.92	7.79	6.43	6.38	7.08	5.86	6.27	7.73	7.73	8.10	6.71	7.34	7.05	7.41	5.92	6.46	6.00	5.01	5.51	0.34
	Associationd	TMED4	TMEM149	TMEM149	TMEM149															TMEM63A	TMEM80	IRF5	IRF5	0	TRAPPC4	I LATI C4								TRAPPOR	TRAPPCS	TRAPPC5		1	RAPGEF1	TBEM1	TREMI	TRIM38	TSPAN14	TSPAN32		
SNF 2	Pos/Mb^{c}	44581986	36219525	36219525	36147315	4799159	133025756	128884559	64268976	90932598	13822381	113317583	147619772	171792273	129595460	233879000	101083974	242889492	21473952	226027323	656845	128593948	128593948	23498358	118887887	166970604	132022957	156404902	242329791	2369415	129644342	9947811	146690926	85439550 7758194	7758194	7758194	228504503	30408765	134635088	157393770	41264577	26044369	82273079	2317951	137947208	238/40880
	Chr.	2.	19	19	19	10	o 0	. 5	000	14	œ	4	-	n	11	N C	10	-	. 5		11	-	4	٠,	11	1 10	o oc	9	:	13	17	4	۲- ;	10	19	19	2	16	0.0	n c	9	9	10	11	9 (N C
	rs ID	rs17725246	rss106959	rs8106959	rs7254601	rs10508289	rs10819626	rs1401098	rs1557335	rs17719594	rs1843357	rs2351458	rs2539000	rs2731711	rs471728	rs6718480	rs0920382	rs914940	rs9509428	rs4149226	rs4963126	rs10488630	rs10488630	rs11770192	rs3916581	rs3916361	rs1023095	rs1375714	rs1393299	rs17763599	rs7313362	rs7694997	rs7800935	rs856638	rs17159840	rs17159840	rs10179572	rs12921440	rs1887778	rs963354	rs2395771	rs2032447	rs10748526	rs12800998	rs620607	rs1198819
	Associationd				SNX26	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149							TRAPPCE	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPCS										MYBPC3	TSPAN32	ECGFI
SNF 1	Pos/Mb^{c}	132389627	27925288	45207005	36268923	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	36219525	30219525	36219525	36219525	36219525	72890603	58058246	4859303	22287303	23528927	113531675	7758194	7758194	7758194	7758194	7758194	7758194	7758194	7758194	7758194	45128454	11272861	7762978	7762978	7762978	7762978 85749398	108256422	158808416	27194634	47663049	2317951	2000/1200
	Chr.	11	22	20	19	19	61.	67	13	13	19	19	19	19	13	1.0	5 -	61	61	13	19	6	20	٠,	2 -	17	19	19	19	19	19	19	19	13 23	21	20	19	19	13	13	101	-	17	:::	11	7 0
	rs ID	rs1940400	rs5762235	rs6090518	rs807491	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs8106959	rs1254086	rs1548475	rs1537146	rs199793	rs7776572	rs1278760	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs3916995	rs6040514	rs7246264	rs7246264	rs7246264	rs7246264 rs10862975	rs12412964	rs2527180	rs968726	rs10838738	rs12800998	rs140522
	Chr.	2.	19	19	19	19	61.	. o	61	10	19	19	19	19	61	- 67	5 0	61	61	-	11	-1	-	۲ ;	Ξ:	16	19	19	19	19	19	19	19	5 0	19	19	19	19	13	61	9	9	10	11	11	7 0
Expression trait	Probe ID ^b	ILMN_1804148	ILMN_1786426	ILMN_1786426	ILMN_1786426	ILMN_1786426	ILMIN_1786426	II.MN 1786426	ILMN_1786426	ILMN_1786426	ILMN_1786426	ILMN_1786426	ILMN_1786426	ILMN_1786426	ILMN-1786426	ILMIN-1786426	ILMIN_1786426	II.MN 1786426	ILMN 1786426	ILMN_1719649	ILMN_1708482	ILMN_1683811	ILMN_1683811	ILMN_1731043	ILMN_1814650	II.MN 2372639	ILMN_2372639	ILMN-2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN_2372639	ILMN 1688231	ILMN_1688231	ILMN_1697971	ILMN_1785060	ILMN_1718621	ILMN_2389970	ILMIN-3223126						
	Gene ID ^a	TMED4	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEM149	TMEMI49	TMEM149	TMEM149	TMEM149	TMEM63A	TMEM80	TNPO3	TNPO3	TRAZA	TRAPPC4	TRAPPC5	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPOS	TREMI	TRIM38	TSPAN14	TSPAN32	TSPAN32	TYME

_	_	_					_	_	_	_	_	_	_	_	_	_	_	_	_					_	_	_
	ice / Mbh			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
/ - log10 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	0.02	0.54	0.17	1.38	0.13	1.35	0.61	1.43	0.17	0.36	0.27	0.01
Interaction statistic,	${ m Fehrmann}^{ m f}$	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
Interacti	BSGS _e I	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	ZXX
SNP 2	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
S	Chr.	16	1	17	19	9	9	9	9	9	9	9	9	9	9	18	10	19	က	က	က	8	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
	Associationd	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
00	Chr.	21	21	17	19	7	20	22	11	7	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	8	17	16	16	-1
Expression trait	Probe ID ^b	ILMN_2338348	ILMN_2338348	ILMN_1697227	ILMN_1743646	ILMN_1678939	ILMN_1678939	ILMN_1678939	ILMN_1678939	ILMN_1804935	ILMN_1804935	ILMN_1804935	ILMN_1804935	ILMN_2387680	ILMN_2387680	ILMN_1763455	ILMN_1763455	ILMN_1763455	ILMN_1762103	ILMN_1762103	ILMN_1762103	ILMN_1669484	ILMN_2370573	ILMN_1684628	ILMN_1700238	ILMN_1701875
Exi	Gene ID ^a	UBASH3A	UBASH3A	USP36	VASP	VNN2	VNN2	VNN2	VNN2	VNN3	VNN3	VNN3	VNN3	VNN3	VNN3	VSTM1	VSTM1	VSTM1	WDR48	WDR48	WDR48	WDR6	XAF1	ZFP90	ZNF500	ZYX

Table S1 - continued from previous page

a Phenotypes are expression levels of RefSeq Genes
Dilumina probe ID used to measure gene expression
Physical SNP position in base pairs (HG19)
d RefSeq Gene ID of gene expression level that is influenced by the SNP (BSGS discovery dataset, significance threshold = 1.29 × 10⁻¹¹)
Interaction - log₁₀ p-value from discovery dataset
Interaction - log₁₀ p-value from meta analysis of replication datasets on the statement of the

Table S2: Estimation of additive and non-additive variance components from pedigree information Taken from previous analysis in Powell et al 2013^{21}

		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

Test	Interactions	Dataset	\overline{n}	Expected	Observed	<i>p</i> -value
1 ^a	All	EGCUT	434	217.00	306	6.69×10^{18}
		Fehrmann	434	217.00	278	5.04×10^{09}
		Both	434	108.50	221	5.56×10^{31}
	Significant	EGCUT	30	15.00	25	3.25×10^{04}
		Fehrmann	30	15.00	24	1.43×10^{03}
		Both	30	7.50	22	3.76×10^{08}
2^{b}	All	EGCUT	434	54.25	92	4.22×10^{07}
		Fehrmann	434	54.25	79	6.18×10^{04}
		Both	434	6.78	30	2.55×10^{11}
	Significant	EGCUT	30	3.75	19	9.46×10^{11}
		Fehrmann	30	3.75	19	9.46×10^{11}
		Both	30	0.47	18	2.23×10^{25}
3^{c}	All	EGCUT	434	27.12	34	1.65×10^{01}
		Fehrmann	434	27.12	35	1.35×10^{01}
		Both	434	1.70	2	6.89×10^{01}
	Significant	EGCUT	30	1.88	8	3.92×10^{04}
		Fehrmann	30	1.88	9	6.22×10^{05}
		Both	30	0.12	1	1.11×10^{01}
4^{d}	All	EGCUT	1133	566.50	775	7.10×10^{36}
		Fehrmann	1133	566.50	726	1.90×10^{21}
		Both	1133	283.25	562	1.39×10^{70}
	Significant	EGCUT	73	36.50	55	1.69×10^{05}
		Fehrmann	73	36.50	55	1.69×10^{05}
		Both	73	18.25	46	7.86×10^{12}

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

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

 $^{^{\}rm c}$ The sign of all four epistatic variance components are identical in the discovery and the replication.

^d 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: Details on linkage disequilibrium and relative positions of all discovery cis-cis interactions

Chr	Gene	SNP 1	SNP 2	Position 1	Position 2	Distance / Mb	R^2	D'		
19	TMEM149	rs807491	rs7254601	36268923	36147315.0	0.122	0.000	0.001		
17	FN3KRP	rs898095	rs9892064	80890638	80827903.0	0.063	0.063	0.088		
21	CSTB	rs9979356	rs3761385	45230974	45198355.0	0.033	0.041	0.066		
3	MBNL1	rs16864367	rs13079208	152234166	152116652.0	0.118	0.041	0.117		
10	ADK	rs2395095	rs10824092	76446305	75929517.0	0.517	0.013	0.020		
11	CTSC	rs7930237	rs556895	88117962	88077479.0	0.040	0.012	0.045		
17	GAA	rs11150847	rs12602462	78153130	78146016.0	0.007	0.000	0.001		
8	NAPRT1	rs2123758	rs3889129	144663661	144613680.0	0.050	0.053	0.060		
1	LAX1	rs1891432	rs10900520	203877662	203780591.0	0.097	0.065	0.106		
18	MBP	rs8092433	rs4890876	74747424	74732087.0	0.015	0.035	0.053		
11	SNORD14A	rs2634462	rs6486334	17339127	17015557.0	0.324	0.008	0.012		
21	C21ORF57	rs9978658	rs11701361	48027084	47764477.0	0.263	0.032	0.065		
16	RPL13	rs352935	rs2965817	89648580	89513234.0	0.135	0.054	0.060		
19	ATP13A1	rs4284750	rs873870	19810050	19738554.0	0.071	0.008	0.015		
2	NCL	rs7563453	rs4973397	232301670	232291471.0	0.010	0.027	0.029		
5	HNRPH1	rs6894268	rs4700810	179032488	178991794.0	0.041	0.000	0.001		
19	VASP	rs1264226	rs2276470	46063167	45974668.0	0.088	0.018	0.022		
7	TRA2A	rs7776572	rs11770192	23528927	23498358.0	0.031	0.064	0.064		
21	PRMT2	rs2839372	rs11701058	48063862	47776382.0	0.287	0.100	0.122		
12	OAS1	rs13311	rs2072133	113448652	113409260.0	0.039	0.002	0.016		
16	N4BP1	rs12444224	rs11649236	87580855	48632478.0	38.948	0.007	0.021		
5	CAST	rs12719343	rs7733671	125369113	96000269.0	29.369	0.001	0.001		
7	DNAJB6	rs2286842	rs3779589	157216093	157163614.0	0.052	0.005	0.006		
1	OVGP1	rs10802822	rs1264898	240132968	111992823.0	128.140	0.008	0.030		
20	CD93	rs2868504	rs1884655	37771578	23074375.0	14.697	0.000	0.002		
11	PHCA	rs493642	rs10736812	123097386	76708086.0	46.389	0.002	0.008		
21	MX1	rs459498	rs8130120	42795027	29363604.0	13.431	0.000	0.000		
16	AKTIP	rs2896940	rs13332406	57721127	53489705.0	4.231	0.000	0.001		
17	CDK5R1	rs9905940	rs11655031	46614102	30833162.0	15.781	0.000	0.000		
2	CYBRD1	rs888427	rs7591849	172368120	160112881.0	12.255	0.000	0.000		
8	HMBOX1	rs587639	rs7837237	132725731	28876221.0	103.850	0.001	0.001		
11	TRAPPC4	rs1793823	rs3916581	131018917	118887887.0	12.131	0.001	0.002		
12	PEX5	rs10444467	rs4329748	128052636	7364442.0	120.688	0.000	0.000		
12	FLJ20489	rs17615703	rs3782908	117036766	48169526.0	68.867	0.001	0.002		
16	PRKCB1	rs2188355	rs10492793	23867776	12639800.0	11.228	0.000	0.000		
14	MRPL52	rs1950857	rs3811188	26710271	23299135.0	3.411	0.002	0.004		
17	C17ORF60	rs9907897	rs7405659	63502633	59874129.0	3.629	0.004	0.011		
6	FLJ43093	rs6906101	rs13214069	36667610	32705248.0	3.962	0.000	0.000		
19	TRAPPC5	rs17159840	rs17763599	7758194	2369415.0	5.389	0.000	0.000		
22	PISD	rs715572	rs6518754	33234931	32097775.0	1.137	0.001	0.003		
12	DIP2B	rs871257	rs12427378	117994348	51074199.0	66.920	0.001	0.001		
12	GPR162	rs2272500	rs2707210	79685913	6902002.0	72.784	0.003	0.005		
17	USP36	rs2279308	rs7225546	76794981	75151717.0	1.643	0.000	0.000		