Detection and replication of epistasis influencing transcription in humans

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Abstract

Epistasis is the phenomenon whereby one polymorphism's effect on a trait depends on other polymorphisms present in the genome. The extent to which epistasis influences complex traits¹ and contributes to their variation^{2,3} is a fundamental question in evolution and human genetics. Though epistasis has been demonstrated in artificial gene manipulation studies in model organisms, 4,5 and 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). 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, $A \times A$, $A \times D$, $D \times A$, $D \times D$) 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 ($p << 1.0 \times 10^{-16}$, 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, median distance between interacting SNPs is 1.83Mb), 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 Figure S9), TRAPPC5 (Supplementary Figur tary 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. Ideally one would approach this question from a whole genome perspective 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. 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

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	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

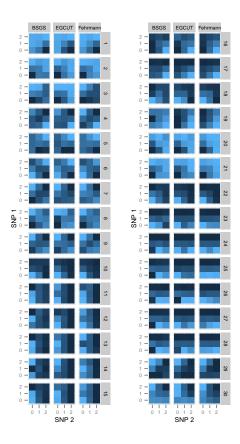


Figure 1: Replication of GP maps in two independent populations The GP maps for each epistatic interaction that is significant at the Bonferroni level in both replication datasets are shown. Each GP map consists of nine tiles where each tile represents the expression level for that two-locus genotype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

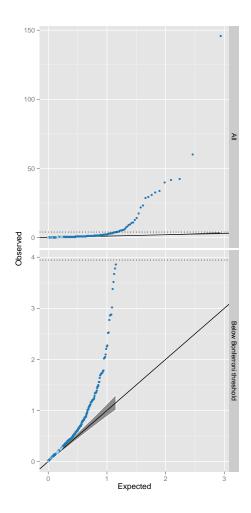


Figure 2: \mathbf{Q} - \mathbf{Q} plots of interaction p-values from replication datasets. The top panel shows all 434 discovery SNPs that were tested for interactions. Observed p-values (y-axis, $-\log_{10}$ scale) are plotted against the expected p-values (x-axis, $-\log_{10}$ scale). The multiple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

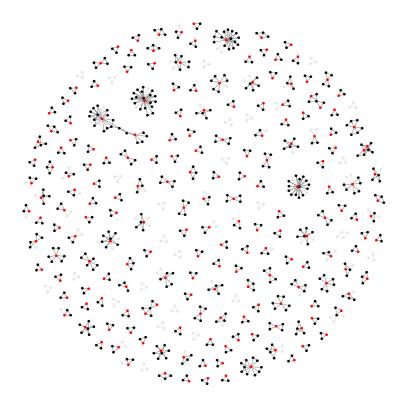


Figure 3: Discovery and replication of epistatic networks All 434 putative genetic interactions (edges) with data common to discovery and replication sets is shown, where black nodes represent SNPs and red nodes represent traits (gene expression probes). Three hundred and forty-five interactions had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

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Supplementary Figures

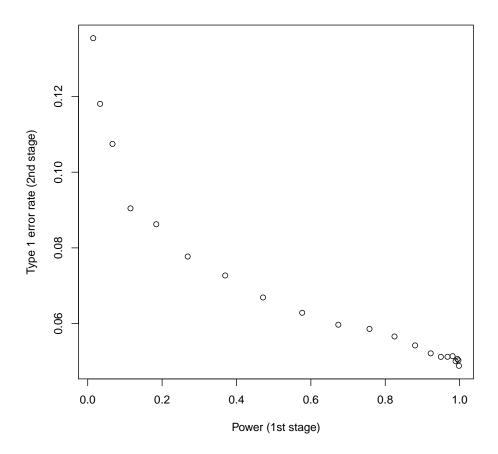


Figure S1: Type 1 error rate of two stage design In stage 1 SNPs are tested for full genetic effects (8 d.f.) and those that surpass a threshold for multiple testing are then tested for significant interaction terms in stage 2. These interaction p-values are then adjusted (Bonferroni) for the total number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

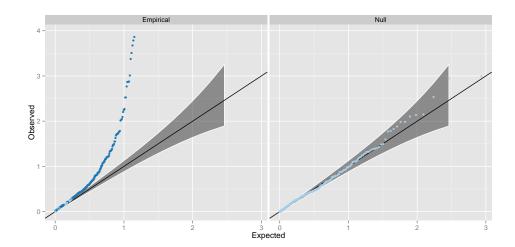


Figure S2: Q-Q plots of interaction p-values from replication datasets, excluding the 30 points significant at the Bonferroni level The right panel (Null) shows the interaction p-values from a meta analysis across two independent datasets on 434 randomly drawn SNP pairs. The left panel (Empirical) shows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

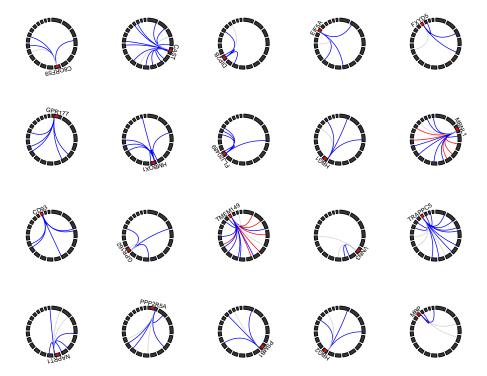


Figure S3: Gene expression traits with four or more genetic interactions Circle plots represent the genomic positions for SNPs (linking lines) and expression probes (red points). Chromosomes are represented by black blocks and ordered from 1 to 22 clockwise, starting from the top. Grey lines represent 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 S4: Location of SNPs relative to genomic features We used chromatin segmentation 27 as a method for labelling genomic features. All SNPs within 1Mb and $r^2 > 0.8$ of each cis- and trans-SNP were taken to find which genomic features (x-axis) were covered by the SNPs that compose the 501 significant interactions. Green bars represent the proportion (y-axis) of the 528,509 SNPs used in the analysis that fall within the range of the different genomic features. There is enrichment for cis-acting SNPs (red bars) in promotor regions, but trans-acting SNPs (blue bars) are not enriched for genomic features. The labels on the x-axis are as follows: E = Predicted enhancer, E CTCF enriched element, E Predicted weak enhancer or open chromatin cis regulatory element, E Predicted promoter flanking region, E Predicted promoter region including transcriptional start site, E Predicted transcribed region, E Predicted Repressed or Low Activity region

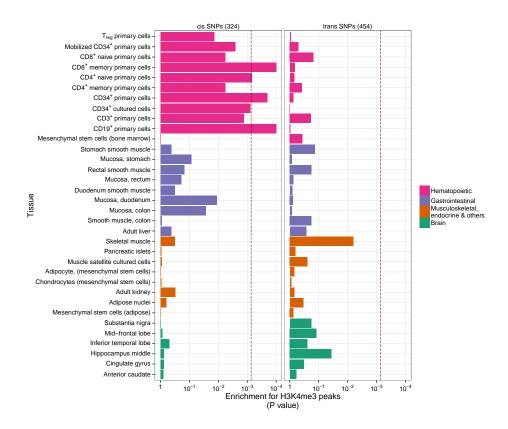


Figure S5: Tissue specific enrichment of SNPs in transcriptionally active regions The locations of transcriptional activity can be predicted by chromatin marks, assayed by H3K4me3. Enrichment p-values are calculated using permutation analysis for 34 different cell types (y-axis) in four tissue types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

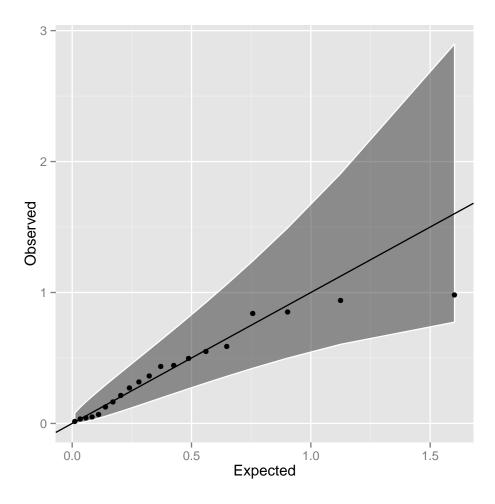


Figure S6: Q-Q plot of interaction p-values in the CDHWB dataset Twenty of the 501 discovery SNP pairs passed filtering in the CDHWB dataset (mainly due to small sample size). There is no evidence for enrichment of interaction terms, most likely due to insufficient power given the limited sample size.

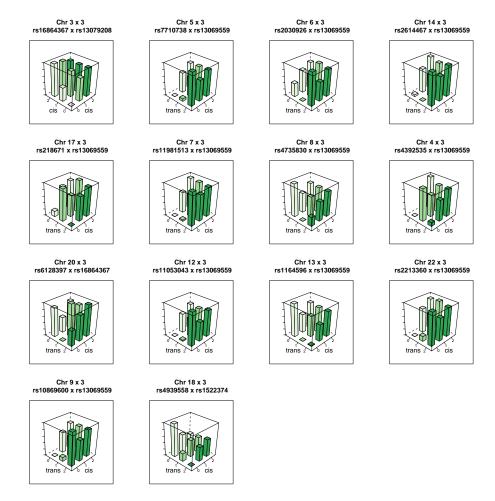


Figure S7: Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1 Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions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

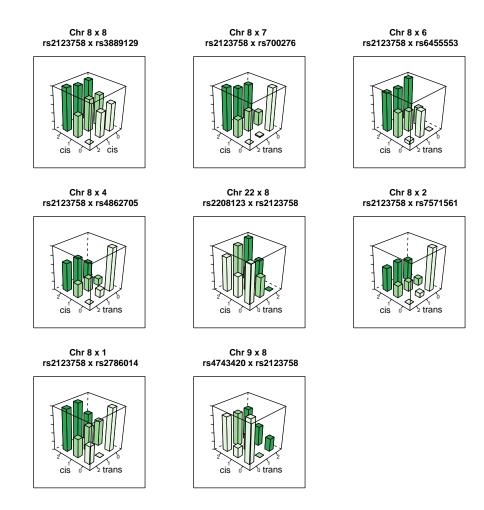


Figure S9: Genotype-phenotype maps for 8 interactions influencing the expression of NAPRT1 Each bar represents the mean phenotypic value for individuals in that genotype class.

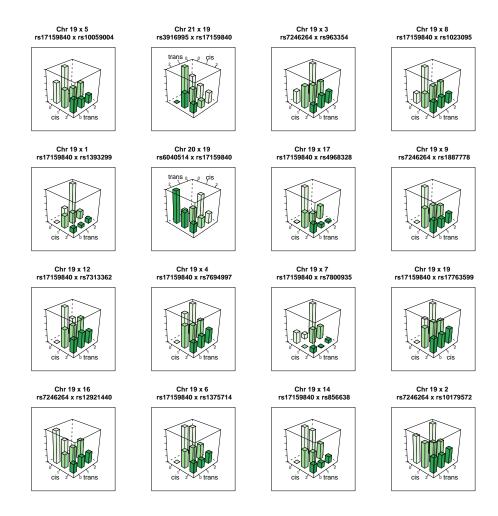


Figure S10: Genotype-phenotype maps for 16 interactions influencing the expression of TRAPPC5 Each bar represents the mean phenotypic value for individuals in that genotype class.

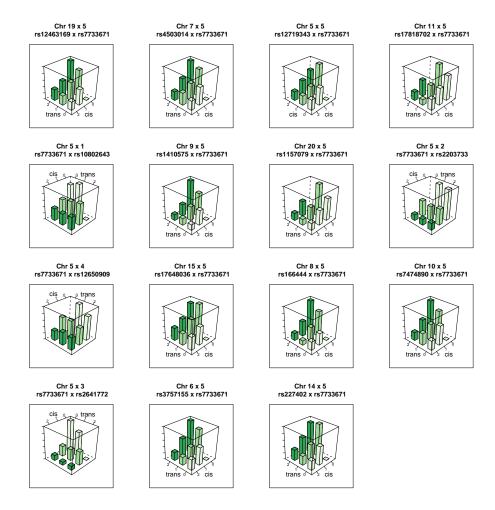


Figure S11: Genotype-phenotype maps for 15 interactions influencing the expression of CAST Each bar represents the mean phenotypic value for individuals in that genotype class.



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.

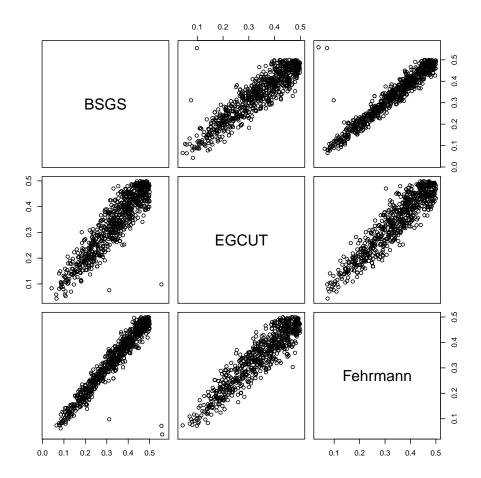


Figure S13: Comparison of allele frequencies for 781 SNPs involved in genetic interactions across independent populations Outliers were removed from the analysis as part of the filtering stage during replication.

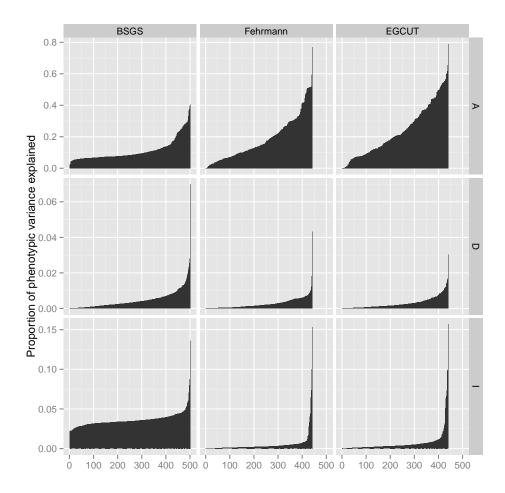


Figure S14: Comparison of variance explained by additive, dominant and epistatic effects from different cohorts How does the estimated variance decomposition change in different cohorts? The proportion of the phenotypic variance that is additive (A), dominant (D), or epistatic (I) for each putative interaction 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

	/ MP _p					0.517			4 231								31.703					0.071																	0.263				
	Distance																60																										1.33
values	Metag	0.09 ^j	0.95	2.02	2.05	39.82	0	20.00	0.0	0.42	0.23	1.01	0.04	06.0	07.0	1.16						14.23	0.14	0.50	0.54	0.43	0.85	0.24							0.19	0.13	0.37	0.28	21.67	0.27	0.07	0.21	1.33
- log10 p-values	$\mathtt{EGCUT}^{\mathrm{f}}$	0.02^{i}	1.81	1.78	0.83	21.21	9	1.93	*0:0 0 0	0.20	0.30	1.37	0.20	1.09	0.17	1.02						3.25	0.40	0.16	0.04	0.50	0.84	0.28							0.05	0.50	0.50	0.08	16.36	0.04	0.02	0.18	0.07
Interaction statistic /	$Fehrmann^{f}$	0.38^{i}	0.02	1.04	2.04	18.33		1.83	0.92	0.71	0.27	0.33	0.02	0.44	0.47	0.80						12.18	90.0	0.87	1.15	0.38	09.0	0.31							0.53	0.01	0.29	0.65	80.9	0.72	0.29	0.38	2.18
Interact	$BSGS^{e}$	5.82	6.10	6.59	6.58	69.9	6.22	7.15 7.45	6.43	5.93	6.18	6.26	5.75	28.00	0.01	5.60	5.96	6.65	7.64	6.26	0. 20 7.00 7.00	5.30	5.84	6.60	5.66	3.87	6.02	5.98 7.15	4.87	4.32	4.40	9 % 0 %	4.61	4.69	6.79	5.90	0 10	4.91	9.42	5.55	5.49	7.62	5.67
	Associationd				ADCK1			AHSAS	AKTIP								ARL17B	ARL17B							21300212	81.710610	C14ORF173	C14ORF173							C17ORF60	CIORFS6	CLORF86	ZNF641		C5ORF4	CSCRF59		CSORF59
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	Associationd	ABCA7 ABCA7	ABCC3	ACATI	ADCNI	ADK	AGAP8	HI.A.C.	5-6-11	AKTIP	AKTIP	ALDH3A2	ANG	ANPEP	ANFER	APPL2			ARL17B	ARL17B	ARLI7B		BID	1	C11ORF17	C13ORF18		C140RF173														C8ORF59	
SNP 1	Pos/Mb^{c}	1047161	48771135	108207393	88462550	76446305	51515534	29938258	57721127	53536345	53536345	19581009	21153299	90363995	300000000	105580918	75768225	35932619	44064851	44064851	44064831	19810050	18213057	18233000	8886260	46913416	37575398	92276674	13819673	77574438	77574438	70416307	51151724	52083552	63502633	110577257	25711358	48052838	48027084	45866512	36577930	86102223	52273663
	Chr.	19	17	11	16	10	10	n u	9	16	16	17	14	15	CT H	12	17	21	17	17	17	19	22	22	11	13	22	15	18	14	4.	14	22	19	17	9 9	91	21	21	18	2 2	9 00	14
	rs ID	rs3752237	rs9455	rs227064	rs12431690 rs8058066	rs2395095	rs2611512	rs10881585	rs2896940	rs7189819	rs7189819	rs3760489	rs9322855	rs11073891	rsii0/3891	rs935251	rs12947580	rs2834541	rs8079215	rs8079215	rs8079215	rs4284750	rs8919	rs181405	rs2568061	rs674754	rs11089825	rs3935344	rs1293455	rs2655991	rs2655991	rs2655991 rs4793445	rs6010061	rs7245800	rs9907897	rs2334323	rs7188668	rs4819271	rs9978658	rs1122762	rs12429804	rs2896452	rs7152284
	Chr.	19	17	11	14	10	010	21.0	4 6	16	16	17	14	15	C I	12	17	17	17	17	17	19	22	22	11	13	14	7 7	14	14	4.5	14	14	14	17			21	21	ഹ	ж о	000	8
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Exp	Gene ${ m ID}^{ m a}$	ABCA7 ABCA7	ABCC3	ACATI	ADCK1	ADK	AGAP6	AHSA2 AHSA2	AKTIP	AKTIP	AKTIP	ALDH3A2	ANG	ANPEP	ANFEF	APPL2	ARL17B	ARL17B	ARL17B	ARL17B	ARLI7B	ATP13A1	BID	BID	C110RF17	C13ORF18	C14ORF173	C14ORF173	C14ORF4	C14ORF4	C14ORF4	C14ORF4	C14ORF4	C14ORF4	C17ORF60	CIORFS6	CIORES	C21ORF57	C21ORF57	C5ORF4	CSORFS	CSORF59	C8ORF59

4	1			SNP 1				SNF 2		Interac	Interaction statistic / $-\log_{10} p$ -values	$-\log_{10} p$	values	
Probe ID ^D	Chr.	rs ID	Chr.	Pos/Mb^{c}	Association	rs ID	Chr.	Pos/Mb^{C}	Association	BSGSe	Fehrmann ^f	$EGCUT^{t}$	Metag	Distance / Mb ⁿ
ILMN_1653205	ж с	rs8051751	16	7188323	COORE79	rs2896452	∞ -	86102223	C8ORF59	5.79	1.39	0.18	0.87	
LMN_1731064		rs12765847	10	4353908		rs3738725		227174210	CABC1	6.36	0.94	0.00	0.34	
LMN_1712532	6	rs4266763	6	139289825	INPP5E	rs684040	-1	82128660		5.81				
LMN_1712532	6	rs4573661	11	6026661		rs4077515	6	139266496	INPP5E	6.61	0.09	98.0	0.42	
LMN_1717234	rO r	rs1157079	20	6778978		rs7733671	ı, ı	96000269	CAST	7.07	0.23	0.96	0.62	
LMN-1717234	O H	rs12463169	61.	17321669		rs7733671	υn	96000269	CAST	2.73	0.02	2.85	I.75	
ILMIN 1717234) IC	rs12719343	o r	195369113		rs7733671	o ro	96000269	CAST	7.68	98 0	1 Y	1 20	96 96
ILMIN_1717534	o m	rs12/19545	ာင	78955630		rs//550/1	o m	96000269	Take Take	 	0.30	1.07	0.78	29.509
LMN 1717234) 1C	rs166444	n ox	78392770		127733671	'nΩ	9600096	CAST	7.03	0.13	1.07 4.07	3,10	
LMN_1717234	10	rs17648036	12.0	27311111		rs7733671	10	96000269	CAST	7.81	0.97	0.03	0.41	
LMN_1717234	'n	rs17818702	11	86107920		rs7733671	ıΩ	96000269	CAST	6.62	1.15	0.59	1.09	
LMN_1717234	10	rs227402	14	70496867		rs7733671	10	96000269	CAST	6.12	0.11	0.01	0.01	
LMN_1717234	10	rs2822124	21	15166804		rs7733671	10	96000269	CAST	6.87				
ILMN_1717234	10	rs3757155	9	136458593		rs7733671	10	96000269	CAST	7.24	0.07	0.33	0.12	
ILMN_1717234	10	rs4503014	-1	31149140		rs7733671	10	96000269	CAST	5.88	0.92	1.56	1.72	
ILMN_1717234	ro	rs7474890	10	59590078		rs7733671	20	96000269	CAST	6.74	0.49	0.12	0.23	
LMN_1717234	ro	rs7733671	20	96000269	CAST	rs10802643	1	238120177		7.42	0.75	0.78	0.93	
LMN_1717234	rO	rs7733671	10	96000269	CAST	rs12650909	4	170192890		7.42	0.23	0.78	0.50	
LMN_1717234	ນ	rs7733671	70	96000269	CAST	rs2203733	5	224093101		6.07	0.22	0.87	0.54	
LMN_1717234	ນ	rs7733671	70	96000269	CAST	rs2641772	8	195531841		6.93	0.19	0.26	0.15	
LMN_1651705	11	rs872311	18	66175386		rs11032695	11	34447586	CAT	6.41	0.26	0.30	0.22	
LMN_1772208	11	rs2353203	19	17099980		rs541207	11	64125142	CCDC88B	5.68	0.33	0.37	0.31	
LMN_1772208	11	rs694739	11	64097233	CCDC88B	rs12771349	10	96998193		5.62	0.23	0.18	0.14	
LMN_1784863	-	rs3211834	7	80280117		rs1254900	73	85816334	VAMP8	6.93	0.15	0.01	0.02	
LMN_1800540	-	rs750801	11	76033374		rs6700168	1	207502534	CD55	5.09	80.0	0.03	0.02	
LMN_1704730	20	rs1884655	20	23074375	CD93	rs10255470	4	157182040		90.9	1.74	0.24	1.20	
LMN_1704730	20	rs1884655	20	23074375	CD93	rs4696726	4	7992632		5.71	0.13	08.0	0.42	
LMN_1704730	20	rs1884655	20	23074375	CD93	rs7622580	9	196721395		5.56	0.04	0.27	0.08	
LMN_1704730	20	rs1884655	20	23074375	CD93	rs838875	12	125145394		6.31	0.24	1.67	1.16	
LMN_1704730	50	rs1884655	20	23074375	CD93	rs9576388	13	38434472		7.88	0.71	0.22	0.45	
LMN_1704730	50	rs2868504	20	37771578		rs1884655	20	23074375	CD93	5.71	0.64	0.75	0.81	14.697
LMN-1704730	20	rs4813479	20	23076914	CD93	rs10925747	- 1	238899903		7.43				
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LMN_2339796	13	rs861544	14	104162263		rs7324744	13	115008038	CDC16	5.46	0.21	0.14	0.11	
LMN_1730928	17	rs9905940	17	46614102	HOXB2	rs11655031	17	30833162	CDK5R1	5.47	0.95	0.07	0.45	15.781
LMN_1745949	19	rs200609	20	51956250		rs4803481	19	42066556	CEACAM21	6.15	06.0	0.12	0.48	
ILMN_1745949	19	rs4803481	19	42066556	CEACAM21	rs2421050	ro.	158943044		6.67	2.16	0.16	1.44	
LMN_1703754	80	rs6505780	œ ;	13069782	CEP192	rs13132719	4 (180265266	0.00	5.75	0.15	0.24	0.12	
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LMN 2202940	12	rs6539014	12	102277782		rs867578	11	81937002		4.75	0.92	0.02	0.36	
LMN_1663142	17	rs429790	16	84471642		rs7313235	12	10132283	CLEC12A	5.55	0.07	1.28	0.67	
LMN_2403228	12	rs7305054	12	10156646		rs3903088	10	134236688		7.54	0.95	0.36	0.73	
LMN_1674609	n	rs17129799	11	96929337		rs6863172	ю	175595960	CLTB	5.55		0.27		
LMN_1770290	19	rs3752237	19	1047161	ABCA7	rs169130	16	63121080		7.56	0.07	0.07	0.02	
LMN_1770290	19	rs3752237	19	1047161	ABCA7	rs7336017	13	67713633		6.33	1.92	0.28	1.39	
LMN_1654545	00 1	rs4333645	œ ;	145569535		rs1455268	4	61738094		6.34	0.10	0.01	0.01	
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16 First	rs2950520 7	99827148	GATS	6.22	0.42		
16 16 174504270 16 301689955 18 187198445 16 20084475 18 110899955 18 187198445 16 20084475 18 187198465 19 20084475 19 1871980563 16 6478898 12 872872500 12 6478898 13 872707210 12 6902002 GPR162 19 872707210 12 6902002 GPR162 19 872707210 12 124369421 1872557241 6 124369421 1872557241 6 124369421 1872557241 6 1169683 11 8725613 16 1169683 11 87256669 18 70560611 1892590426 17 82988268 187399321 187324647 17 83028634 GSDMB 18745474 13 8028634 GSDMB 18745474 13 80344527 187642807 13 80145560 187642807 13 80145560 187642807 13 80145670 13 80145670 14 87139888 22 83399979 187139888 22 83399979 187139888 22 8339979 187139888 187139888 22 8339979 187139888 187138888 187138888 187138888 187138888 187138888 187138888 187138888 187138888 187138888 187138888 187138888 187138888 187138888	rs2197465 14	48572632					
2 rs4445072 13 11089955 12 rs1880563 16 20084476 12 rs1860563 16 6478898 12 rs27707210 12 7688913 12 rs27707210 12 6902002 13 rs1057333 12 1246803 1 rs1257741 6 1246803 1 rs1257749 7 1246803 1 rs125775613 12793793 1 rs2575613 12793793 1 rs9575047 13 8298268 1 rs6566669 18 7750601 1 rs6566669 18 7750601 1 rs1557467 7 3805863 1 rs1547574 13 8514527 1 rs1547574 13 8514527 1 rs164808 2 38399979 2 rs13888 2 38399979 2 rs13888 2 38399979	rs1015111 4	128972357					
12 rss198646 16 2608476 12 rss272500 12 79685913 13 rs2777210 12 6902002 GPR162 14 rs27077210 12 6902002 GPR162 15 rs2707210 12 6902002 GPR162 1 rs12527241 6 12468639 1 rs1253299 7 12793793 1 rs253299 7 12793793 1 rs256399 7 12793973 1 rs256399 16 11169683 1 rs25950426 18 70506611 1 rs1224677 17 38028634 1 rs124673 10 53192833 1 rs145744 13 85344527 1 rs149886 22 38399979 1 rs1139886 22 38399979 1 rs1139886 22 38399979 1 rs1139886 22 38399979 1 rs11078523 17 4523167 1 rs123868 22 38339979 1 rs139886 24 38339979 1 rs139886 24 38339979 1 rs11078523 17 4523167 1 rs25850399 11 5271671 HBC2		85935282	GNLY		0.02 0.45	0.13	
12 rs2872560 16 6478898 12 rs2772500 12 6902002 GPR162 12 rs2777210 12 6902002 GPR162 1 rs11057383 12 124369421 6902002 GPR162 1 rs11057383 12 124369421 612468039 12793793 8802 17793793 17793793 8802 17793793 17793793 17793793 17793793793 17793793 17793793 17793793 17793793		111164237	GPN3				
12 rs2272500 12 76858513 12 rs2707210 12 6902002 GPR162 12 rs2707210 12 6902002 GPR162 1 rs11057383 12 124369421 rs2757741 1 rs12527741 6 12468039 rs275613 1 rs15527741 6 12468039 rs285618 1 rs255613 1 12793793 rs2856668 1 rs6566669 18 7766011 rs285618 1 rs9575047 17 3805863 GSDMB 1 rs1557467 17 3805863 GSDMB 1 rs1547574 13 8534457 rs154757 1 rs1547574 13 8534957 rs18888 22 rs13888 22 38399979 22 rs13888 22 38399979 11 rs1078523 17 4523167 11 rs245666 19 377671 <		6902002	GPR162				
12 rs2707210 12 6902002 GPR162 1 rs2707210 12 6902002 GPR162 1 rs11057383 12 124669421 GPR162 1 rs120572241 6 120468039 1 rs120572241 6 120468039 1 rs120572241 6 120468039 1 rs120572041 6 1169683 1 rs9575097 13 rs2988268 1 rs1224667 13 rs2988268 1 rs1224667 17 rs1224667 17 rs1224677 11 rs1224677 11 rs1224677 13 rs125560 1 rs129888 22 rs139888 23 rs1398979 22 rs139888 23 rs13889979 22 rs138888 23 rs13889979 22 rs138888 23 rs13889979 23 rs138898 23 rs13889979 23 rs13889979 23 rs138898 23 rs13889979 23 rs13889979 23 rs138898 23 rs13889979 23 rs13889979 23 rs13889979	07210 12	6902002	GPR162				72.784
12 rs2/07/23 12 692002 GPR162 rs10.05738 12 124369421 rs10.05738 12 124369421 rs10.05738 12 124369421 rs12.0527241 6 120466039 1 rs12.0527241 6 120466039 11 rs20.0566669 18 70506011 rs10.057467 17 38028634 GSDMB rs10.057467 17 38028634 GSDMB rs10.057467 17 38029979 rs10.057407 13 85192833 17 rs10.07852 2 rs10.0898 22 38399979 rs10.07852 1 rs10.07852 17 4523167 rs20.066 19 3573531 rs20.07856099 11 rs20.07856099 11 rs20.066 19 3573531 rs20.07856099 11 rs20.07856099 11 rs20.07856099 11 rs20.07856099 11 rs20.07856099 11 rs20.078560999 11 rs20.07856099 11 rs20.07856099 11 rs20.07856099 11 rs20.07856099 11 rs20.07856099 11 rs20.078560999 11 rs20.07856099 11 rs20.07856099 11 rs20.07856099 11 rs20.078560999 11 rs20.078560999 11 rs20.078560999 11 rs20.07856099 11 rs20.07856099 11 rs20.078560999 11 rs20.07856099999 11 rs20.07856099 11 rs20.07856099999 11 rs20.078560999 11 rs20.07856099999 11 rs20.078560999999999999999999999999999999999999	rs4740848 9	6554558					
1 rs12527241 6 124468039 1 rs12527241 6 124468039 1 rs12532999 7 12793793 1 rs12532999 7 127938793 1 rs12532999 7 127938793 1 rs25613 16 11160683 1 rs656669 18 70560011 1 rs2590426 3 717399321 1 rs1224667 17 38028634 CSDMB 1 rs124677 19 38134627 1 rs139888 22 rs139888 1 rs11078523 1 rs11078523 1 rs11078533 1 rs11078533 1 rs110785399 1 rs257671 rs257671 rs12666 19 rs2575301 rs25767639 1 rs277671 rs277677 rs277671 rs2	rs9827054 3	188880113					
1 rs12527241 6 120468039 1 rs12532999 7 12793793 1 rs755613 16 1106683 1 rs756613 16 1106683 1 rs656669 18 71560018 1 rs1224467 13 8028634 1 rs1244574 17 8834833 1 rs1244574 13 8534457 1 rs1244674 13 8534457 1 rs124888 22 8339979 1 rs107883 17 4523167 1 rs1107883 17 4523167 1 rs124666 19 357367 1 rs125666 19 357367 1 rs125666 19 357367 1 rs125666 19 357367 1 rs125666 19 357367 1 rs1257666 19 357367 1 rs1257666 19 357367 1 rs1257666 19 357367 1 rs1257666 10 357367 1 rs1257678 10 3571671 rs1257678 10 rs1257678 rs12688 10 rs12688 rs12688 10 rs12688 r	rs12065581 1	68732819	GPR177				
1 rs42532999 7 12793793 1 rs9575613 11166683 1 rs9575097 13 82986268 1 rs6566669 18 77506011 1 rs9575047 17 38058263 17 rs9520426 3 771399321 17 rs1557467 17 38058634 GSDMB 18 rs1547574 13 8514527 1 1 rs1547574 13 8514527 1 22 rs138898 22 38399979 2 22 rs138888 22 38399979 2 22 rs138888 22 38399979 1 11 rs1078523 17 4523167 11 rs2855039 11 5271671 HBG2	rs12065581 1	68732819	GPR177		_		
1 rs972613 16 1166883 1 rs9775097 13 rs9586669 18 7506011 1 rs95966669 18 7506011 1 rs92900426 3 717399321 1 rs1254674 7 38028634 GSDMB 1 rs12547574 17 38028634 GSDMB 1 rs6492807 13 s916560 22 rs139808 22 rs139808 22 rs139808 22 rs139808 22 rs139808 22 rs139808 11 rs12076823 17 4523167 11 rs1297666 19 3573671 HBG2	065581 1	68732819	GPR177				
1 res9575097 13 82982288 1 res920426 13 70506011 1 res1257467 17 38028634 1 res1248673 10 58192833 1 res12446774 13 8534457 2 res138898 22 38399979 22 res138898 22 38399979 22 res189888 22 38399979 11 res1078523 17 4523167 11 res2850399 11 5771671 HBG2	rs12065581 1	68732819	GPR177				
1 rse5566669 18 70506011 1 rse9290426 3 71399321 1 rse11557467 17 38028634 1 rse11557467 17 38028634 1 rse1547574 13 85149580 2 rse642807 13 9615560 2 rse138898 22 38399979 2 rse139888 22 38399979 1 rse11078523 17 4523167 1 rse129666 19 35728501 1 rse2550399 11 5571671 HBG2	065581 1	68732819	GPR177				
1 rs92204245 3 171393321 GSDMB rs925204246 1 rs1255467 1 53902863 GSDMB rs12548673 1 0 53192833 GSDMB rs12548673 1 1 ss1642867 1 3 83839979 22 rs139898 22 38399979 22 rs139898 22 38399979 1 rs12975066 19 35723501 rs2855039 1 5271671 HBG2	065581 1	68732819	GPR177				
17 rs11524667 17 38028634 GSDMB rs12246673 10 58192863		68732819	GFRI				
1 rs1224574 10 53192833 1 rs16245774 13 56344527 22 rs139808 22 38399979 22 rs139808 22 38399979 11 rs1076823 17 4523167 11 rs1076823 17 4523167 11 rs255666 19 3573501	65745 15	101508261					
1 rslo47574 13 8534527 1 rslo492807 13 8534527 13 8534527 13 8534527 13 8534527 13 rslo3888 22 rslo3888 22 rslo3888 22 rslo3888 11 rslo78553 17 4523167 11 rslo566 19 35723501 1 rs2855039 11 5271671 HBG2	101992 1	110266754	GSTM1				
1 re6422807 13 9615560 22 re138898 22 38399979 22 re138898 22 38399979 11 re11078523 17 4523167 11 re1297666 19 35725361 11 re2555639 11 5271671 HBG2	101992	110266754	GSTM1		0.27	0.79	
22 rs138898 22 38399979 22 rs139898 22 38399979 11 rs11078523 17 4523167 11 rs255066 19 35723501 11 rs285039 11 5271671 HBG2	54446 1	110253241	GSTM1				
22 rs139898 22 38399979 22 rs139888 12 38399979 11 rs12078523 17 4523167 11 rs2297566 19 35723501 11 rs2855039 11 5271671 HBG2		77919015					
22 rs138888 22 3839979 11 rs107853 17 4523167 11 rs2975066 19 35725501 11 rs2855039 11 5271671 HBG2		85877017					
11 rs1107823 17 4533167 11 rs12975066 19 35723501 11 rs2855039 11 5271671 HBG2	83949 21	19532546					
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	55039 11	5271671	HBG2				
11 rs2855039 11 5271671 HBG2	rs2855039 11	5271671	HBG2				
	rs12042181 1	213088494	LQK1				
11 rs2855039 11 5271671 HBG2	rs12503379 4	141533832	000	6.42	0.01 0.46		
17 4523167	rs16912979 11	2309092	HBGZ		0.01 0.41		0.10

Exp	Expression trait			01	SNP 1				SNP 2		Interac	Interaction statistic /	- log10 p-values	values	
Gene IDa	Probe ID ^b	Chr.	rs ID	Chr.	Pos/Mb ^c	Associationd	rs ID	Chr.	Pos/Mb ^c	Associationd	BSGSe	Fehrmann ^f	EGCUT	Metag	Distance / Mb ^h
HBG2	ILMN_2084825	11	rs12975066	19	35723501		rs2855039	11	5271671	HBG2	5.77	80.0	0.13	0.05	
HBG2	ILMN_2084825	11	rs2855039	11	5271671	HBG2	rs12042181	1	213088494	LQK1	6.84	90.0	0.54	0.21	
HBG2	ILMN_2084825	11	rs2855039	11	5271671	HBG2	rs12503379	4	141533832		5.98	0.00	0.46	0.10	
HDAC7	ILMN_3266186	17	rs2109029	91	6036851		rs4760636	12	48173352	HDAC7	5.75		i c	0	
HEBFI	ILMN-1802557	1 5	rs3782567	2 0	13145613	HEBFI	rs17686635	1 x	135220622	COVER	0.0 0.0 0.0	0.15	0.59	0.32	
HLA-DRA	ILMN 2157441	9	rs4899635	2 4	77532672		rs7192	- 9	32411646	HLA-DRB6	5.94	0.90	0.16	0.52	
HLA-F	ILMN_1762861	9	rs11660982	18	75467313		rs2523404	9	29695713	HLA-H	5.69	1.00	0.47	0.86	
HMBOX1	ILMN_1720059	œ	rs12435486	14	98670849		rs7837237	œ	28876221	HMBOX1	6.54	0.92	1.11	1.34	
HMBOX1	ILMN_1720059	œ	rs2837803	21	42112794		rs4732890	œ	28751381	HMBOX1	6.62	0.05	1.01	0.46	
HMBOX1	ILMN_1720059	00	rs4765451	12	127237464		rs8180944	00	28904086	HMBOX1	5.80	0.39	3.13	2.52	
HMBOX1	ILMN_1720059	œ	rs587639	œ	132725731		rs7837237	œ	28876221	HMBOX1	6.58	0.55	0.34	0.44	103.850
HMBOX1	ILMN_1720059	00 0	rs8180944	oo o	28904086	HMBOX1	rs4553956	က၊	189533772		6.88	80.00 80.00	0.03	2.20	
HMBOXI	ILMN_1720059	x0 0	rs8180944	χ <u>-</u>	110804086	HMBOXI	rs7810884	- 0	158276926	TWD OV1	6.12 4.45	0.34	0.66	0.52	
HNRPH1	ILMN 2101920	0 10	rs6894268	3 10	179032488		rs4700810	0 10	178991794	HMBOAL	20.50	5 00 10 10	3.01	10.37	0.041
HSPC157	ILMN_3194087	-	rs555812	16	88882257		rs4654783	-	22439520	HSPC157	5.51		5		
HSPC157	ILMN_3194087	-	rs6063164	20	46486900		rs4654783	-	22439520	HSPC157	6.51				
HSPC157	ILMN_3194087	1	rs662739	12	121229893		rs4654783	1	22439520	HSPC157	6.61				
HSPC157	ILMN_3194087	1	rs7088558	10	101884937	CWF19L1	rs4654783	1	22439520	HSPC157	6.48				
IL32	ILMN_1778010	16	rs1554999	16	3115628	IL32	rs4759890	12	131757163		6.90	0.19	0.50	0.29	
IL32	ILMN_2368530	16	rs765044	19	2560423		rs1554999	16	3115628	IL32	5.53	0.69	0.23	0.44	
INPPSE	ILMN_1811301	61	rs8044524	16	81603771		rs1127152	61	139335599	INPP5E	5.58	1.46	0.84	1.55	
JAZFI	ILMN_1682727		rs757355	7.7	47970693	10000	rs849341	۲.	28288174		8.16	0.02	0.26	0.02	
KCNJIS	ILMN_1675756	77.	rs2186344	17.	39606769	KCNJI5	rs424299	17	1770766		5.04	0.65	0.13	0.00	
KIRZDS5	ILMIN_1691803	6T °	rs649216	5 -	84507110	NIRZDLI	rs6419960	4 0	110110488	KTEI C1	4.7 4.7	0.46	0.09	0.72	
KTELCI	ILMN_1811104	o es	rs6815953	4	183109012		rs6414283	o	119195913	KTELCI	5.45	0.64	0.08	0.28	
L3MBTL2	ILMN_2336109	22	rs4822006	22	41519362	L3MBTL2	rs1294338	-	233438952		5.88	0.33	0.04	0.00	
LAP3	ILMN_1683792	4	rs7042087	6	132602868		rs7658240	4	17588950	LAP3	5.72	0.24	0.47	0.31	
LAX1	ILMN_1769782	1	rs1891432	1	203877662		rs10900520	1	203780591		19.16	18.60	11.22	29.24	0.097
LDLRAP1	ILMN_1809040	-	rs1552032	12	59971635		rs6687605	-	25889632	LDLRAP1	6.00				
LGALS9	ILMN_2412214	17	rs12450521	17	26083392		rs11749727	ທຸ	179608360		5.16	0.35	0.40	0.34	
LILRA5	ILMN_2357419	13	rs3859532	13	54827248	LILRAS	rs714789	200	71561497		6.13	0.23	0.03	0.02	
LIBRC25	ILMN 2150196	10	rsi1247250	22	51151350	LINGI	rs8101804	0 1	18496107	I.RRC25	0.00	0 11	0.15	7.	
LY86	ILMN_1807825	9	rs977785	9	658881	LY86	rs1543675		78946879		5.61	0.13	0.15	0.07	
LYZ	ILMN_1815205	12	rs2168029	12	69734641	LYZ	rs11981725	-	154137150		5.95	0.15	0.03	0.03	
LYZ	ILMN_2162972	12	rs177820	18	77276964		rs2168029	12	69734641	LYZ	5.71	0.49	0.03	0.16	
LYZ	ILMN_2162972	15	rs2168029	15	69734641	LYZ	rs2253135	0.0	130319560		6.31	0.61	0.36	0.49	
MADILI	ILMIN_2358069	- 9	rs//05/15	- 6	102202146	MADILI	rs6414306	၁ဖ	43538441	MADSLIBB	0.0 0.0 0.0	0.25	0.00	0.03	
MAP1LC3A	ILMN_1776188	20	rs974607	21	29435869		rs6060034	20	33351864	MAP1LC3A	25.70	1.18	11:1	60.1	
MBNL1	ILMN_2313158	8	rs10869600	6	78225815		rs13069559	8	152187431	MBNL1	7.96	0.79	0.27	0.54	
MBNL1	ILMN_2313158	3	rs11053043	12	9932070		rs13069559	3	152187431	MBNL1	6.70	80.0	2.21	1.37	
MBNL1	ILMN_2313158	3	rs1164596	13	97100681		rs13069559	3	152187431	MBNL1	7.38	1.43	0.63	1.34	
MBNL1	ILMN_2313158	3	rs11981513	-1	94648239		rs13069559	က	152187431	MBNL1	7.71	0.43	5.36	4.58	
MBNL1	ILMN_2313158	က	rs16864367	က	152234166		rs13079208	က	152116652		13.49	16.25	24.74	41.56	0.118
MBNL1	ILMN_2313158	n	rs2030926	: :	114067127		rs13069559	က	152187431	MBNL1	7.10	0.91	5.80	5.53	
MBNL1	ILMN 2313158	0 00	rs2213360	22	34291750		rs13069559	o e	152187431	MBNL	6.05	0.62	0.07	0.70	
MBNL1	ILMN_2313158	0 00	rs2305802	13	16038535		rs13069559	, m	152187431	MBNL1	6.94	1.67		-	
MBNL1	ILMN_2313158	က	rs2614467	14	99770138		rs13069559	က	152187431	MBNL1	5.74	4.13	2.22	5.30	

Table S1 - continued from previous page

Probe Prop. Prop	Expression trait				SNP 1				SNP 2		Interact	Interaction statistic /	- log10 p-values	values	
10 reduction decided 4	Probe ID ^b	Chr.	rs ID	Chr.	Pos/Mb^{c}	Associationd	rs ID	Chr.	Pos/Mb^{c}	Associationd		Fehrmann ^f	$EGCUT^{t}$	Metag	Distance / Mb ^h
1 10,000	ILMN_3237385	10	rs6025645	20	56157341		rs7923609	10	65133822	NRBF2 NRBF2	5.45				
8 minoson mino	ILMN_1800897	1	rs4852124	- 61	240680022		rs6588415	1	52334047	MINDE	6.13	0.47	0.02	0.17	
12 nillididadi ilitatis 11 11486050 nillididadi ilitatis 11 11486050 nillididadi ilitatis 11 11486050 0AST 413 0.55 0.00 0AST 0.00 <td< td=""><td>ILMN_1787885</td><td>œ</td><td>rs5017351</td><td>11</td><td>25453482</td><td></td><td>rs1005901</td><td>œ</td><td>21964378</td><td>NUDT18</td><td>5.44</td><td>0.03</td><td>0.46</td><td>0.15</td><td></td></td<>	ILMN_1787885	œ	rs5017351	11	25453482		rs1005901	œ	21964378	NUDT18	5.44	0.03	0.46	0.15	
12 mistages m	ILMN_1658247	12	rs11613438	12	113480510		rs1047944	9	163997467		8.59	1.27	1.55	2.03	
10. 1.00 1	ILMN_1658247	12	rs13311	12	113448652		rs2072133	12	113409260		4.13	4.12	0.81	3.86	0.039
1 17,8555507 2 17,755469 CSPP1 CSP	ILMN_1675640	77.	rs2892233	61	49160255		rs3741981	7.	00000	OASI	4.38	0.87	0.46	0.76	
11 17,220,079 2.1 2.00,024.23 2.00,024.24 2.00	ILMN-2381899	01	rs7192613	16	74286646		rs17512962	01	13169066	OFTN	5.64	0.42	0.06	0.14	
9 FATABOLIS DE CONTRILIS PATABOLIS DE CONTRILICATION FATABOLIS DE CONTRILICATION </td <td>ILMN_2307032</td> <td>11</td> <td>rs2829679</td> <td>21</td> <td>26662543</td> <td></td> <td>rs998639</td> <td>11</td> <td>3149249</td> <td>OSBPL5</td> <td>5.00</td> <td>0.36</td> <td>0.00</td> <td>0.07</td> <td></td>	ILMN_2307032	11	rs2829679	21	26662543		rs998639	11	3149249	OSBPL5	5.00	0.36	0.00	0.07	
1 FAZZASTO 1 CONDENS CONDENS 1 CALL CALL <td>ILMIN_1742456</td> <td>n 0</td> <td>rs17780195</td> <td>1.7</td> <td>70624189</td> <td></td> <td>rs22/37/0</td> <td>ומ</td> <td>77755469</td> <td>CSTFI</td> <td>5.42</td> <td>0.16</td> <td>0.87</td> <td>0.49</td> <td></td>	ILMIN_1742456	n 0	rs17780195	1.7	70624189		rs22/37/0	ומ	77755469	CSTFI	5.42	0.16	0.87	0.49	
1 0.00000000 1.00000000 1.00000000 1.000000000 1.0000000000	ILMN-1742456	n ,	rs2273770	n ,	77755469	OSTFI	rs7718088	Ω,	179590952		5.42	1.20	80.0	0.62	000
1 1	ILMN_1734542	-	rs10802822	-	240132968		rs1264898	-	111992823	OVGP1	5.43	0.13	1.48	0.88	128.140
5 ##3248340 5 ##324840 6 ##324840 6 ##324840 7 ##324840 7 ##324840 7 ##324840 8 ##324840 9 PAM ##32440 PAM ##324840 PAM PAM PAM PAM <t< td=""><td>ILMN_1734542</td><td>- 1</td><td>rs347331</td><td>n :</td><td>140148107</td><td></td><td>rs1264894</td><td>-</td><td>111969719</td><td>CVGFI</td><td>6.04</td><td>0.25</td><td>1.21</td><td>0.82</td><td></td></t<>	ILMN_1734542	- 1	rs347331	n :	140148107		rs1264894	-	111969719	CVGFI	6.04	0.25	1.21	0.82	
15 FRANKSHOUND 1 JARY 2019 PEX.D A.18 A.18 <td>ILMN_2313901</td> <td>ı n</td> <td>rs28092</td> <td>io i</td> <td>102149795</td> <td>PAM</td> <td>rs784600</td> <td>- 0</td> <td>40139553</td> <td>HPCAL4</td> <td>5.59</td> <td>0.66</td> <td>0.44</td> <td>0.59</td> <td></td>	ILMN_2313901	ı n	rs28092	io i	102149795	PAM	rs784600	- 0	40139553	HPCAL4	5.59	0.66	0.44	0.59	
12 12 12 12 12 12 12 12	ILMN_1815951	o	rs2438490	c	148726162	PCYOXIL	rs2731939	n	21395989		6.20	0.19	0.26	0.16	
12 Fig405797 15 74,246,642 Fig4328748 12 7364442 PEX 5 5.74 0.34 0.09 11 rest3288233 12 49151303 rest3284233 12 49151404 rest3284233 19 40029446 PGLYRP1 rest3288233 19 40029446 PGLYRP1 rest3288233 19 40029446 PGLYRP1 rest3288233 19 40029446 PGLYRP1 rest328233 19 70000 0.00 </td <td>ILMN_1660232</td> <td>12</td> <td>rs10444467</td> <td>12</td> <td>128052636</td> <td></td> <td>rs4329748</td> <td>12</td> <td>7364442</td> <td>PEX5</td> <td>5.85</td> <td>0.09</td> <td>0.71</td> <td>0.32</td> <td>120.688</td>	ILMN_1660232	12	rs10444467	12	128052636		rs4329748	12	7364442	PEX5	5.85	0.09	0.71	0.32	120.688
13 18131090 22 401511030 PGTAPRA 5.64 0.87 0.36 21 18131090 22 140151030 PGCS9467 1.4 2195267 PGAPA 6.51 0.65 0.65 22 1847072 22 3167518 PHKZH 1778808 PHCA 6.51 0.69 0.60 22 1847072 22 3167518 PHKZH 18208887 PKZH 0.50 0.00 0.00 22 1867672 22 3199917 PHKZH 18208687 0.00 0.00 0.00 22 1867672 22 3199917 PHKZH 18208687 0.00 0.00 0.00 22 1867672 22 3199917 PHKZH 18208787 0.00 <td>ILMN_1660232</td> <td>12</td> <td>rs7495797</td> <td>15</td> <td>27246462</td> <td></td> <td>rs4329748</td> <td>12</td> <td>7364442</td> <td>PEX5</td> <td>5.74</td> <td>0.34</td> <td>0.00</td> <td>0.13</td> <td></td>	ILMN_1660232	12	rs7495797	15	27246462		rs4329748	12	7364442	PEX5	5.74	0.34	0.00	0.13	
11 pt.12982333 19 46.52466 PCLYRP1 rs12082367 14 212982367 6.51 0.03 0.05 22 rs4414404 22 3157186 PRINT rs401464 5.51 0.03 0.00 22 rs440440 22 3157186 PRINT rs506841 1 7178657 5.00 0.00 0.00 22 rs440440 22 3157186 PRINT 1 7178657 5.00 0.00 0.00 22 rs47087 22 33234931 PISD rs565844 2 31094776 5.00 0.00 0.00 2 rs75587 22 33234931 PISD rs565046 2 1101244767 PPPRBA 5.01 0.00 0.00 11 rs12040307 1 rs1204767 PPPRBA 5.01 0.01 0.01 0.01 12 rs12040307 1 rs1204767 PPPRBA 5.01 0.01 0.01 0.01	ILMN_1797893	13	rs131969	22	49151303		rs7328733	13	33126737	PFAAP5	5.64	0.87	0.36	0.67	
21 residand 2 11 12007368 PHK3IP1 residand 2 12 1200736 0.00 0.00 0.00 22 residand 2 2 31999177 PHK3IP1 residand 2 2 3100777 0.00<	ILMN_1704870	19	rs12982353	19	46529456	PGLYRP1	rs1263806	14	21982957		6.51	0.03	0.65	0.24	
2.2 ried/14/14/40 2. 314/75/18/2 products 1 61728/67 1 61728/67 1 61728/67 1 61728/67 1 61728/67 1 1 61728/67 1 1 61728/67 1 1 61728/67 1 <	II.MN 1812552	-	rs493642	=	123097386		rs10736812	-	76708086	PHCA	10	0.36	0 0	0.70	46 389
2.2 ind/10072 2. 2026333 PISD ind/100833 14 30368867 5.2 0.62 0.87 0.87 2.2 ind/10072 2. 32364031 PISD ind/10072 2. 3036918 PISD ind/10072 2. 3036040 0.0 1.0 0.0 <	11.MN 1719986	66	ro4141404	000	31675185	PIK3ID1	200000000000000000000000000000000000000	-	61798507		100	00.0	0.00	0 03	
2.2 Fight 10.2 2.2 STATION 2.2 2.2 </td <td>11 Men 1703034</td> <td>1 0</td> <td>10111111</td> <td>1 0</td> <td>99969191</td> <td>T TOTAL</td> <td>12000041</td> <td></td> <td>000000000000000000000000000000000000000</td> <td></td> <td>00.0</td> <td>000</td> <td>0.00</td> <td>0000</td> <td></td>	11 Men 1703034	1 0	10111111	1 0	99969191	T TOTAL	12000041		000000000000000000000000000000000000000		00.0	000	0.00	0000	
2.2 F. 180.1877.2 2.2 3.199.117 F. 1.5 F. 1.5 F. 1.1 O. 0.0 0.1.9 2.2 1.875.187.2 2.2 3.139.187 F. 1.5 1.1 1.1 1.1 1.1 1.1 1.1 0.00 0.1.2 0.04 2. 1.875.10.10 4.05.20.10 4.05.20.10 4.04.20.10 0.31 0.04 0.04 1.1 1.891.10.10 2. 3.32.34.34.3 1.1 7.55.30.0 0.04 0.04 0.04 1.1 1.891.10.10 2. 3.05.30.0 1.1 7.55.30.0 0.04 <	ILMIN_1,93934	7 0	2100153	7 0	10100270	LISD	FSIO490313	# ·	0.000000		0.70	0.02	0.0	0.00	
2 ref.15572 2 3524834 ref.15572 7 4.12 0.05 0.04 9 ref.15572 2 150878164 2 32048475 PISD 0.06 0.04 9 ref.15579 0 465878164 ref.28046 9 14087108 PNFLAT 5.15 0.05 0.04 1 ref.1231969 16 4527109 ref.28046 9 14087108 PPFLAT 5.15 0.05 0.04 1 ref.1231403 15 16839947 ref.1210009 1 212447167 PPFRBA 5.15 0.03 0.04 1 ref.12402256 12 135350044 ref.1210009 1 21244767 PPFRBA 5.65 0.03 0.03 1 ref.12402256 12 135050044 ref.1210009 1 21244767 PPFRBA 5.65 0.03 0.03 1 ref.104040 1 21244767 PPFRBA 5.75 0.08 0.03	ILMIN_I 793934	7.7	rsp518752	7.7	31999127	FISD	rs954627	-	18236681		7.11	0.00	1.19	0.48	
2 res6869411 5 ISSERSIGO4 res407884 2 219182481 PNKD 6:35 0.16 0.704 1 res1163998 6 4527100 res428064 9 14487108 0.31 0.73 0.73 14 res1163998 6 4527109 res22664 res1116887 1 755990 PPPPRRA 5.63 0.72 0.43 14 res129365 1 2659664 res12120009 1 212447167 PPPPRRA 5.63 0.72 0.43 1 res122355 13 66222691 res12120009 1 212447167 PPPPRRA 5.61 0.03 0.13 1 res8622694 1 107417238 res1120009 1 212447167 PPPPRRA 5.61 0.03 0.13 1 res862267 1 107417238 res1120009 1 212447167 PPPPRRA 5.61 0.03 0.14 1 res1022846 1 12147167 PPP	ILMN_1793934	7.7	rs715572	7.7	33234931		rs6518754	7.7	32097775	PISD	4.12	0.05	0.42	0.15	1.137
9 res163998 16 4557109 res92804 9 140487108 PPFIBP2 4.44 0.31 0.37 14 res1291019 20 49668256 res92864 19 140487108 6.15 5.15 0.33 0.33 14 res12910109 20 5836086 res1120000 1 212447167 PPPRR5A 5.63 0.72 0.48 1 res1280367 13 66222691 res12120009 1 212447167 PPPRR5A 5.67 0.08 0.36 1 res188352 13 66222691 res12120009 1 212447167 PPPRR5A 5.67 0.08 0.36 1 res1082037 14 9504042 res12120009 1 212447167 PPPRR5A 5.65 0.36 0.36 1 res1082031 14 9504042 res1120009 1 212447167 PPPRR5A 5.65 0.36 0.36 1 res1082023 16 1202447167	ILMN_1774604	7	rs6869411	S	158781604		rs4672884	7	219182481	PNKD	6.35	0.16	0.04	0.04	
11 re9911019 20 49688255 res475840 PFPRBP2 444 0.29 0.33 14 re9104409 2 49688255 res47864 5.830880 6.836886 <td>ILMN_1662587</td> <td>6</td> <td>rs11639998</td> <td>16</td> <td>4527109</td> <td></td> <td>rs928046</td> <td>6</td> <td>140487108</td> <td>PNPLA7</td> <td>5.15</td> <td>0.31</td> <td>0.78</td> <td>0.56</td> <td></td>	ILMN_1662587	6	rs11639998	16	4527109		rs928046	6	140487108	PNPLA7	5.15	0.31	0.78	0.56	
14 rs12914603 15 58350896 rs11168875 14 36198146 PPP2RAG 5.81 0.12 0.44 1 rs12914603 15 5835064 rs11156875 14 36198146 PPP2RAG 5.63 0.72 0.48 1 rs12422255 12 125596064 rs12120009 1 21447167 PPP2RAG 5.63 0.05 0.95 1 rs682334 11 107417238 rs12120009 1 21447167 PPP2RAG 5.63 0.05 0.36 1 rs682334 11 107417238 rs12120009 1 212447167 PPP2RAG 5.63 0.05 0.36 1 rs767367 1 12447167 PPP2RAG 5.73 0.06 0.30 1 rs8019823 14 2504088 1 12447167 PPP2RAG 5.73 0.06 0.30 1 rs8019823 14 2504088 1 12447767 PPP2RAG 5.64 0.06	ILMN_1675656	11	rs911019	20	49668255		rs4758001	11	7559930	PPFIBP2	4.44	0.29	0.33	0.26	
1 rss1020009 1 212447167 PPP2R5A 5.63 0.72 0.48 1 rss1032055 2 166399467 rss12120009 1 212447167 PPP2R5A 5.63 0.72 0.95 1 rs1689083 13 162526691 rs12120009 1 212447167 PPP2R5A 5.65 0.13 0.05 1 rs682334 11 107417238 rs12120009 1 212447167 PPP2R5A 5.65 0.13 0.05 1 rs7871178 9 271444775 rs1000099 1 212447167 PPP2R5A 5.65 0.13 0.05 1 rs7871178 9 271444775 rs1000990 1 212447167 PPP2R5A 5.72 0.06 0.13 1 rs7871177 rs1000990 1 212447167 PPP2R5A 5.72 0.16 0.13 1 rs20188555 16 2386774 rs11049773 16 12633867 PRDX5 7.34 <td< td=""><td>ILMN_1662617</td><td>14</td><td>rs12914603</td><td>15</td><td>58350896</td><td></td><td>rs11156875</td><td>14</td><td>35619816</td><td>PPP2R3C</td><td>5.81</td><td>0.12</td><td>0.42</td><td>0.19</td><td></td></td<>	ILMN_1662617	14	rs12914603	15	58350896		rs11156875	14	35619816	PPP2R3C	5.81	0.12	0.42	0.19	
1 rest8492835 12 12555664 res12120009 1 212447167 PPP2R5A 5.72 0.08 0.05 1 res682334 11 10741228 res12120009 1 212447167 PPP2R5A 5.61 0.08 0.03 1 res682334 11 10741238 res12120009 1 212447167 PPP2R5A 5.62 0.08 0.03 1 res682334 11 10741238 res12120009 1 212447167 PPP2R5A 5.62 0.08 0.37 1 res682834 16 28867776 res1200099 11 212447167 PPP2R5A 5.73 0.05 0.11 2 res1209231 23 24867776 res1200099 11 21244767 PPP2R5A 5.73 0.05 0.11 2 res1209231 23 24867776 res1200099 11 21244767 PPPRA 5.73 0.01 0.14 2 res1209231 21 4793468	ILMN_1738784	1	rs10930170	73	166399467		rs12120009	-	212447167	PPP2R5A	5.63	0.72	0.48	99.0	
1 res6889083 13 66222691 res121200009 1 212447167 PPP2R5A 5.61 0.36 0.28 1 res6829083 13 66222691 res121200009 1 212447167 PPP2R5A 5.65 1.60 0.28 1 res7757871 6 135030045 res12120009 1 212447167 PPP2R5A 5.65 1.60 0.38 1 res7757871 6 135030045 res121200099 1 212447167 PPP2R5A 5.65 0.36 0.36 1 res1282355 16 42867776 res11000990 1 212447167 PPP2R5A 5.65 0.36 0.36 1 res1282355 16 42867776 res11701058 21 47776382 C210RF57 5.60 0.03 0.03 6 res28805648 18 43808354 FSMB1 res1220714 6 17087444 PSMB1 5.14 0.06 0.04 6 res6060390 2	ILMN_1738784	1	rs12423255	12	123595064		rs12120009	-	212447167	PPP2R5A	5.72	0.08	0.95	0.46	
1 rs652334 1 107417238 rs12120009 1 212447167 PPP2R5A 5.65 1.69 0.28 1 rs7571778 9 27144475 rs12120009 1 212447167 PPP2R5A 5.95 0.16 0.06 1 rs7571778 9 27144475 rs12120009 1 212447167 PPP2R5A 5.95 0.16 0.06 1 rs28019823 14 95040482 rs1100099 1 212447167 PPP2R5A 5.72 0.16 0.03 1 rs28019823 2 2887776 rs1000990 1 212447167 PPP2R5A 5.73 0.06 0.11 2 rs2801923 2 47931653 C210RF57 rs1107058 2 777474 PSMB1 7.34 0.05 0.14 5 rs2802954 1 47087682 2 17087744 PSMB1 5.14 0.04 0.21 6 rs6008980 2 170877444 PSMB1	ILMN_1738784	1	rs1889083	13	66222691		rs12120009	-	212447167	PPP2R5A	5.61	0.36	0.13	0.17	
1 res7757871 6 135030045 res12120009 1 212447167 PPP2R5A 5.95 0.37 0.06 11 res7757871 6 271444475 res12120009 11 212447167 PPP2R5A 5.95 0.37 0.08 11 res8019823 14 95040482 res11600990 11 64082807 PRDX5 6.43 0.81 0.14 15 res288372 21 47931653 C210RF57 res16407346 6.43 0.63 0.03 2 res28839372 21 47031653 C210RF57 res1600934 PSMB1 5.60 0.19 0.03 2 res28839372 21 42062843 6 17080084 PSMB1 5.14 0.00 0.03 6 res6060830 18 43983354 PSMB1 res282643 6 17080084 PSMB1 5.14 0.00 0.20 6 res6060830 20 30347824 PSMB1 res2826415 6	ILMN_1738784	1	rs682334	11	107417238		rs12120009	Т	212447167	PPP2R5A	5.65	1.69	0.28	1.21	
1 resp8719278 9 27144475 res12120009 1 210442867 PPP2R5A 5.72 0.16 0.30 16 res2188355 16 23867776 res1060990 1 6442887 PRDX5 6.43 0.14 0.14 21 res2188355 16 23867776 res10609279 16 12639800 7.34 0.15 0.13 21 res2188355 16 23867776 res1049273 16 12639800 7.34 0.55 0.11 21 res3862607 21 47931653 C210RF57 res1207114 6 17687744 PSMB1 5.79 0.05 0.14 6 res6060330 20 31347842 res12207114 6 17682379 PSMB1 5.14 0.04 0.21 6 res6060330 20 31347744 PSMB1 5.44 0.24 0.21 6 res6082843 6 17685423 1 77628275 PSMB1 5.44 0.24<	ILMN_1738784	Т	rs7757871	9	135030045		rs12120009	1	212447167	PPP2R5A	5.95	0.37	90.0	0.12	
11 res6019823 14 95040482 res11600990 11 64082807 PRDX5 6.43 0.81 0.14 16 res1029231 21 473467776 res0402739 16 1263900 7.34 0.53 0.01 0.03 21 res283972 21 47931653 C21ORF57 res928437 21 4777340 5.60 0.19 0.03 21 res2839372 21 45068862 C21ORF57 res1207114 PARBH 5.79 0.03 0.044 6 res4890648 18 43983954 res13207114 FSMBH 5.79 0.00 0.04 6 res608030 20 30047822 pre608089 1 2777444 PSMBH 5.74 0.00 0.26 6 res608080 20 30047823 res12207144 PSMBH 5.74 0.04 0.26 1 res7299449 12 137287957 res1220714 1702877957 4.58 0.08 0.08	ILMN_1738784	1	rs7871178	6	27148475		rs12120009	1	212447167	PPP2R5A	5.72	0.16	0.30	0.16	
16 res188355 16 22867776 res10492793 16 12639800 7.34 0.53 0.11 21 res108355 21 42038653 C210RF57 res049377 18 34934653 C210RF57 6.60 0.19 0.45 21 res283972 21 48063862 res048362 1.81777638 21 4777638 6.79 0.09 0.44 7 6 res3802648 18 438938544 res0383843 6 17080334 PSMB1 5.14 0.00 0.26 6 res060830 20 3034782 res030415 6 170823379 PSMB1 5.14 0.04 0.26 6 res060830 20 30347824 res10320714 6 17087744 PSMB1 5.14 0.04 0.05 12 res060830 20 3034782 res10320714 6 170877444 PSMB1 5.14 0.04 0.05 12 res031562 1 7521825<	ILMN_1711606	11	rs8019823	14	95040482		rs11600990	11	64082807	PRDX5	6.43	0.81	0.14	0.44	
21 res1029321 21 47931653 C21ORF57 18 31497346 5.60 0.19 0.03 6 res280923 21 47931653 C21ORF57 18 41777344 PSMB1 5.76 0.19 0.04 6 res380507 11 121774705 res928843 6 170877444 PSMB1 5.74 0.00 0.26 6 res4800648 18 43983854 res928433 6 17089784 PSMB1 5.14 0.00 0.21 6 res6028843 6 res6028843 6 17089784 PSMB1 5.14 0.00 0.21 6 res6028843 6 res6028843 6 17089034 PSMB1 5.14 0.00 0.21 12 res6028846 17089034 1 12277976 6 17089034 1.03 0.03 0.44 12 res615622 1 1 170877444 PSMB1 1.084804 0.00 0.02 0.44<	ILMN_1713603	16	rs2188355	16	23867776		rs10492793	16	12639800		7.34	0.53	0.11	0.25	11.228
21 rs2839372 21 48068862 rs11701058 21 4775382 C210RF57 4.81 0.69 4.47 6 rs386267 11 121774705 rs13207114 6 17087744 PSMB1 5.79 0.04 6 rs488626843 2 3034782 rs6928445 6 17082379 PSMB1 5.14 0.00 0.26 6 rs6060830 20 3034782 rs780714 6 17082379 PSMB1 0.04 0.05 6 rs6060803 2 3034782 rs7106083 6 17082379 7 4.58 0.04 0.02 12 rs6060803 2 3034782 rs7106083 1 2721825 PSMB1 6.14 0.00 0.03 12 rs608020 1 76588123 rs11036212 1 5221825 PTDSS1 5.00 0.03 0.08 12 rs631562 1 1 7221825 PTDSS1 5.70 0.03	ILMN_1675038	21	rs1029231	21	47931653	C21ORF57	rs958127	18	31497346		5.60	0.19	0.03	0.04	
6 res8ec667 11 12177476 res13207114 6 170877444 PSMB1 5.79 0.44 0.24 6 res600830 20 30347832 res029543 6 170823379 PSMB1 5.14 0.04 0.26 6 res600830 20 30347832 res29543 6 170823379 PSMB1 5.14 0.04 0.21 6 res60830 20 30347832 res276964 1 22579787 5.44 0.44 0.21 12 res635367 14 9478823 res1020714 6 170823379 PSMB1 5.42 0.32 12 res631562 17 76588123 res1030714 1 5221825 PTDSS1 5.00 0.03 0.43 12 res631562 17 76588123 res10020773 4 17526823 QDPR 5.75 0.02 0.03 12 res631562 1 1 22521825 PTDSS1 5.70 <t< td=""><td>ILMN_1675038</td><td>21</td><td>rs2839372</td><td>21</td><td>48063862</td><td></td><td>rs11701058</td><td>21</td><td>47776382</td><td>C21ORF57</td><td>4.81</td><td>0.69</td><td>4.47</td><td>4.06</td><td>0.287</td></t<>	ILMN_1675038	21	rs2839372	21	48063862		rs11701058	21	47776382	C21ORF57	4.81	0.69	4.47	4.06	0.287
6 re4890648 18 43983644 PSMB1 FSMB1 5.14 0.00 0.26 6 re5028643 6 170890384 PSMB1 FSMB1 FS.14 0.00 0.26 6 re5028643 6 170829384 6 170829384 6 170829384 6 170829384 6 170829384 6 1708744 7542 1.35 0.64 0.21 1 re3729676 1 2779797 4.58 1.35 0.63 1.35 0.64 0.63 0.64 0.63 1 re372836 1 70277977 1 521825 PTDSS1 5.00 0.08 0.63 0.64 1 re434862 1 76598123 re11036212 11 5221825 PTDSS1 5.00 0.08 0.08 0.08 1 re4345704 re1005627 1 7023672 QPR 2.70 0.02 0.08 1 re1077728 1 4 <th< td=""><td>ILMN_1789176</td><td>9</td><td>rs3862607</td><td>11</td><td>121774705</td><td></td><td>rs13207114</td><td>9</td><td>170877444</td><td>PSMB1</td><td>5.79</td><td></td><td>0.44</td><td></td><td></td></th<>	ILMN_1789176	9	rs3862607	11	121774705		rs13207114	9	170877444	PSMB1	5.79		0.44		
6 res0060830 20 3034783 PSMB1 5.44 0.44 0.1 6 res0608330 20 3034783 PSMB1 res99545 6 17087344 PSMB1 4.58 1.18 0.54 0.64 6 res729749 12 131727816 res2720836 1 2574744 PSMB1 5.45 1.18 0.32 12 res2383 67 1 568123 res10320714 6 17087744 PSMB1 5.50 0.03 0.048 12 res2383 67 1 7658123 1 521825 PTDSS1 5.00 0.03 0.08 12 res631562 1 7658123 res1036212 1 5221825 PTDSS1 5.70 0.02 0.03 12 res631562 1 7628424 1 7628682 QPPR 5.75 0.03 0.03 13 res041730 2 3337574 RFMD RFMD 1 70233726 QPPR 6	ILMN_1789176	9	rs4890648	18	43983954		rs6928843	9	170890384	PSMB1	5.14	00.0	0.26	0.04	
6 rs6928843 6 170890384 PSMB1 rs2769959 1 225797957 4.58 1.95 0.64 12 rs7239674 12 131727816 rs12207114 6 17087744 PSMB1 5.42 1.95 0.64 12 rs238367 14 9.5478823 rs1038212 11 5221825 PTDSS1 5.00 0.03 0.48 12 rs4669205 17 76584246 rs1008212 11 5221825 PTDSS1 5.70 0.03 0.48 12 rs4669205 17 76584246 rs1008212 11 5221825 PTDSS1 5.70 0.03 0.48 12 rs491762 6 106348246 rs10020773 4 17526682 QDPR 5.75 0.03 0.46 12 rs2404788 RABACI rs78051628 11 120174174 6.42 0.25 0.03 11 rs9931702 16 55526551 AKTIP rs18492379 11 <td>ILMN_1789176</td> <td>9</td> <td>rs6060930</td> <td>20</td> <td>30347832</td> <td></td> <td>rs9295415</td> <td>9</td> <td>170823379</td> <td>PSMB1</td> <td>5.44</td> <td>0.44</td> <td>0.21</td> <td>0.27</td> <td></td>	ILMN_1789176	9	rs6060930	20	30347832		rs9295415	9	170823379	PSMB1	5.44	0.44	0.21	0.27	
6 res7299749 12 137727816 res13207114 6 170877444 PSMB1 5.42 1.18 0.32 12 res2396774 1 1.2085243 res1036212 11 5221825 PTDSS1 5.90 0.08 0.08 12 res631602 1 76598123 res11036212 11 5221825 PTDSS1 5.90 0.08 0.08 12 res631602 1 76598138 res11036212 11 5221825 PTDSS1 5.90 0.08 0.08 4 res631602 1 765982438 res11036212 11 5221825 PTDSS1 5.70 0.08 0.08 1 res041730 2 33375704 res10020773 1 7723726 QDPR 6.55 0.25 0.08 1 res042279 1 27023726 QDPR 6.38 0.03 0.31 1 res0422579 1 32136436 RCNI res14740645 6.42 0.04	ILMN_1789176	9	rs6928843	9	170890384	PSMB1	rs2769689	1	225797957		4.58	1.95	0.64	1.78	
12 res255367 14 99478823 res1036212 11 5221825 PTDSS1 5.00 0.03 0.48 12 res631562 11 12685423 res11036212 11 5221825 PTDSS1 5.70 0.02 0.03 12 res631562 11 126854248 res11036212 11 5221825 PTDSS1 5.70 0.02 0.03 12 res494676 6 1063428246 res10020773 4 17526682 QDPR 5.75 1.03 0.05 19 res1075728 12 33377504 1 70263177 0.02 0.05 0.05 16 res2087702 16 5526551 AKTIP res492279 11 32136436 RCNI 6.32 0.03 0.31 11 res4922579 11 res4922579 11 21244645 0.04 0.04 0.06	ILMN_1789176	9	rs7299749	12	131727816		rs13207114	9	170877444	PSMB1	5.42	1.18	0.32	98.0	
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4 res4946705 6 106348246 res10020773 4 17526682 QDPR 5.75 1.03 1.25 12 res421730 22 33375704 res736507 12 70235726 6.55 0.28 0.28 0.084 19 res045788 19 45462788 RABACI res1863464 15 226938488 6.38 0.03 0.31 11 res0831702 16 55526551 AKTIP res1863464 15 226938488 6.38 0.03 0.31 11 res10875911 12 213343486 RCNI res192579 11 32136436 RCNI 8 141174488 0.58 0.03 0.03 11 res4922579 11 32136436 RCNI res11417468 RCNI 6.38 0.04 0.04 0.06	ILMN_1743049	12	rs631562	11	126852438		rs11036212	11	5221825	PTDSS1	5.70	0.05	0.40	0.11	
12 rs241730 22 33375704 rs7305307 12 70235726 6.55 0.25 0.08 19 rs1075728 16 43262788 RAFAP rs765344 15 26938488 6.38 0.03 0.31 11 rs1087702 16 5352651 AKTIP rs4892879 11 32136436 RCNI 6.38 0.03 0.31 11 rs4922579 11 32136436 RCNI rs11416997 8 11177468 4.32 0.41 0.09 11 rs4922579 11 32136436 RCNI rs1341899 1 102740645 5.40 0.04 0.26	ILMN_1672443	4	rs4946705	9	106348246		rs10020773	4	17526682	QDPR	5.75	1.03	1.25	1.55	
19 rs1075728 19 42467788 RABACI rs7951628 11 120161117 6.42 0.28 0.84 16 rs9931702 16 53526551 AKTIP rs1863364 15 26938488 6.42 0.28 0.31 11 rs1927313 12 41147155 rs1427557 11 32136436 RCN1 rs11177468 4.32 0.41 0.09 11 rs4922579 11 32136436 RCN1 rs1341899 1 102740645 5.40 0.04 0.26	ILMN_1803197	12	rs241730	22	33375704		rs7305307	12	70235726		6.55	0.25	0.08	0.09	
16 re9931702 16 5552555 AKTIP rs1863464 15 296934488 6.38 0.03 0.31 11 rs102879131 12 41147155 RCN1 rs19292579 11 32136436 RCN1 5.23 0.58 0.37 11 rs4922579 11 32136436 RCN1 rs11166957 8 14177468 4.32 0.41 0.09 11 rs4922579 11 32136436 RCN1 rs1341899 1 102740645 5.40 0.04 0.26	ILMN_2207363	19	rs1075728	19	42462788	RABACI	rs7951628	11	120161117		6.42	0.28	0.84	0.59	
11 rs1087931 12 41147155 RCNI rs4922579 11 32136436 RCNI 65.23 0.58 0.37 11 rs4922579 11 32136436 RCNI rs1146957 8 14177468 4.32 0.41 0.09 11 rs4922579 11 32136436 RCNI rs1341899 1 102740645 5.40 0.04 0.26	ILMN_1756999	16	rs9931702	16	53526551	AKTIP	rs1863464	15	26938488		6.38	0.03	0.31	0.08	
11 rs4922579 11 32136436 RCN1 rs11166957 8 141177468 4.32 0.41 0.09 11 rs4922579 11 32136436 RCN1 rs1341899 1 102740645 5.40 0.04 0.26	ILMN_1800276	11	rs10879131	12	41147155		rs4922579	11	32136436	RCN1	5.23	0.58	0.37	0.47	
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	ILMN_1800276	11	rs4922579	11	32136436	RCN1	rs1341899	1	102740645		5.40	0.04	0.26	0.02	

- 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		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
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	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
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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	ILMN 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 ⁿ					0.122																				0.031		12.131				10 00 00 00	0000														45.345		
	Metag Dis	0.70	0.26			145.78	3.67	08.0	3.78	2.52	0.03	2.87	00.9	8.00	2.27	0.19	3.51	7.36	10.72	2.10	9.20	4.47	0	0.32	0.07	4.09	0.29	0.36	1.07	0.68	80.0	0.59	0.44	0.25	0.22	0.16	80.0	1.01	0.56	0.02	0.13	0.40	0.69	1.69	0.39	90.0			
assis d'Olesa	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	1.89	0.40	0.01	1.60	0.87	0.18	0.47	0.38	0.65	0.36	0.33	0.07	0.78	0.55	0.02	0.26	0.86	0.90	1.23	0.91	0.18			
٠l	Fehrmann ^f	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	1.03	1.03 3.19	0.28	0.93	0.21	0.37	0.12	0.63	0.50	0.04	0.20	0.15	0.24	0.85	0.51	0.14	0.14	0.08	0.36	1.20	0.04	0.07			
	BSGS ^e F	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	5.01	20.08	5.61	5.52	5.97	6.92	7.79	0.45	6.51	7.08	5.86	6.27	0.73 7.83	7.73	8.10	6.71	7.34	7.05	7.41	20.00	6.46	00.9	5.01	5.51	6.34
	Associationd	TMED4	TMEM149	TMEM149	TMEM149	TMEM149																	TMEM63A	TMEMSO	IRF5	IRFO	TRAPPC4	TRAPPC4									TR A DDC 5	TRAPPCS	TRAPPC5			RAPGEF1	TDENG	TREMI	TRIM38	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	23498358	118887887	118887887	166970604	132022957	156404902	24.2529791 2369415	57495457	129644342	9947811	146690926	85439550	7758194	7758194	228504503	30408765	134635088	157393770	41264577	26044369	82273079	2317951	137947208	238746880
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	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	rs11770192	rs3916581	rs3916581	rs10059004	rs1023095	rs1375714	rs1595299	rs4968328	rs7313362	rs7694997	rs7800935	rs856638	rs17159840	rs17159840	rs10179572	rs12921440	rs1887778	rs963354	rs2395771	rs2032447	rs10748526	rs12800998	rs620607	re1198819
	Associationd					SNX26	TMEM149							TRAPPC5	TRAPPC5	TRAPPC5	TRAPPOS	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPOS										MYBPC3	TSPAN32	100 E															
	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	23528927	113531675	131018917	7758194	7758194	7758194	7758194	7758194	7758194	7758194	7758194	7758194	45128454	11272861	7762978	7762978	7762978	7762978	108256422	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	5 0	7	- 62	11	19	19	13	61.	13	19	19	13	19	2 2	20	19	19	19	61	3 5		17	11	11	22
	rs ID	rs1940400	rs2839013	rs5762235	rs6090518	rs807491	rs8106959	rs1254086	rs1548475	rs1537146	rs199795	rs1278760	rs1793823	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs17159840	rs3916995	rs6040514	rs7246264	rs7246264	rs7246264	rs7246264	rs12412964	rs2527180	rs968726	rs10838738	rs12800998	rs140522															
	Chr.	7	19	19	19	19	19	19	19	19	16	19	19	19	19	19	19	19	19	19	19	19	- ;	11	- 1	- 1-	- []	111	19	19	13	n 0	19	19	19	19	. o	61	19	19	19	19	 6I	 o @	9	10	11	11	55
	Probe ID ^D	ILMN_1804148	ILMN_1786426	ILMN_1719649	ILMN_1708482	TI MM 1693611	ILMN-1683811 II.MN 1731043	ILMN_1814650	ILMN_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	II.MN 1688231	ILMN_1697971	ILMN_1785060	ILMN_1718621	ILMN_2389970	II.MN 3223126																			
ı	Gene ID ^a	TMED4	TMEM149	TMEM63A	TMEMSO	TNFO3	TBA2A	TRAPPC4	TRAPPC4	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPOS	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPOS TRAPPOS	TRAPPCS	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TRAPPC5	TREMI	TRIM38	TSPAN14	TSPAN32	TSPAN32	TYMP																			

	Distance / Mb ^h			1.643	0.088																					
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	2.22	1.63	0.15	0.46	0.05
$' - \log_{10} p$	\mathtt{EGCUT}^{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 / $-\log_{10} p$ -values	$Fehrmann^{f}$	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
Interac	BSGSe	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
	Association ^d					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
	Chr.	16	1	17	19	9	9	9	9	9	9	9	9	9	9	18	10	19	က	8	က	က	15	16	16	2
	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
	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	က	8	က	က	17	16	16	7
Expression trait	Probe ID ^b	ILMN_2338348	ILMN_2338348	ILMN_1697227	ILMN_1743646	ILMN_1678939	ILMN_1678939	ILMN_1678939	ILMN_1678939	ILMN_1804935	ILMN_1804935	ILMN_1804935	ILMN_1804935	ILMN_2387680	ILMN_2387680	ILMN_1763455	ILMN_1763455	ILMN_1763455	ILMN_1762103	ILMN_1762103	ILMN_1762103	ILMN_1669484	ILMN_2370573	ILMN_1684628	ILMN_1700238	ILMN_1701875
E	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 ^a	Dataset	n^{b}	Expected ^c	Observed ^d	p-value
$1^{\rm e}$	All	EGCUT	434	217.00	306	6.69×10^{-18}
		Fehrmann	434	217.00	278	5.04×10^{-9}
		Both	434	108.50	221	5.56×10^{-31}
	Significant	EGCUT	30	15.00	25	3.25×10^{-4}
		Fehrmann	30	15.00	24	1.43×10^{-3}
		Both	30	7.50	22	3.76×10^{-8}
2^{f}	All	EGCUT	434	54.25	92	4.22×10^{-7}
		Fehrmann	434	54.25	79	6.18×10^{-4}
		Both	434	6.78	30	2.55×10^{-11}
	Significant	EGCUT	30	3.75	19	9.46×10^{-11}
		Fehrmann	30	3.75	19	9.46×10^{-11}
		Both	30	0.47	18	2.23×10^{-25}
$\overline{3^{\mathrm{g}}}$	All	EGCUT	1133	566.50	775	7.10×10^{-36}
		Fehrmann	1133	566.50	726	1.90×10^{-21}
		Both	1133	283.25	562	1.39×10^{-70}
	Significant	EGCUT	73	36.50	55	1.69×10^{-5}
		Fehrmann	73	36.50	55	1.69×10^{-5}
		Both	73	18.25	46	7.86×10^{-12}

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

^b Number of tests for concordance

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

^d Observed number of concordant cases

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

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

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

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

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

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

^b Number of tests for concordance.

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

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

Table S5: Details on linkage disequilibrium and relative positions of all discovery cis-cis interactions

TMEMI49	Chr	Gene	SNP 1	SNP 2	Position 1	Position 2	Distance / Mb	R^2	D'
CSTB	19	TMEM149	rs807491	rs7254601	36268923	36147315	0.122	0.000	0.001
MBNL1	17	FN3KRP	rs898095	rs9892064	80890638	80827903	0.063	0.063	0.088
10 ADK	21	CSTB	rs9979356	rs3761385	45230974	45198355	0.033	0.041	0.066
11 CTSC rs7930237 rs556895 88117962 88077479 0.040 0.012 0.041 17 GAA rs11150847 rs12602462 78153130 78146016 0.007 0.000 0.001 8 NAPRT1 rs2123758 rs3889129 144663680 0.050 0.053 0.060 1 LAX1 rs1891432 rs10900520 203875662 203780591 0.097 0.065 0.106 18 MBP rs8092433 rs4890876 74747424 74732087 0.015 0.035 0.053 11 SNORD14A rs2648634 17339127 17015557 0.324 0.008 0.012 21 C21ORF57 rs9978658 rs11701361 48027084 47764477 0.263 0.032 0.065 16 RPL13 rs352935 rs2965817 8964580 89513234 0.015 0.051 0.060 19 ATP13A1 rs4284750 rs8783870 19810050 19738554 0.071 0.0	3	MBNL1	rs16864367	rs13079208	152234166	152116652	0.118	0.041	0.117
Trace	10	ADK	rs2395095	rs10824092	76446305	75929517	0.517	0.013	0.020
8 NAPRT1 rs2123758 rs3889129 144663661 144613680 0.050 0.053 0.060 1 LAX1 rs1891432 rs10900520 203877662 203780591 0.097 0.065 0.106 18 MBP rs809433 rs4890876 74747424 74732087 0.015 0.035 0.032 11 SNORD14A rs2634462 rs648634 17339127 17015557 0.324 0.008 0.012 21 C21ORF57 rs9978658 rs11701361 48027084 47764477 0.263 0.032 0.065 16 RPL13 rs352935 rs2965817 89648580 89513234 0.135 0.054 0.065 19 ATP13A1 rs4284750 rs873870 19810050 19738554 0.071 0.008 0.015 2 NCL rs7563453 rs4973397 232201670 232291471 0.010 0.001 0.021 3 NCL rs7563453 rs470010 1793248 1789	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
11 SNORD14A rs2634462 rs6486334 17339127 17015557 0.324 0.008 0.012 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 rs7776572 rs11701052 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs11701058 48063862	1	LAX1	rs1891432	rs10900520	203877662	203780591	0.097	0.065	0.106
21 C21ORF57 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 rs7776572 rs11770192 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs11701058 48663862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 1	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 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 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 48	11	SNORD14A	rs2634462	rs6486334	17339127	17015557	0.324	0.008	0.012
Nation	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 rs7776572 rs11770192 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs11701058 48663862 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 rs773569 157216093 157163614 0.052 0.005 0.006 1 OVGP1 rs10808222 rs1264898 240132968	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 rs1170105 23528927 23498358 0.031 0.064 0.064 21 PRMT2 rs2839372 rs1170105 48063862 47776382 0.287 0.100 0.122 12 OAS1 rs13311 rs2072133 113448652 113409260 0.039 0.002 0.016 16 N4BP1 rs1244224 rs11649236 87580855 48632478 38.948 0.007 0.021 5 CAST rs12719343 rs773671 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	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 48663862 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 rs773671 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 rs184655 37771578 <t< td=""><td>2</td><td>NCL</td><td>rs7563453</td><td>rs4973397</td><td>232301670</td><td>232291471</td><td>0.010</td><td>0.027</td><td>0.029</td></t<>	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 rs2868504 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 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	19	VASP	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 0.000 16 AKTIP rs2896940 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 rs11655031 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 rs11655031 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 rs88427 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 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 12 PEX5 rs10444467 rs4329748 128052636	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 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 <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 rs3811188 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 6 FLJ43093 rs6906101 rs13214069 366	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 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 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	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 0.000	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 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	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	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	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	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	14	MRPL52	rs1950857	rs3811188	26710271	23299135	3.411	0.002	0.004
19 TRAPPC5 rs17159840 rs17763599 7758194 2369415 5.389 0.000 0.000	17	C17ORF60	rs9907897	rs7405659	63502633	59874129	3.629	0.004	0.011
	6	FLJ43093	rs6906101	rs13214069	36667610	32705248	3.962	0.000	0.000
22 PISD rs715572 rs6518754 33234931 32097775 1.137 0.001 0.003	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	DIP2B	rs871257	rs12427378	117994348	51074199	66.920	0.001	0.001
$12 \text{GPR} \\ 162 \text{rs} \\ 2272500 \text{rs} \\ 2707210 79685913 6902002 72.784 0.003 0.005$	12	GPR162	rs2272500	rs2707210	79685913	6902002	72.784	0.003	0.005
17 USP36 rs2279308 rs7225546 76794981 75151717 1.643 0.000 0.000	17	USP36	rs2279308	rs7225546	76794981	75151717	1.643	0.000	0.000