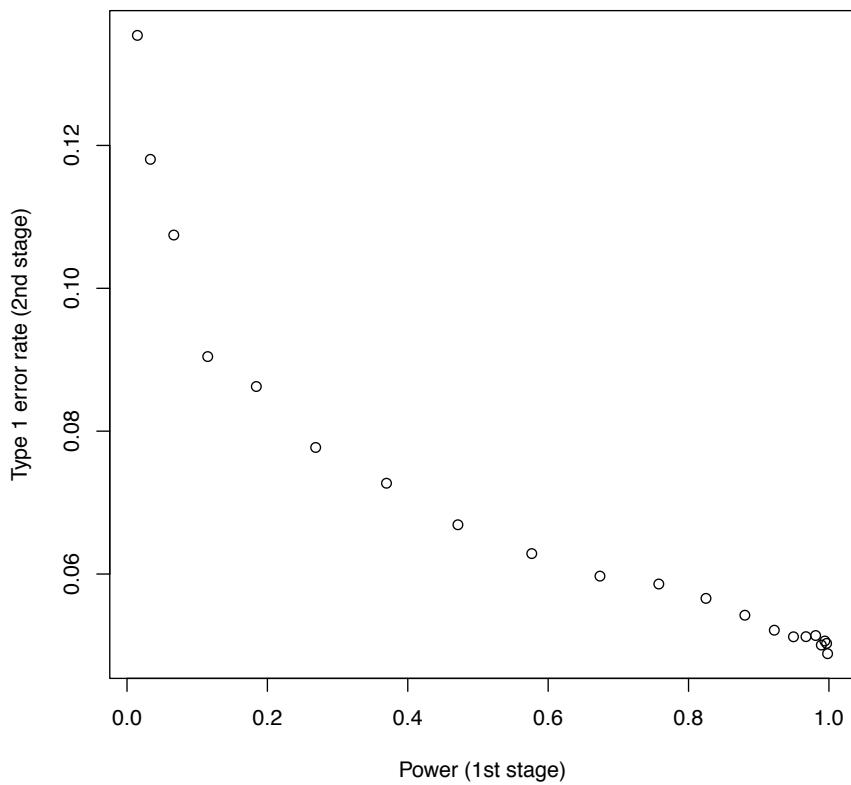
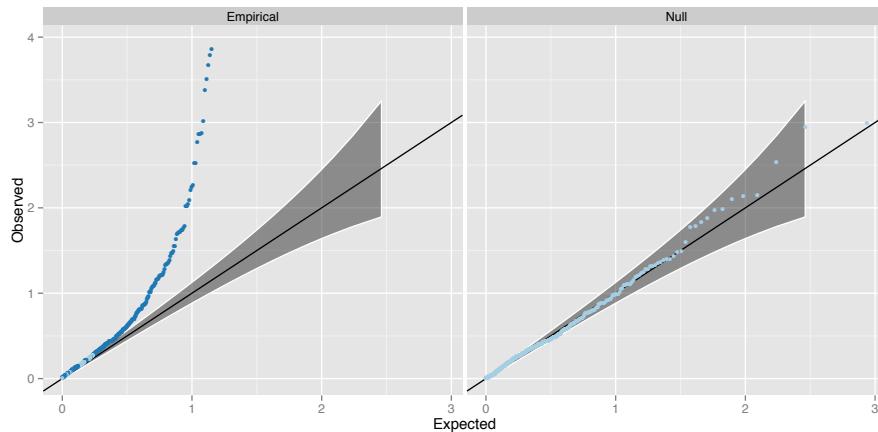


# SUPPLEMENTARY INFORMATION

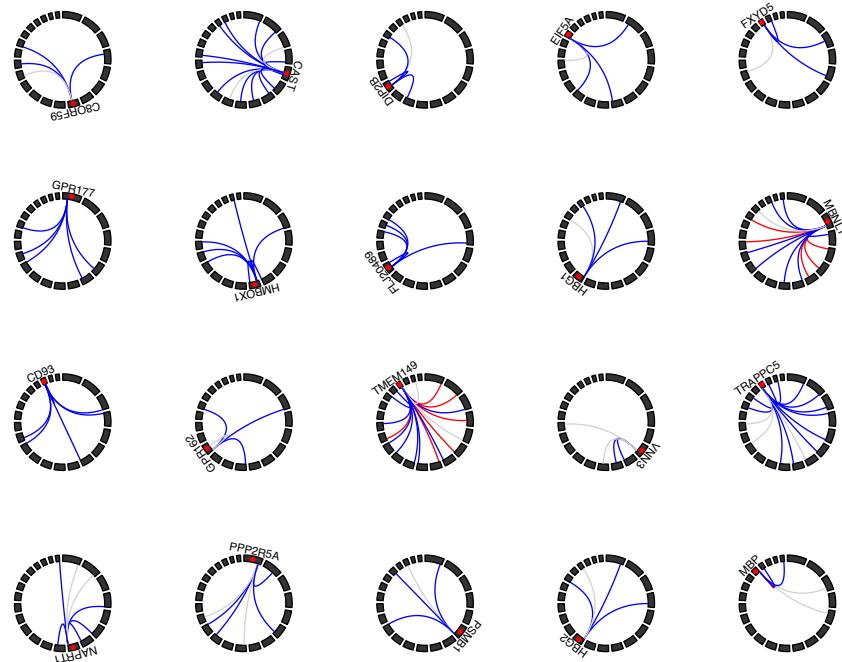
doi:10.1038/nature13005



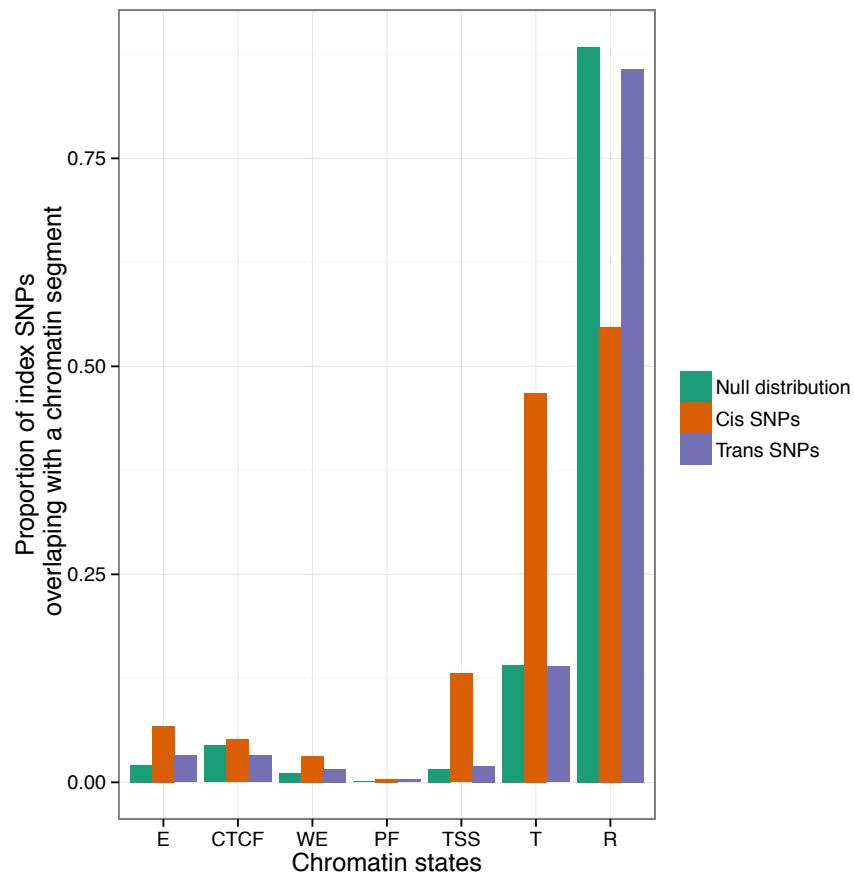
**Figure S1: Type 1 error rate of two stage design assuming a null model of one large additive effect and no epistasis** In stage 1 SNPs are tested for full genetic effects (8 d.f.) and those that surpass a threshold for multiple testing are then tested for significant interaction terms in stage 2. These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



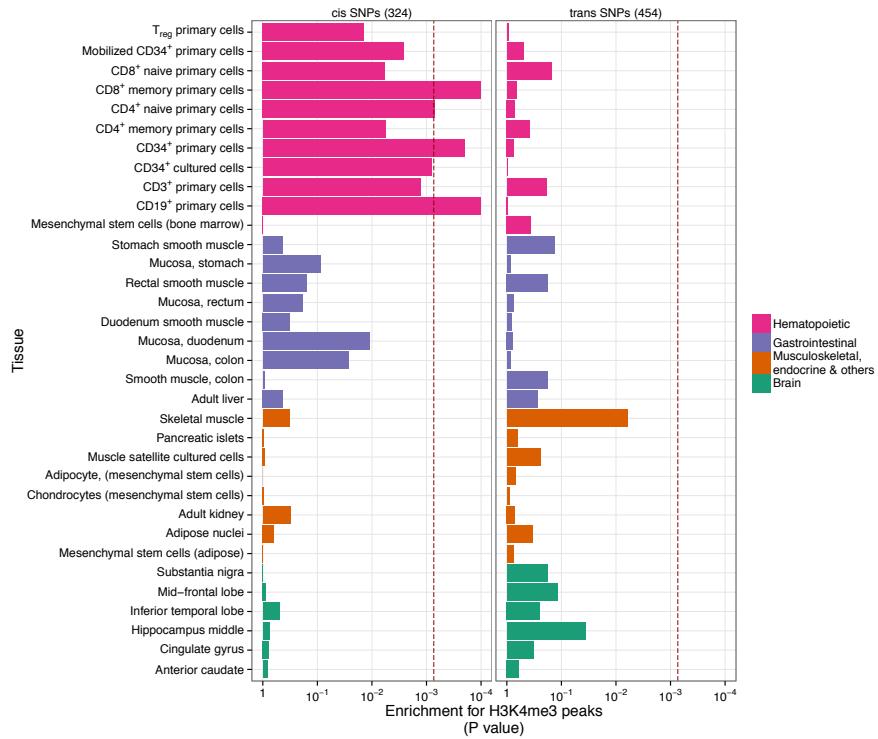
**Figure S2: Q-Q plots of interaction  $p$ -values from replication datasets, excluding the 30 points significant at the Bonferroni level** The right panel (Null) shows the interaction  $p$ -values from a meta analysis across two independent datasets on 434 SNP pairs where one SNP has a marginal effect.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



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



**Figure S4: Location of SNPs relative to genomic features** We used chromatin segmentation<sup>28</sup> 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 promoter 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, CTCF = CTCF enriched element, WE = Predicted weak enhancer or open chromatin cis regulatory element, PF = Predicted promoter flanking region, TSS = Predicted promoter region including transcriptional start site, T = Predicted transcribed region, R = 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.<sup>27</sup> Enrichment *p*-values are calculated using permutation analysis for 34 different cell types (*y*-axis) in four tissue types (Rows of boxes). The dotted red line denotes significance (Bonferroni correction for 34 cell types, *x*-axis). There is enrichment for *cis*-acting SNPs in Haematopoietic tissue types only. *Trans*-acting SNPs have no tissue specificity.

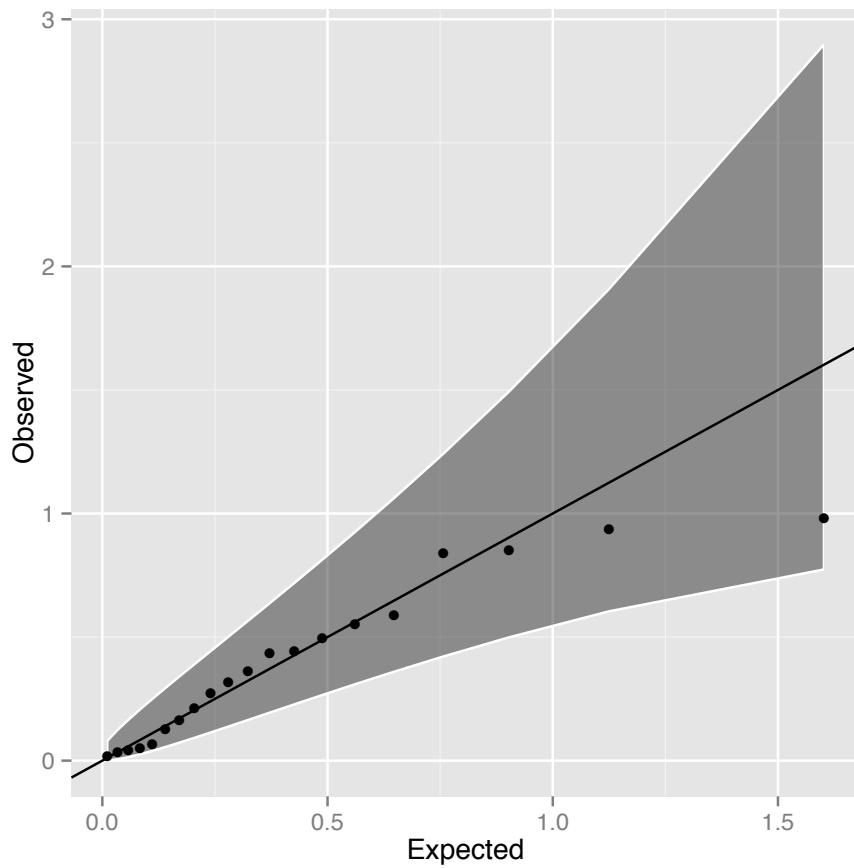
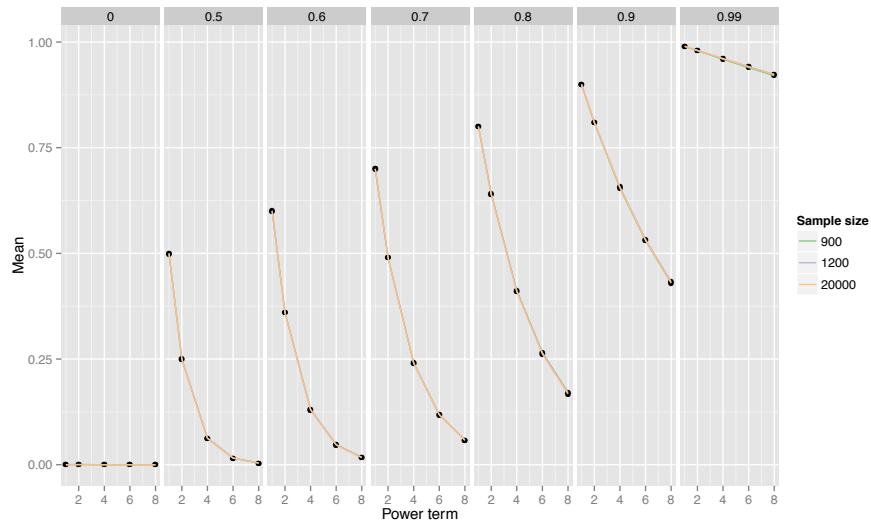
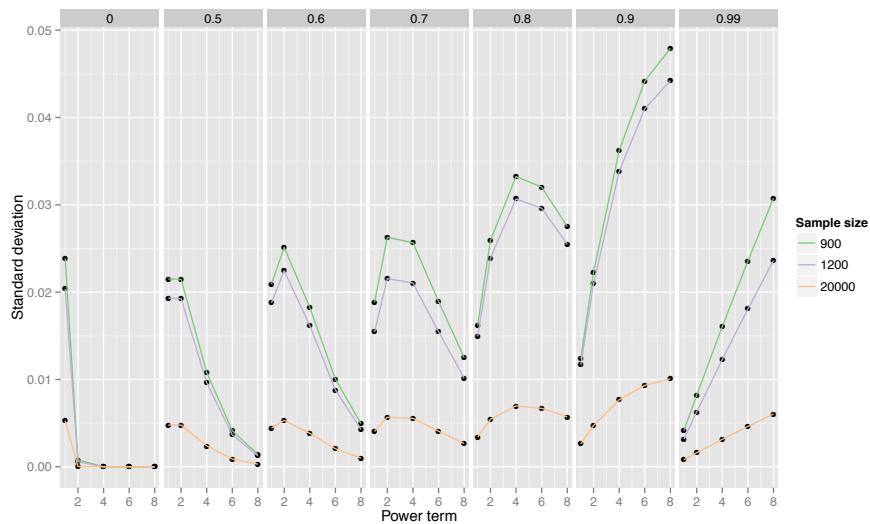


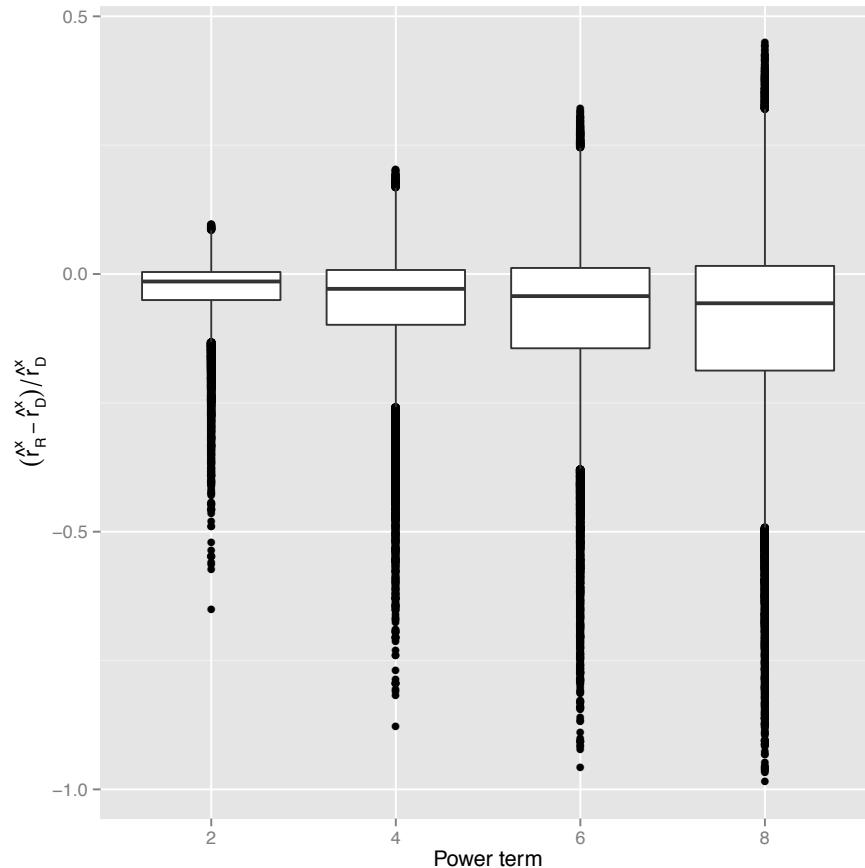
Figure S6: **Q-Q plot of interaction  $p$ -values in the CDHWB dataset**  
Twenty of the 501 discovery SNP pairs passed filtering in the CDHWB dataset (mainly due to small sample size). There is no evidence for enrichment of interaction terms, most likely due to insufficient power given the limited sample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



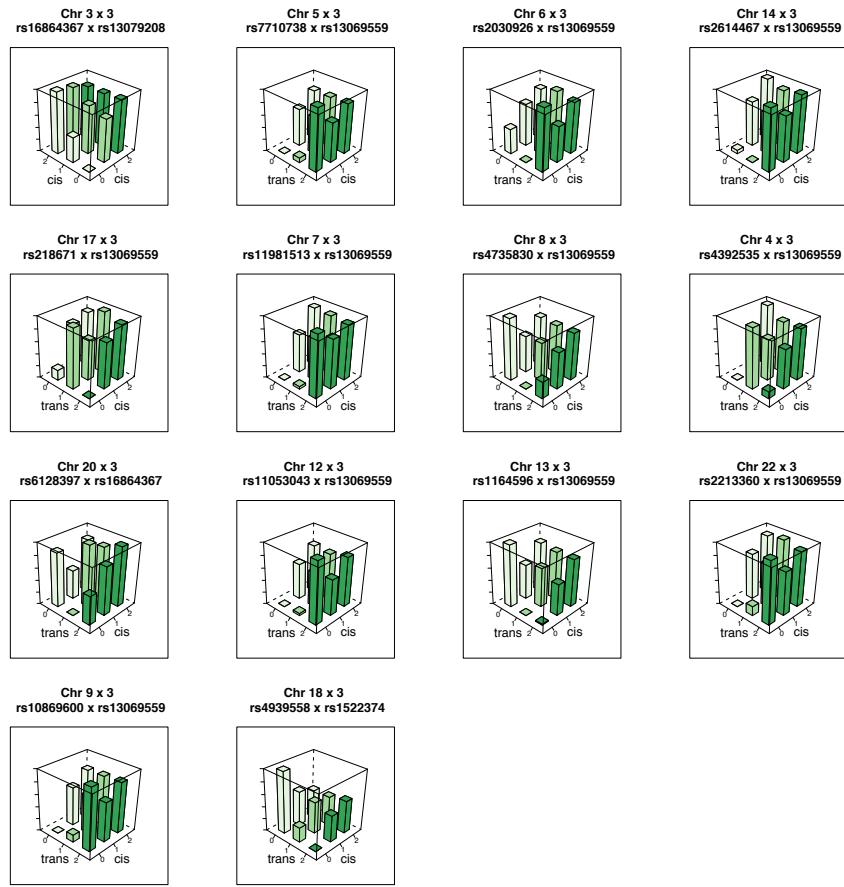
**Figure S7: Sampling mean for different power terms of population  $r$  values** Power of detection and replication of epistatic interactions depends not on  $r^2$  between causal variants and observed SNPs, but on  $r^4, r^6, r^8$ . For a given population value of LD  $r$  (columns of plots), plotted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



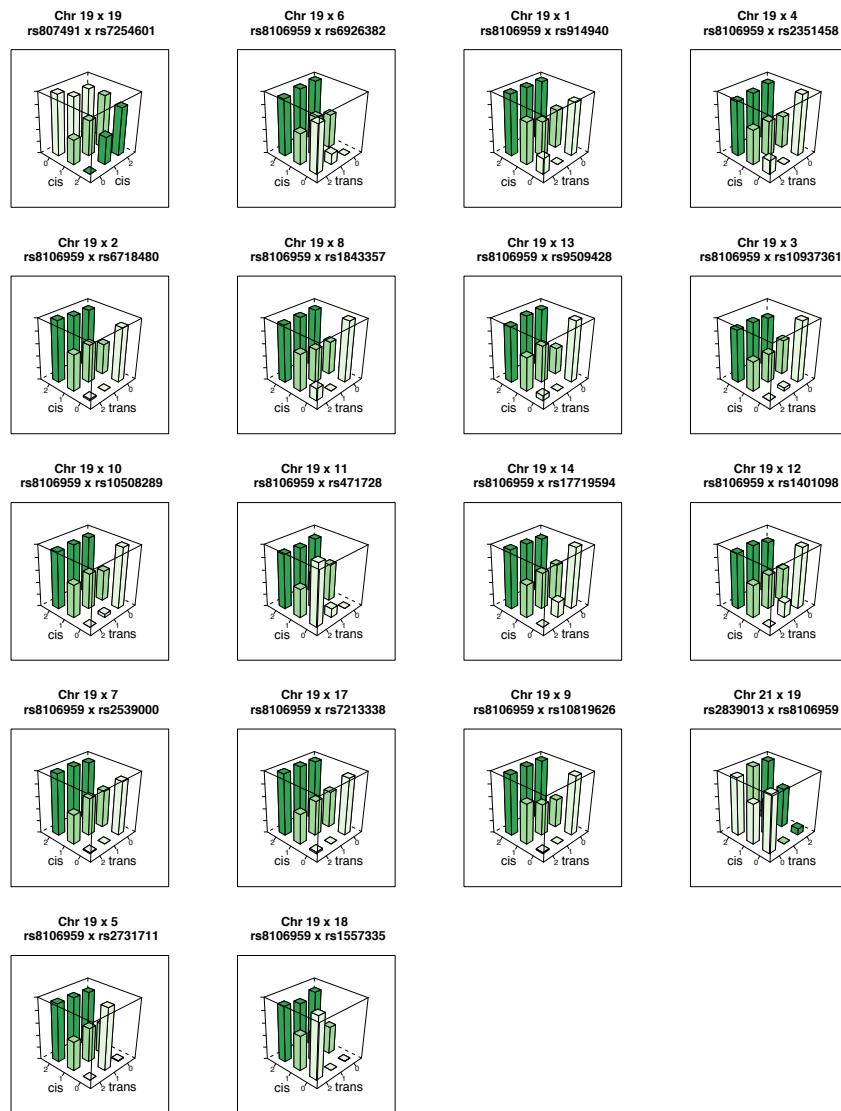
**Figure S8: Sampling standard deviation for different power terms of population  $r$  values** Power of detection and replication of epistatic interactions depends not on  $r^2$  between causal variants and observed SNPs, but on  $r^4, r^6, r^8$ . For a given a population value of LD  $r$  (columns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



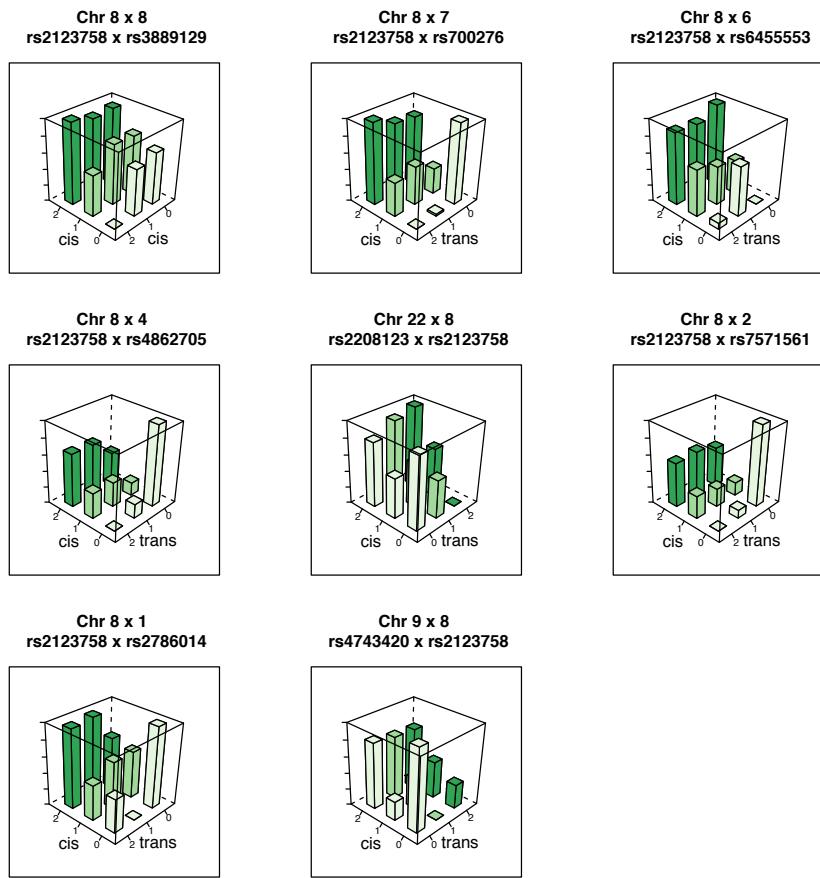
**Figure S9: Reduction in LD as estimated in replication data after ascertaining for high LD in discovery data** 100,000 “unobserved” causal variants (CVs) were tested for LD against a panel of 528,509 “observed” discovery markers (DMs). DM/CV pairs with LD  $r^2 > 0.9$  were then tested in an independent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



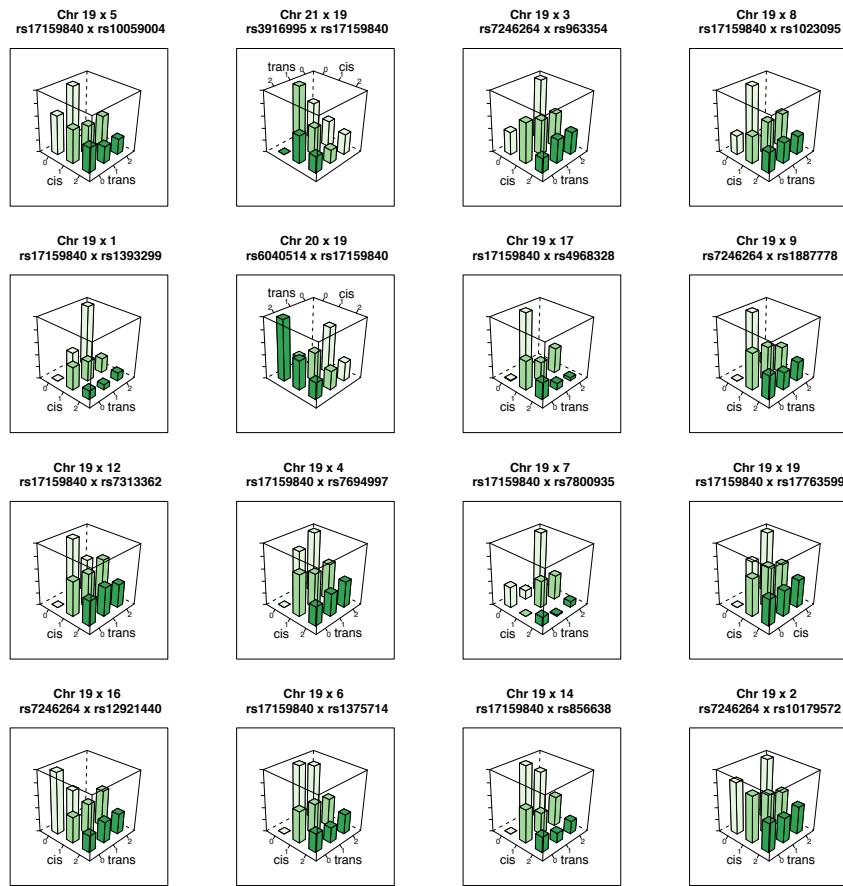
**Figure S10: Genotype-phenotype maps for 14 interactions influencing the expression of MBNL1** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of MBNL1, but in many of these interactions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



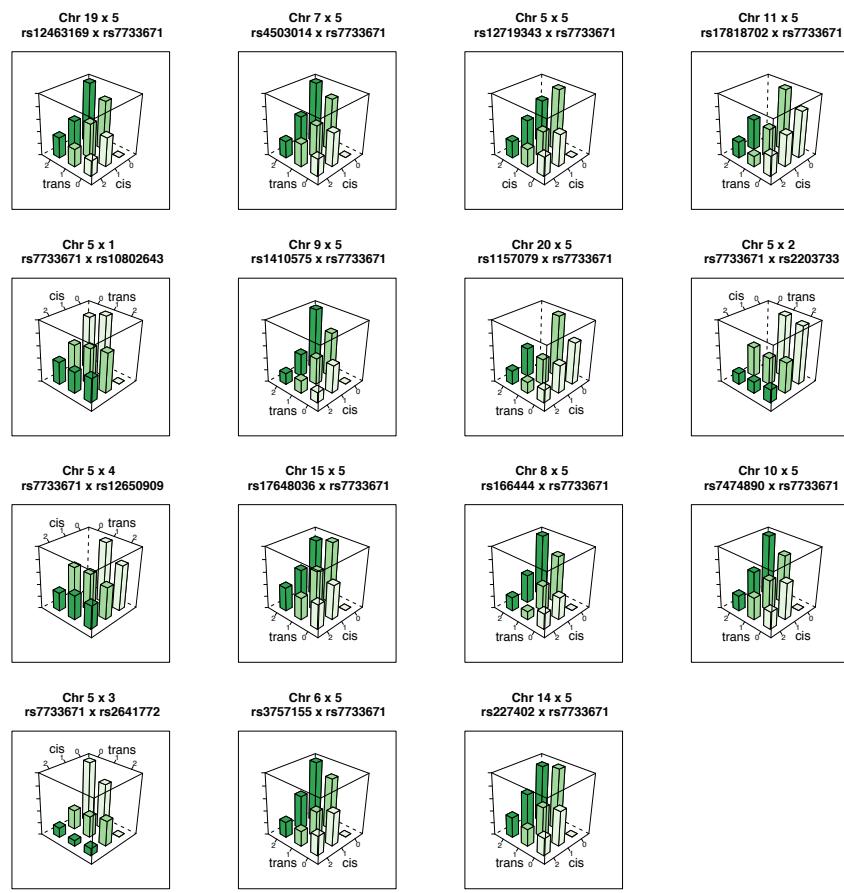
**Figure S11: Genotype-phenotype maps for 19 interactions influencing the expression of TMEM149** Each bar represents the mean phenotypic value for individuals in that genotype class. The rs13069559 SNP typically has a *cis*-additive decreasing effect on the expression of TMEM149, but in many of these interactions the *cis* effect is masked when the *trans* SNP is homozygous for the masking allele.



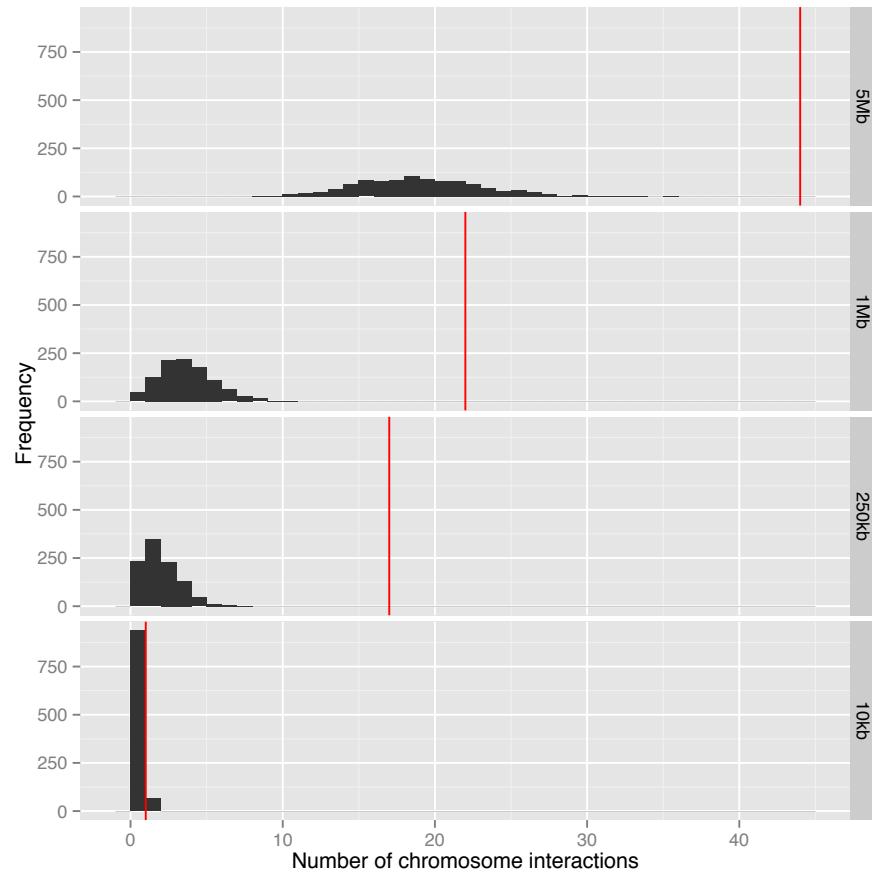
**Figure S12: Genotype-phenotype maps for 8 interactions influencing the expression of NAPRT1** Each bar represents the mean phenotypic value for individuals in that genotype class.



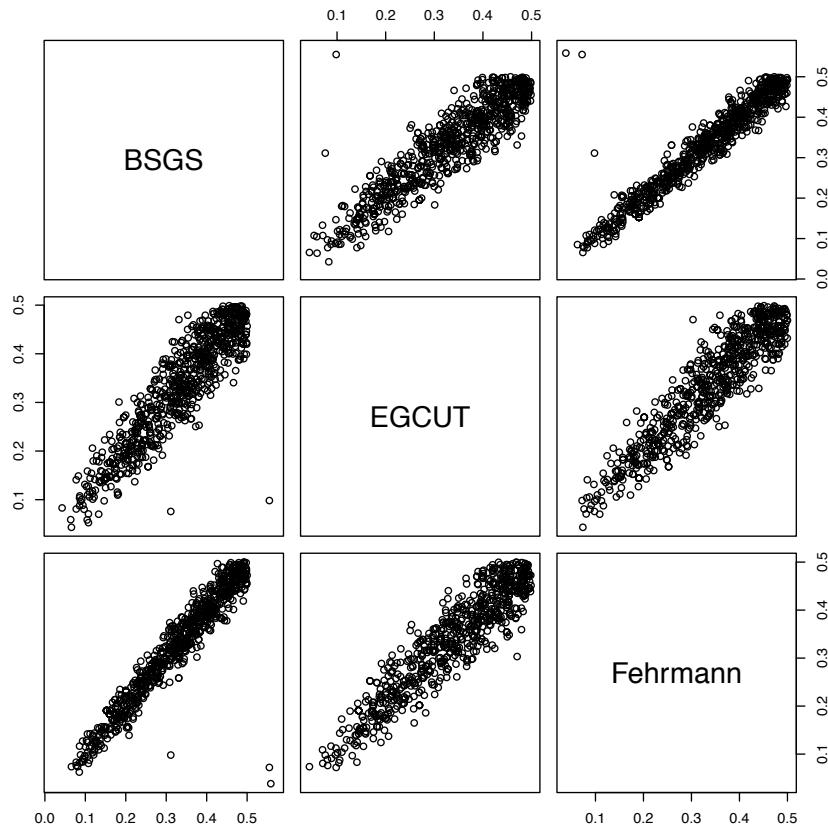
**Figure S13: Genotype-phenotype maps for 16 interactions influencing the expression of TRAPPC5** Each bar represents the mean phenotypic value for individuals in that genotype class.



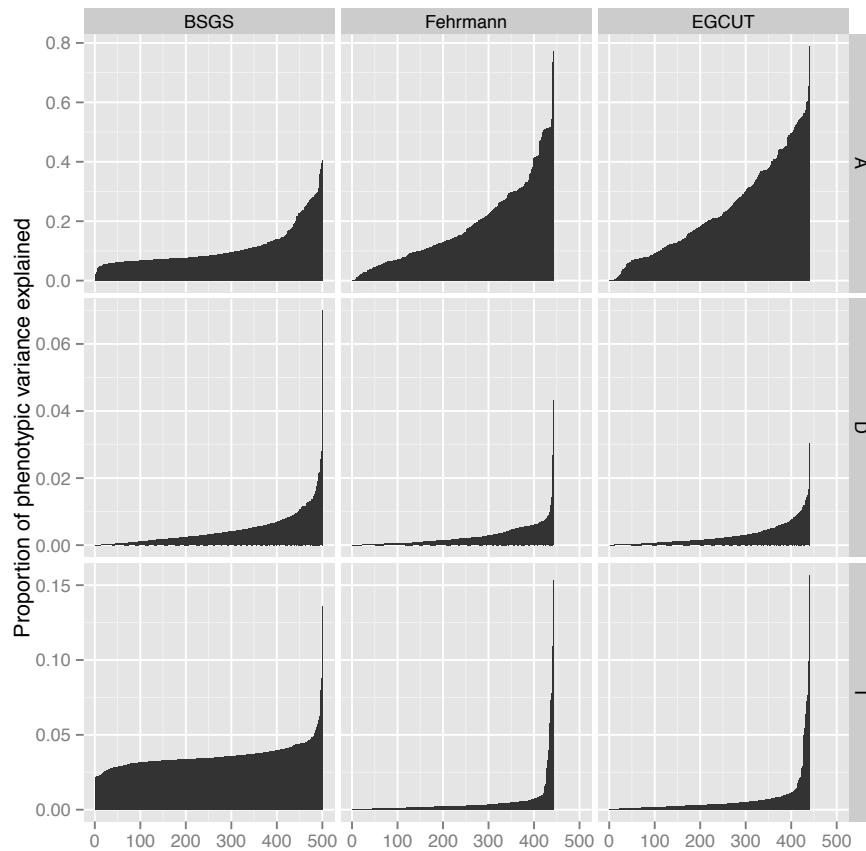
**Figure S14: Genotype-phenotype maps for 15 interactions influencing the expression of CAST** Each bar represents the mean phenotypic value for individuals in that genotype class.



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



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



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

Table S1: Details on 501 interactions discovered in BSGS dataset

Expression trait	Gene ID <sup>a</sup>	Probe ID <sup>b</sup>	Chr.	SNP 1			SNP 2			Interaction statistic / - log <sub>10</sub> p-values					Distance / Mb <sup>b</sup>	
				rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	BSGS <sup>e</sup>	Fehrmann <sup>f</sup>	EGCUT <sup>g</sup>	Meta <sup>g</sup>	
ABCAT7	ILMN_1743205	19	rs3752237	19	1047161	ABCAT7	rs500183	6	158100199			5.82	0.38 <sup>i</sup>	0.02 <sup>i</sup>	0.09 <sup>j</sup>	
ABCAT7	ILMN_1743205	19	rs3752237	19	1047161	ABCAT7	rs914737	9	130522101			5.50				
ABC C3	ILMN_1677814	17	rs9455	17	48771135	ABC C3	rs4732202	7	136057883			6.10	0.02	1.81	0.95	
ACAT1	ILMN_1804008	11	rs227064	11	108207393	ACAT1	rs4744894	9	72001517			6.59	1.04	1.78	2.02	
ADCK1	ILMN_1698777	14	rs22431896	14	78088813	ADCK1	rs4833241	4	122933601			5.59	0.36	1.14	0.87	
ADCK1	ILMN_1698777	14	rs8058066	16	88462550		rs12431806	14	78088813	ADCK1		6.58	2.04	0.83	2.05	
ADK	ILMN_2358626	10	rs2395095	10	76446305	ADK	rs10824092	10	75929513			6.69	18.33	21.21	39.82	0.517
AGAP6	ILMN_3239130	10	rs2611512	10	51515534	AGAP6	rs2547906	5	95174319			6.22				
AHSA2	ILMN_1798308	2	rs10881585	9	13712421		rs8426476	2	61119471			7.15	1.83	1.93	2.88	
AHSA2	ILMN_1798308	2	rs2523971	6	299838258	HLA-G	rs1177303	2	61388355	AHSA2		5.45	0.92	0.64	0.94	
AKTIP	ILMN_1665982	16	rs2896940	16	57721217		rs1332406	16	53489705	AKTIP		6.91	0.16	0.99	0.57	4.231
AKTIP	ILMN_1665982	16	rs7189819	16	53536345	AKTIP	rs1362032	7	125543391			5.93	0.71	0.20	0.42	
AKTIP	ILMN_1665982	16	rs7189819	16	53536345	AKTIP	rs1473017	4	179323762			6.18	0.27	0.30	0.23	
ALDH3A2	ILMN_2401641	17	rs3760489	17	19581009	ALDH3A2	rs11720112	3	161996349			6.26	0.33	1.37	1.01	
ANG	ILMN_1760727	14	rs9322855	14	21153299	ANG	rs4865116	5	3032625			5.75	0.02	0.20	0.04	
ANPEP	ILMN_1763837	15	rs11073891	15	90363995	ANPEP	rs3823523	7	154511163			5.85	0.44	1.09	0.90	
ANPEP	ILMN_1763837	15	rs11073891	15	90363995	ANPEP	rs6846031	4	178019148			6.31	0.47	0.17	0.26	
AP3B1	ILMN_1768867	5	rs6453374	5	77508159	AP3B1	rs4684443	3	4818792			5.94	0.05			
APPL2	ILMN_1765076	12	rs935251	12	105580918	APPL2	rs2769594	9	87918528			5.60	0.80	1.02	1.16	31.703
ARL17B	ILMN_3231952	17	rs12947580	17	75768225		rs8079215	17	44064851	ARL17B		5.96				
ARL17B	ILMN_3231952	17	rs2834541	21	35932619		rs8079215	17	44064851	ARL17B		6.65				
ARL17B	ILMN_3231952	17	rs8079215	17	44064851	ARL17B	rs1950646	14	94722497			7.64				
ARL17B	ILMN_3231952	17	rs8079215	17	44064851	ARL17B	rs2197777	12	125831219			6.26				
ATP13A1	ILMN_21342424	19	rs4284750	19	19810050		rs873870	19	19738554			5.30	12.18	3.25	14.23	0.071
BID	ILMN_1763386	22	rs8919	22	18213057	BID	rs9804943	12	129906275			5.84	0.06	0.40	0.14	
BID	ILMN_2372413	22	rs181405	22	18233000		rs10888267	1	248059423			6.60	0.87	0.16	0.50	
C11ORF17	ILMN_1752988	11	rs2568061	11	8886260	C11ORF17	rs6553184	4	189150656			5.66	1.15	0.04	0.54	
C13ORF18	ILMN_2196550	13	rs2110603	16	6259852		rs674754	13	46913416	C13ORF18		6.66	0.28	0.28	0.22	
C13ORF18	ILMN_2196550	13	rs674754	13	46913416	C13ORF18	rs6857876	4	153610164			3.87	0.38	0.50	0.43	
C14ORF173	ILMN_2393450	14	rs11089825	22	37575398		rs4983382	14	105189504	C14ORF173		6.02	0.60	0.84	0.85	
C14ORF173	ILMN_2393450	14	rs395344	15	92276764		rs4983382	14	105189504	C14ORF173		5.98	0.31	0.28	0.24	
C14ORF173	ILMN_2393450	14	rs4983382	14	105189504	C14ORF173	rs10754644	1	23872474			7.15	0.42	0.34	0.35	
C14ORF4	ILMN_1804396	18	rs1293455	18	13819673		rs2655991	14	77574438			4.87				
C14ORF4	ILMN_1804396	18	rs2655991	14	77574438		rs10972462	9	35427324			4.32				
C14ORF4	ILMN_1804396	18	rs2655991	14	77574438		rs6445340	3	63371601			4.40				
C14ORF4	ILMN_1804396	18	rs2655991	14	77574438		rs7978151	1	63179138			4.05				
C14ORF4	ILMN_1804396	18	rs4793495	17	70414397		rs2655991	14	77574438			3.35				
C14ORF4	ILMN_1804396	18	rs4793495	17	70414397		rs2655991	14	77574438			4.61				
C17ORF60	ILMN_1747347	17	rs9907897	17	63502633		rs7405650	17		C17ORF60		6.79	0.53	0.05	0.19	
C10RF86	ILMN_1726980	1	rs2334323	6	110577257		rs2257182	1	2028566	C10RF86		5.90	0.01	0.50	0.13	
C10RF86	ILMN_2097790	1	rs2279474	18	46384412		rs2460002	1	2119833	C10RF86		5.65		0.03		
C10RF86	ILMN_2097790	1	rs7188668	16	25711358		rs2460002	1	2119833	C10RF86		5.59	0.29	0.50	0.37	
C21ORF57	ILMN_1795836	21	rs4819271	21	48052838		rs901964	12	48676038	ZNF641		4.91	0.65	0.08	0.28	
C21ORF57	ILMN_1795836	21	rs9978658	21	48027084		rs11701361	21	23764474			9.42	6.08	16.36	21.67	0.263
C50RF4	ILMN_1728742	5	rs1122762	18	45866512		rs2865951	5	154348552	C50RF4		5.55	0.72	0.04	0.27	
C8ORF59	ILMN_1653205	8	rs12429804	13	36577930		rs2896452	8	86102233	C8ORF59		5.49	0.29	0.02	0.07	
C8ORF59	ILMN_1653205	8	rs12454561	18	31272238		rs2896452	8	86102233	C8ORF59		5.45	0.31			
C8ORF59	ILMN_1653205	8	rs2896452	8	86102233		rs1004564	4	55242625	C8ORF59		7.62	0.38	0.18	0.21	
C8ORF59	ILMN_1653205	8	rs7152284	14	52273663		rs2896452	8	86102233	C8ORF59		5.67	2.18	0.07	1.33	
CSORF59	ILMN_1653205	8	rs8051751	16	7188323		rs2896452	8	86102223	CSORF59		5.79	1.39	0.18	0.87	
C9ORF72	ILMN_1741881	9	rs10122902	9	27556780	C9ORF72	rs2526698	1	242092101	C9ORF72		6.36	0.96	0.01	0.37	
CABC1	ILMN_1731064	1	rs12765897	10	435908		rs3738725	1	227174210	CABC1		6.36	0.94	0.00	0.34	
CARD9	ILMN_1712532	9	rs4266763	9	139289825	INPP5E	rs684040	1	82128660			5.81				
CARD9	ILMN_1712532	9	rs4573661	11	6026661		rs4077515	9	139266496	INPP5E		6.61	0.09	0.86	0.42	
CAST	ILMN_1717234	5	rs1157079	20	6778978		rs7733671	5	9600269	CAST		7.07	0.23	0.96	0.62	
CAST	ILMN_1717234	5	rs12463169	19	17321669		rs7733671	5	9600269	CAST		5.73	0.02	2.85	1.75	
CAST	ILMN_1717234	5	rs12599264	16	81840122		rs7733671	5	9600269	CAST		7.00				
CAST	ILMN_1717234	5	rs12599264	16	81840122		rs7733671	5	9600269	CAST		7.68	0.36	1.57	1.20	29.369
CAST	ILMN_1717234	5	rs1661344	8	75111111		rs7733671	5	9600269	CAST		7.11	0.27	0.52	0.37	
CAST	ILMN_1717234	5	rs1661344	8	75111111		rs7733671	5	9600269	CAST		7.81	0.97	0.03	0.41	
CAST	ILMN_1717234	5	rs1661344	8	75111111		rs7733671	5	9600269	CAST		6.62	1.15	0.59	1.09	
CAST	ILMN_1717234	5	rs1661344	8	75111111		rs7733671	5	9600269	CAST		6.12	0.11	0.01	0.01	
CAT	ILMN_1651705	11	rs872311	18	66175386		rs11032695	11	34447586	CAT		6.41	0.26	0.30	0.22	
CCDC88B	ILMN_1772208	11	rs2353203	19	17099890		rs541207	11	641521542	CCDC88B		5.68	0.33	0.37	0.31	
CCDC88B	ILMN_1772208	11	rs694739	11	64097233		rs12771349	10	96991983			5.62	0.23	0.18	0.14	
CD36	ILMN_1784863	7	rs3211834	7	80281117		rs254900	2	85816334	VAMP8		6.93	0.15	0.01	0.02	
CD55	ILMN_1805040	1	rs750801	11	76033374		rs6701608	1	207502534	CD55		5.09	0.08	0.03	0.02	
CD93	ILMN_1704730	20	rs1884655	20	23074375	CD93	rs10254470	7	157182040			6.06	1.74	0.24	1.20	
CD93	ILMN_1704730	20	rs1884655	20	23074375	CD93	rs4696726	4	7992632			5.7				

Table S1 – continued from previous page

Expression trait			SNP 1						SNP 2						Interaction statistic / -log <sub>10</sub> p-values					Distance / Mb <sup>h</sup>
Gene ID <sup>a</sup>	Probe ID <sup>b</sup>	Chr.	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	BSGS <sup>e</sup>	Fehrmann <sup>f</sup>	EGCUT <sup>f</sup>	Meta <sup>g</sup>						
CPVL	ILMN_1682928	7	rs2835998	21	39202070		rs245884	7	29188475	CPVL	5.55	0.19	0.03	0.04						
CRIP1	ILMN_1813256	2	rs2131290	4	188859908		rs1531133	2	46843631	CRIP1	5.47	0.28	0.10	0.12						
CRLS1	ILMN_1737685	20	rs6139887	20	5986234	CRLS1	rs1473927	5	62406408		6.18	0.10	0.36	0.15						
CSTB	ILMN_1761797	21	rs9979356	21	45230974		rs3761385	21	45198355		11.99	25.20	16.72	42.27	0.033					
CTNNA1	ILMN_1804854	5	rs924943	18	69500505		rs176382	5	138226767	CTNNA1	5.74	0.02	0.41	0.11						
CTSC	ILMN_1696347	11	rs2457684	11	88139983	CTSC	rs7079264	10	108679892		5.67	0.92	0.74	1.03						
CTSC	ILMN_1696347	11	rs5752236	22	26250645		rs7128352	11	88087357	CTSC	5.84	0.49	0.80	0.73						
CTSC	ILMN_2242463	11	rs7930237	11	88117962		rs556895	11	88077479		7.16	18.76	15.06	33.53	0.040					
CWF19L1	ILMN_1651886	10	rs7108734	11	11456027		rs12784396	10	102027407	CWF19L1	5.42	0.21	0.01	0.03						
CYBRD1	ILMN_1712305	2	rs2592948	4	129994690		rs888427	2	172368120	CYBRD1	5.89	0.23	0.53	0.34						
CYBRD1	ILMN_1712305	2	rs7852475	9	140698856		rs888427	2	172368120	CYBRD1	5.68	0.20	0.02	0.04						
CYBRD1	ILMN_2087692	2	rs11257679	10	12318284		rs888427	2	172368120	CYBRD1	5.81	0.39	1.87	1.47						
CYBRD1	ILMN_2087692	2	rs6137908	20	23344590		rs888427	2	172368120	CYBRD1	5.53	0.05	0.83	0.36						
CYBRD1	ILMN_2087692	2	rs888427	2	172368120	CYBRD1	rs75918149	2	160112881		5.85	0.87	0.10	0.44						12.255
CYP27A1	ILMN_1704985	2	rs6021982	20	36571928		rs933994	2	172965166	CYP27A1	5.42	0.29	0.86	0.60						
DAB2	ILMN_2128428	5	rs7778910	7	110451383		rs835223	5	39381357	DAB2	5.44	0.48	0.41	0.44						
DCAKD	ILMN_1811648	17	rs99000173	17	43111688		rs1343244	6	82076988		9.12	0.00	0.58	0.14						
DDT	ILMN_1690982	22	rs5760102	22	24248761	DDT	rs2378341	3	187475208		5.62	0.64	0.25	0.42						
DDX58	ILMN_1797001	9	rs4937097	11	12596245		rs7042042	9	32451144		5.31	0.61	0.29	0.44						
DEM1	ILMN_1783996	1	rs10120023	9	137810259	COQ10A	rs2519515	7	88204888		5.47	0.08	0.41	0.16						
DEM1	ILMN_1783996	1	rs12363827	11	106703727		rs10120023	9	137810259	COQ10A	6.39	0.77	0.02	0.29						
DHRS9	ILMN_1733998	2	rs1519956	12	89468283		rs7566044	2	169960422	DHRS9	6.00	0.06	1.17	0.58						
DHRS9	ILMN_1733998	2	rs1285259	7	147132505		rs7566044	2	169960422	DHRS9	6.48	0.37	0.34	0.32						
DHRS9	ILMN_2384181	2	rs2831914	21	29959453		rs2161037	2	16989393	DHRS9	5.51	0.88	0.04	0.37						
DHRS9	ILMN_2384181	2	rs766104	4	18777641		rs2161037	2	16989393	DHRS9	7.64	0.05	0.11	0.03						
DIF2B	ILMN_1755589	12	rs1080134	22	2916503		rs1116932	12	50410976	LASS5	4.65	0.32	0.05	0.10						
DIF2B	ILMN_1755589	12	rs1116932	15	50410976	LASS5	rs2872008	7	18134888	LASS5	5.31	0.30	0.22	0.19						
DIF2B	ILMN_1755589	12	rs338585	19	14711815		rs7134595	12	50730458	LASS5	4.40	0.37								
DIF2B	ILMN_1755589	12	rs7134595	15	50730458	LASS5	rs1808634	8	61971140	LASS5	5.03	0.09	0.02	0.01						
DIF2B	ILMN_1755589	12	rs7312252	12	50744171	LASS5	rs4532958	10	115214154	LASS5	5.92	0.48	0.00	0.11						66.920
DIF2B	ILMN_1755589	12	rs871257	12	17994348		rs124727378	12	51074199	LASS5	5.79	0.23	1.45	0.97	0.052					
DNAJB6	ILMN_1793770	7	rs2286842	7	157216093		rs7799589	7	157163614	DNAJB6	4.81	0.27	0.04	0.04						
DPH3	ILMN_2349610	3	rs12232308	15	93409054		rs1566972	3	1620360	DPH3	6.17	1.58	0.27	1.12						
ECGF1	ILMN_2109708	22	rs140522	22	50971266	ECGF1	rs4891884	18	6406407		4.81	0.15	1.18	0.70						
ECHDC2	ILMN_1671568	1	rs4240941	2	241911027		rs11206043	1	53402552	ECHDC2	6.19	0.22	0.35	0.22						
ECHDC2	ILMN_1671568	1	rs5992637	22	17675900		rs11206043	1	53402552	ECHDC2	5.58	0.64	0.16	0.35						
EHD4	ILMN_1720083	15	rs10403312	19	53244938		rs1048166	15	42192040	EHD4	6.98	0.90	0.47	0.79						
EIF2B2	ILMN_1713380	14	rs6567288	18	60218334		rs1754504	14	55790340	EIF2B2	5.56	0.23	0.11	0.10						
EIF5A	ILMN_1794522	17	rs7216490	17	7221707	EIF5A	rs15534374	2	43955676		5.55	0.28	0.59	0.41						
EIF5A	ILMN_1794522	17	rs7216490	17	7221707	EIF5A	rs4471434	11	126387391		5.52	0.05	1.12	0.53						
EMR2	ILMN_2353633	19	rs2827076	21	23196243		rs9305048	19	14879034	EMR2	6.51	0.36	0.04	0.11						
EMR2	ILMN_2353633	19	rs6132112	20	18761714		rs9305048	19	14879034	EMR2	5.56	0.45	0.40	0.41						
EPHX2	ILMN_1709237	8	rs1107764	11	127909396		rs132699693	8	27400604	EPHX2	5.70	0.20	0.58	0.35						
ERICH1	ILMN_1731001	8	rs10894861	11	134611176		rs12115088	8	578742	ERICH1	5.43	0.25	1.20	0.81						
ERICH1	ILMN_1731001	8	rs5766218	22	45337329		rs4735900	8	607161	ERICH1	6.11	0.20	0.11	0.09						
ERICH1	ILMN_2104696	8	rs726145	18	31187910		rs1517297	4	182786760		5.63	0.67	1.03	1.06						
EXOC3	ILMN_1789419	5	rs187076	10	55228462		rs12188164	5	428236	EXOC3	6.83	0.74	0.19	0.44						10.736
FAHD1	ILMN_2246661	16	rs1560104	16	12708208		rs344363	16	1972548	FAHD1	5.61	1.38								
FCN1	ILMN_1668063	9	rs19501144	19	1278110093		rs107123039	9	128780638	FCN1	6.34	0.27	0.20	0.20						
FEZ2	ILMN_1739586	2	rs2356400	19	44321776		rs13406184	2	36791226	FEZ2	5.78	0.14	0.33	0.16						
FEZ2	ILMN_1739586	2	rs969010	4	159963132		rs11691600	2	36810133	FEZ2	6.59	0.14	0.28	0.14						
FGD2	ILMN_2115005	6	rs4803848	19	46205050		rs831486	6	37001267	FGD2	5.69	0.12	0.25	0.11						
FLJ20489	ILMN_1778144	12	rs17615703	12	117036766		rs3782908	12	48169526	FLJ20489	5.49	1.20	0.11	0.66						68.867
FLJ20489	ILMN_1778144	12	rs3782908	12	48169526	FLJ20489	rs897511	4	167695661		5.53	0.03	0.11	0.02						
FLJ20489	ILMN_1778144	12	rs4792199	17	7992118		rs3782908	12	48169526	FLJ20489	5.74	0.19	0.02	0.04						
FLJ20489	ILMN_1778144	12	rs4984440	15	97033129		rs3782908	12	48169526	FLJ20489	6.49	0.31	0.47	0.36						
FLJ20489	ILMN_1778144	12	rs7204135	16	50621965		rs3782908	12	48169526	FLJ20489	6.90	0.38	0.17	0.21						
FLJ20718	ILMN_1763663	16	rs9325634	21	43818790		rs2287197	16	50105694	FLJ20718	6.04	0.14	0.95	0.53						
FLJ43093	ILMN_2123450	6	rs6906101	6	36667610	FLJ43093	rs13214069	6	32705248		5.44	0.00	0.64	0.18						3.962
FNK3RP	ILMN_1652333	17	rs898093	17	80890638		rs9892064	17	80827903		16.16	28.24	29.39	59.95						0.063
FUCA1	ILMN_17528	1	rs4971478	2	1401063		rs1274386	2												

Table S1 – continued from previous page

Expression trait				SNP 1				SNP 2				Interaction statistic / -log <sub>10</sub> p-values				
Gene ID <sup>a</sup>	Probe ID <sup>b</sup>	Chr.	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	BSSG <sup>e</sup>	Fehrmann <sup>f</sup>	EGCUT <sup>f</sup>	Meta <sup>g</sup>	Distance / Mb <sup>h</sup>	
HBC2	ILMN_2084825	11	rs129750066	19	357723501		rs2855039	11	5271671	HBC2	5.77	0.08	0.13	0.05		
HBC2	ILMN_2084825	11	rs2855039	11	5271671	HBC2	rs12042181	1	213088494	LQK1	6.84	0.06	0.54	0.21		
HBC2	ILMN_2084825	11	rs2855039	11	5271671	HBC2	rs1250379	4	141533832		5.98	0.00	0.46	0.10		
HDAC7	ILMN_3266186	12	rs2109029	16	6036851		rs4760636	12	48173352	HDAC7	5.75					
HEBP1	ILMN_1802557	12	rs3782567	12	13145613	HEBP1	rs17686635	8	135220622		5.98	0.15	0.59	0.32		
HEXDC	ILMN_1741180	17	rs1942719	18	71237270		rs7213057	17	80378939	HEXDC	5.81	1.61	0.34	1.22		
HLA-DRA	ILMN_2157441	6	rs489635	14	77532672		rs7192	6	31411646	HLA-DRA	5.94	0.90	0.16	0.52		
HLA-F	ILMN_1762861	6	rs11660982	18	75467313		rs253404	6	29695713	HLA-F	5.69	1.00	0.47	0.86		
HMBOX1	ILMN_1720059	8	rs12435486	14	98670849		rs7837237	8	28876221	HMBOX1	6.54	0.92	1.11	1.34		
HMBOX1	ILMN_1720059	8	rs2837803	21	42112794		rs4732890	8	28751381	HMBOX1	6.62	0.05	1.01	0.46		
HMBOX1	ILMN_1720059	8	rs4765451	12	127237464		rs8180944	8	28904086	HMBOX1	5.80	0.39	3.13	2.52		
HMBOX1	ILMN_1720059	8	rs587639	8	132752731		rs7837237	8	28876221	HMBOX1	6.58	0.55	0.34	0.44	103.850	
HMBOX1	ILMN_1720059	8	rs8180944	8	28904086	HMBOX1	rs7810884	7	158276926		6.12	0.34	0.66	0.52		
HMBOX1	ILMN_1720059	8	rs9521666	13	110897444		rs8180944	8	28904086	HMBOX1	5.45	0.67	0.26	0.45		
HNRPH1	ILMN_2101920	5	rs6894268	5	179032488		rs4700810	5	178991794		15.38	8.55	3.01	10.37	0.041	
HSPC157	ILMN_3194087	1	rs555812	16	88882257		rs4654783	1	22439520	HSPC157	5.51					
HSPC157	ILMN_3194087	1	rs6063164	20	46468900		rs4654783	1	22439520	HSPC157	6.51					
HSPC157	ILMN_3194087	1	rs662739	12	121229893		rs4654783	1	22439520	HSPC157	6.61					
HSPC157	ILMN_3194087	1	rs7088558	10	10184937	CWF19L1	rs4654783	1	22439520	HSPC157	6.48					
IL32	ILMN_1778010	16	rs1554999	16	3115628		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		
INPP5E	ILMN_1811301	9	rs8044524	16	81603771		rs1127152	9	13933559	INPP5E	5.58	1.46	0.84	1.55		
JAZF1	ILMN_1682727	7	rs757355	12	47970693		rs849341	7	28288174		8.16	0.02	0.26	0.05		
KCNJ15	ILMN_1675756	21	rs2186344	21	39606769	KCNJ15	rs424299	11	5570771		5.64	0.65	0.13	0.33		
KIR2DS5	ILMN_1691803	19	rs649216	19	55324635	KIR2DL1	rs64199660	4	189055298		4.74	0.46	0.89	0.77		
KTEL1C1	ILMN_1811104	3	rs4390934	13	84597119		rs727905	3	119119433	KTEL1C1	5.53	0.08	0.80	0.37		
KTEL1C1	ILMN_1811104	3	rs6815953	4	183109012		rs6414283	3	119195913	KTEL1C1	5.45	0.64	0.08	0.28		
L3MBTL2	ILMN_2336109	22	rs4822006	22	41519362	L3MBTL2	rs129438	1	233438952		5.88	0.33	0.04	0.09		
LAP3	ILMN_1683792	4	rs7042087	9	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	
LDRRAP1	ILMN_1680940	6	rs152040232	15	5681635		rs7605	1	158869362	LDRRAP1	6.0					
LGALS9	ILMN_2412144	17	rs2440821	17	26083392		rs11749727	5	170083400		5.16	0.35	0.40	0.34		
LRRA5	ILMN_2357419	19	rs3859532	19	54872718	LRRA5	rs7149872	18	7150497		6.13	0.23	0.03	0.05		
LINS1	ILMN_2338197	15	rs11247226	15	111120963	LINS1	rs728287	10	127804531		5.89					
LRRK2C5	ILMN_2150196	6	rs977785	6	6588881	LYR86	rs1543675	19	78946879	LYR86	5.61	0.13	0.15	0.07		
LYR86	ILMN_1807825	6	rs977785	6	6588881	LYR86	rs11981725	7	154137150	LYR86	5.95	0.15	0.03	0.03		
LYZ	ILMN_1815203	12	rs2168029	12	69734641		rs2168029	12	69734641	LYZ	5.71	0.49	0.03	0.16		
LYZ	ILMN_2162972	12	rs2168029	12	69734641	LYZ	rs2253135	9	130319560		6.31	0.61	0.36	0.49		
MAD1L1	ILMN_2358069	7	rs7783715	7	1923385	MAD1L1	rs6414306	3	127011798		5.62	0.25	0.88	0.59		
MAD2L1BP	ILMN_1694711	6	rs7983718	13	103203146		rs1096699	6	43528441	MAD2L1BP	5.93	0.63	1.11	1.00		
MAP1LC3A	ILMN_1776188	20	rs974607	21	29435869		rs6060034	20	33351864	MAP1LC3A	5.78	1.18				
MBNL1	ILMN_2313158	3	rs10869600	9	78252815		rs13069559	3	152187431	MBNL1	7.96	0.79	0.27	0.54		
MBNL1	ILMN_2313158	3	rs11053043	12	9932070		rs13069559	3	152187431	MBNL1	6.70	0.08	2.21	1.37		
MBNL1	ILMN_2313158	3	rs1164596	13	97100681		rs13069559	3	152187431	MBNL1	7.38	1.43	0.63	1.34		
MBNL1	ILMN_2313158	3	rs11981513	7	94648239		rs13069559	3	152187431	MBNL1	7.71	0.43	5.36	4.58		
MBNL1	ILMN_2313158	3	rs16864367	3	152234166		rs13079208	3	152116652		13.49	16.25	24.74	41.56	0.118	
MBNL1	ILMN_2313158	3	rs2030926	6	110467127		rs13069559	3	152187431	MBNL1	7.10	0.91	5.80	5.53		
MBNL1	ILMN_2313158	3	rs218671	17	6604708		rs13069559	3	152187431	MBNL1	7.63	0.62	5.82	5.23		
MBNL1	ILMN_2313158	3	rs2213360	22	34291750		rs13069559	3	152187431	MBNL1	6.05	0.52	0.72	0.70		
MBNL1	ILMN_2313158	3	rs2305802	19	16038535		rs13069559	3	152187431	MBNL1	6.94	1.67				
MBNL1	ILMN_2313158	3	rs2614467	14	99770138		rs13069559	3	152187431	MBNL1	5.74	4.13	2.22	5.30		
MEGF9	ILMN_2290118	9	rs1039689	20	51920271		rs966396	9	123453281	MEGF9	4.63	1.13	1.33	1.71		
MFPN2	ILMN_1651385	1	rs798985	13	109401737		rs4846085	1	12050634	MFPN2	5.76	0.61	0.25	0.41		
MGC13057	ILMN_1787526	2	rs12718598	7	50428445	MGC13057	rs11725347	4	171860973		5.81	0.13	0.30	0.14		
MGC13057	ILMN_1787526	2	rs674608	18	69070772		rs21728598	7	50428445	MGC13057	5.57	0.07	1.03	0.50		
MGC13057	ILMN_1787526	2	rs0508518	16	82628245		rs2051344	18	74715653	MGBP	5.56	0.03	0.23	0.05		
MGC72104	ILMN_1688318	20	rs845787	20	26197931	MGC72104	rs26600665	8	137526799	MGBP	6.26	0.10	0.03	0.02		
MGST3	ILMN_1751956	1	rs740441	17	55779644		rs4147592	1	165601646	MGST3	5.45	0.57	0.27	0.40		
MGBP	ILMN_2398939	18	rs8092433	18	74747424		rs4890876	18	74732087		5.40	7.06	21.91	28.73	0.015	
MGBP	ILMN_2398939	18	rs1271856	22	37107630		rs1805	11	118076069	MGBP	5.64	0.97	1.08	1.35		
MIRPL36	ILMN_180197	5	rs17469061	10	8436432		rs750495	5	1782046	MIRPL36	6.89	0.34	0.18	0.19		
MIRPL43	ILMN_2258774	10	rs6564769	16	80641040		rs2863095	10	102746503	MIRPL43	5.71	0.26				
MIRPL52	ILMN_1713966	14	rs1950857	14	26710271		rs3811188	14	12670382	MIRPL52	6.56	0.14	0.44	0.22		
MIRPS10	ILMN_1663664	6	rs1095512	8	810202320		rs722269	6	42194916	MIRPS10	7.48	0.46	0.70	0.64		
MIRPS10	ILMN_1663664	6	rs11698155	20	15063214		rs2395803	6	152158596	MIRPS10	6.85	0.31	0.63	0.46		
MIRPS10	ILMN_1663664	6	rs1420537	16	52453567		rs13217993	6	42164401	MIRPS10	6.21	0.41	0.25	0.28		
MTMR15	ILMN_2152178	15	rs1718735	15	31215953	MTMR10	rs12431444	14	20686889		5.18	1.87	1.87	2.86		
MX1	ILMN_1662355	21	rs459498	21	42795027		rs1160227	14	9551456		6.31	0.46	0.52	0.50		
MX1	ILMN_1662355	21	rs459498	21	42795027		rs4973801	3	26703682		5.83	0.11	0.50	0.23		
MYBPC3	ILMN_178184	11	rs1434030	14	61593110		rs171749	11	4748085	MYBPC3	6.78	0.29	0.92	0.65	13.431	
MYBPC3	ILMN_178184	11	rs7324769	13												

Table S1 – continued from previous page

Expression trait				SNP 1			SNP 2			Interaction statistic / -log <sub>10</sub> p-values					
Gene ID <sup>a</sup>	Probe ID <sup>b</sup>	Chr.	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	BSSG <sup>e</sup>	Fehermann <sup>f</sup>	EGCUT <sup>f</sup>	Meta <sup>g</sup>	Distance / Mb <sup>h</sup>
NRBF2	ILMN_3237385	10	rs6025645	20	56157341		rs7923609	10	65133822	NRBF2	5.45				
NRBF2	ILMN_3237385	10	rs6517815	21	19819016		rs7923609	10	65133822	NRBF2	6.11				
NRD1	ILMN_1800897	1	rs4852124	2	240680022		rs6588415	1	52334047		6.13	0.47	0.05	0.17	
NUDT18	ILMN_1787885	8	rs5017351	11	25453482		rs1005901	8	21964378	NUDT18	5.44	0.03	0.46	0.15	
OAS1	ILMN_1658247	12	rs11613438	12	113480510		rs1047944	6	163997467		8.59	1.27	1.55	2.03	
OAS1	ILMN_1658247	12	rs13311	12	113448652		rs2072133	12	113409260		4.13	4.12	0.81	3.86	0.039
OAS1	ILMN_1675640	12	rs2892233	19	49160255		rs3741981	12		OAS1	4.38	0.87	0.46	0.76	
OPTN	ILMN_2381899	10	rs7192613	16	74286646		rs17512962	10	13169066	OPTN	5.64	0.42	0.06	0.14	
OSBPL5	ILMN_2307032	11	rs2829679	21	26662543		rs998639	11	3149249	OSBPL5	5.00	0.36	0.00	0.07	
OSTF1	ILMN_1742456	9	rs17780195	17	70624189		rs2273770	9	77755469	OSTF1	5.42	0.16	0.87	0.49	
OSTF1	ILMN_1742456	9	rs2273770	9	77755469	OSTF1	rs7718088	5	17959052		5.42	1.20	0.08	0.62	
OVGP1	ILMN_1734542	1	rs10802822	1	240132968		rs1264989	1	11992823	OVGP1	5.43	0.13	1.48	0.88	128.140
OVGP1	ILMN_1734542	1	rs347331	3	140148107		rs1264984	1	11969719	OVGP1	6.04	0.25	1.21	0.82	
PAM	ILMN_2313901	5	rs28092	5	102149795	PAM	rs784600	1	40139553	HPCAL4	5.59	0.66	0.44	0.59	
PCYOX1L	ILMN_1815951	5	rs2438490	5	148726162	PCYOX1L	rs2731939	3	21350989		6.20	0.19	0.26	0.16	
PEX5	ILMN_1660232	12	rs10444467	12	128052636		rs4329748	12	736442	PEX5	5.85	0.09	0.71	0.32	
PEX5	ILMN_1660232	12	rs7459757	15	27246462		rs4329748	12	736442	PEX5	5.74	0.34	0.09	0.13	
PFAPA5	ILMN_1797893	13	rs131969	22	49151303		rs7328733	13	33126737	PFAPA5	5.64	0.87	0.36	0.67	
PGLYRP1	ILMN_1704870	19	rs12982353	19	46529456	PGLYRP1	rs1263806	14	21982957		6.51	0.03	0.65	0.24	
PHCA	ILMN_1812552	11	rs49362	11	123097386		rs10736812	11	70670806	PHCA	5.51	0.36	0.90	0.70	46.389
PIK3IP1	ILMN_1719986	22	rs4141404	22	31675185	PIK3IP1	rs2065841	1	61728597		5.60	0.20	0.01	0.03	
PISD	ILMN_1793934	22	rs470072	22	32263131	PISD	rs10498313	14	30398876		5.23	0.02	0.87	0.33	
PISD	ILMN_1793934	22	rs6518752	22	31999127	PISD	rs954627	1	18236681		7.11	0.00	1.19	0.48	
PISD	ILMN_1793934	22	rs715572	22	33234931		rs6518754	22	32097757	PISD	4.12	0.05	0.42	0.15	1.137
PNKD	ILMN_1774604	5	rs686911	5	15878804		rs4672884	2	219182481	PNKD	6.35	0.16	0.04	0.04	
PNPPLA7	ILMN_1642587	9	rs11639098	16	51878804		rs928696	9	14011086	PNPPLA7	5.15	0.31	0.78	0.56	
PPFBP2	ILMN_1675653	11	rs651919	20	40838255		rs4809001	11	75559010	PPFBP2	4.44	0.29	0.33	0.26	
PPPR29C	ILMN_1661617	14	rs3914603	15	58530896		rs11156875	14	35619816	PPPR29C	5.81	0.12	0.42	0.19	
PPPR25A	ILMN_1738784	1	rs10930170	2	166399467		rs12120009	1	212447167	PPPR25A	5.63	0.72	0.48	0.66	
PPPR25A	ILMN_1738784	1	rs12423255	1	123550564		rs12120009	1	212447167	PPPR25A	5.72	0.08	0.95	0.46	
PPPR25A	ILMN_1738784	1	rs1880083	13	66226961		rs12120009	1	212447167	PPPR25A	5.61	0.36	0.13	0.17	
PPPR25A	ILMN_1738784	1	rs682334	11	10742728		rs12120009	1	212447167	PPPR25A	5.65	1.69	0.28	1.21	
PPPR25A	ILMN_1738784	1	rs7757871	6	135030045		rs12120009	1	212447167	PPPR25A	5.95	0.37	0.06	0.12	
PPPR25A	ILMN_1738784	1	rs7871178	9	27148475		rs12120009	1	212447167	PPPR25A	5.72	0.16	0.30	0.16	
PRDX5	ILMN_1716106	11	rs8019823	14	95040482		rs11600990	11	64082807	PRDX5	6.43	0.81	0.14	0.44	
PRKCBB1	ILMN_1713603	16	rs2188355	16	23867776		rs10492793	16	12639800		7.34	0.53	0.11	0.25	11.228
PRMT2	ILMN_1675038	21	rs1029231	21	47931653	C21ORF57	rs958128	18	31497346		5.60	0.19	0.03	0.04	
PRMT2	ILMN_1675038	21	rs2839372	21	48063862		rs117010588	21	47776382	C21ORF57	4.81	0.69	4.47	4.06	0.287
PSMB1	ILMN_1789176	6	rs3862607	11	121774705		rs32071114	6	170877444	PSMB1	5.79	0.44	0.44	0.27	
PSMB1	ILMN_1789176	6	rs6060930	20	30347832		rs6928843	6	170893084	PSMB1	5.14	0.00	0.26	0.04	
PSMB1	ILMN_1789176	6	rs6928843	6	170890384	PSMB1	rs2769689	1	225797957		4.58	1.95	0.64	1.78	
PSMB1	ILMN_1789176	6	rs7299749	12	131727816		rs32071114	6	170877444	PSMB1	5.42	1.18	0.32	0.86	
PWP1	ILMN_1743049	12	rs2353567	14	95478823		rs11036212	11	5221825	PTDSS1	5.00	0.03	0.48	0.15	
PWP1	ILMN_1743049	12	rs4969205	17	76598123		rs11036212	11	5221825	PTDSS1	5.90	0.80	0.08	0.38	
PWP1	ILMN_1743049	12	rs631562	11	126852438		rs11036212	11	5221825	PTDSS1	5.70	0.02	0.40	0.11	
QDPR	ILMN_1672443	4	rs4946705	6	106348246		rs10020773	4	17526682	QDPR	5.75	1.03	1.25	1.55	
RAB31P	ILMN_1803197	12	rs2417310	22	33375704		rs7305307	12	20735276		6.55	0.25	0.08	0.09	
RABAC1	ILMN_2207363	19	rs1075728	19	42462788	RABAC1	rs7951628	11	120161117		6.42	0.28	0.84	0.59	
RBL2	ILMN_1756999	16	rs9931702	16	53526551	AKTIP	rs1863464	15	26938488		6.38	0.03	0.31	0.08	
RCN1	ILMN_1800276	11	rs10879131	12	41417455		rs4922579	11	32136436	RCN1	5.23	0.58	0.37	0.47	
RCN1	ILMN_1800276	11	rs4922579	11	32136436	RCN1	rs1166957	8	141177468		4.32	0.41	0.09	0.17	
RCN1	ILMN_1800276	11	rs4922579	11	32136436	RCN1	rs1341899	1	102740645		5.40	0.04	0.26	0.07	
RERE	ILMN_1802380	1	rs4982058	14	24987865		rs301819	1	8501786	RERE	5.66	0.61	1.23	1.17	
RERE	ILMN_1802380	1	rs7697290	4	135248366		rs301819	1	8501786	RERE	5.74	0.14	0.10	0.06	
RERE	ILMN_2327795	1	rs11058529	19	13174312		rs301819	1	8501786	RERE	5.12	0.21	0.32	0.21	
RERE	ILMN_2327795	1	rs3852011	3	112844086		rs301819	1	8501786	RERE	5.71	0.08	0.60	0.26	
RNASE6	ILMN_1780533	14	rs11628398	14	21182800	RNASE6	rs7324365	13	100610327		5.48	0.42	0.21	0.26	
RNASE6	ILMN_1780533	14	rs3852011	3	112844086		rs1628398	14	21182800	RNASE6	5.11	0.09	0.22	0.08	
RNF167	ILMN_1794726	17	rs400688	17	48399308	RNF167	rs11076900	3	36348968		5.59	0.71	0.46	0.64	
RNNEP	ILMN_1738347	1	rs8071611	17	67153386		rs2819365	1	201983242		6.27	0.11	0.30	0.13	
RNNEP	ILMN_1738347	1	rs8071611	17	67153386		rs2819365	1	201983242		4.32	0.52	1.48	0.28	
RPL13	ILMN_2413278	16	rs352935	16	89648580		rs2965817	16	89513234	RPL23AP7	4.98	3.79	14.41	17.24	0.135
RPL23AP7	ILMN_2227570	11	rs1401202	16	80320506		rs4849261	7	114450028	RPL23AP7	5.55	0.13	0.73	0.38	
RPL36AL	ILMN_2189933	14	rs3007033	14	50103816	RPL36AL	rs17495030	9	138038093		5.46	0.09	0.06	0.02	
RPL36AL	ILMN_2189933	14	rs4909028	14	50020817	RPL36AL	rs1502991	6	66137260		5.86	0.32	0.20	0.19	
RPL8	ILMN_1764721	8	rs2958482	8	145984615	RPL8	rs1619856	1	23458790		4.59	0.10	0.37	0.15	
RPL8	ILMN_1764721	8	rs4143674	20	4741304		rs2058482	8	145984615	RPL8	4.33	0.13	0.45	0.22	
SEC13	ILMN_3297880	3	rs4889214	16	80913946		rs696221	3	10342876	SEC13	6.48	0.02	0.51	0.15	
SEMA4A	ILMN_1702787	1	rs17085428	5	95388015		rs7695	1	156147326	SEMA4A	5.70	0.22	1.73	1.17	
SESN3	ILMN_1694027	11	rs355391	15	46519793		rs684856	11	9						

Table S1 – continued from previous page

Expression trait				SNP 1				SNP 2				Interaction statistic / -log <sub>10</sub> p-values				
Gene ID <sup>a</sup>	Probe ID <sup>b</sup>	Chr.	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	rs ID	Chr.	Pos/Mb <sup>c</sup>	Association <sup>d</sup>	BSGS <sup>e</sup>	Fehrmann <sup>f</sup>	EGCUT <sup>g</sup>	Meta <sup>h</sup>	Distance / Mb <sup>i</sup>	
TMEM149	ILMN_1786426	7	rs1340400	11	132389627		rs17725246	7	44581986	TMEM149	5.70	0.06	1.34	0.70		
TMEM149	ILMN_1786426	19	rs2839013	21	47248981		rs8106959	19	36219525	TMEM149	8.41	0.16	0.48	0.26		
TMEM149	ILMN_1786426	19	rs5762235	22	2278238		rs8106959	19	36219525	TMEM149	6.79					
TMEM149	ILMN_1786426	19	rs6090518	20	45207005		rs8106959	19	36219525	TMEM149	11.09		0.76			
TMEM149	ILMN_1786426	19	rs807491	19	36268923	SNX26	rs7254601	19	36147315	TMEM149	12.16	81.55	45.78	145.78	0.122	
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs10508289	10	47990159		8.12	1.55	3.09	3.67		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs10819626	9	133025756		8.02	0.40	0.09	0.80		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs10937361	3	188359436		8.39	3.61	1.18	3.78		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs1401098	12	128884559		7.37	2.41	1.00	2.52		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs1557335	18	64268976		6.95	0.08	0.07	0.03		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs17719594	14	90932598		6.93	3.06	0.77	2.87		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs1843357	8	13822381		6.21	3.72	3.33	6.00		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs2351458	4	113317583		7.30	0.04	9.61	8.00		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs2539000	7	147619772		6.70	1.57	1.52	2.27		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs2731711	5	171792273		5.92	0.19	0.33	0.19		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs471728	11	129595460		8.89	0.90	3.62	3.51		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs67178480	2	233879066		8.55	3.31	5.15	7.36		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs6926382	6	161683974		5.80	3.06	8.80	10.72		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs7213338	17	80357420		5.49	0.07	3.14	2.10		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs914940	1	242889492		6.22	3.36	6.96	9.20		
TMEM149	ILMN_1786426	19	rs8106950	19	36219525	TMEM149	rs9509428	13	21473952		9.44	0.10	5.75	4.47		
TMEM63A	ILMN_1719649	1	rs12540846	13	72890603		rs4149226	1	226027323	TMEM63A	5.60					
TMEM80	ILMN_1708482	11	rs1548475	19	58058246		rs4963126	11	656845	TMEM80	5.79	0.64	0.12	0.32		
TNP03	ILMN_1683811	7	rs1537146	9	4859303		rs10488630	7	128593948	IRF5	5.61	0.11	0.15	0.07		
TNP03	ILMN_1683811	7	rs199793	20	22827303		rs10488630	7	128593948	IRF5	5.52	1.03	0.17	0.62		
TRA2A	ILMN_1731043	7	rs7776572	7	23528927		rs11770192	7	23498358		8.23	3.19	1.89	4.09	0.031	
TRAPPC4	ILMN_1814650	11	rs1278760	13	113531675		rs3916581	11	118887887	TRAPPC4	5.61	0.28	0.40	0.29		
TRAPPC5	ILMN_1814650	11	rs1793823	11	131018917		rs3916581	11	118887887	TRAPPC4	5.52	0.93	0.01	0.36	12.131	
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs10059904	5	166970604		5.97	0.21	1.60	1.07		
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs1023095	8	13022957		6.92	0.37	0.87	0.68		
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs1375714	6	156409402		7.79	0.12	0.18	0.08		
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs1393299	1	242329791		6.43	0.63	0.47	0.59		
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs17763599	19	2369415		6.38	0.21	0.24	0.16	5.389	
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs4968328	17	57495457		6.51	0.50	0.38	0.44		
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs7313362	12	129644342		7.08	0.04	0.65	0.25		
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs7694997	4	9947811		5.86	0.20	0.36	0.22		
TRAPPC5	ILMN_1814650	19	rs17159840	19	7758194	TRAPPC5	rs7808035	7	146691926		6.27	0.15	0.33	0.16		
TRAPPC5	ILMN_1814650	19	rs380768	22	23740855		rs17159840	19	8543950		6.03	0.24	0.07	0.08		
TRAPPC5	ILMN_1814650	19	rs391695	21	45149454		rs17159840	19	7758194	TRAPPC5	7.58					
TRAPPC5	ILMN_1814650	19	rs6040514	20	11272861		rs17159840	19	7758194	TRAPPC5	7.73	0.85	0.78	1.01		
TRAPPC5	ILMN_1814650	19	rs7246264	19	7762978		rs1017972	2	228504503		8.10	0.51	0.55	0.56		
TRAPPC5	ILMN_1814650	19	rs7246264	19	7762978		rs102117440	16	30408765		6.71	0.14	0.02	0.02		
TRAPPC5	ILMN_1814650	19	rs7246264	19	7762978		rs1887778	9	134635088	RAPGEF1	7.05	0.08	0.86	0.40		
TRAPPC5	ILMN_1814650	19	rs7246264	19	7762978		rs9633554	3	157393770		7.41	0.36	0.90	0.69		
TREM1	ILMN_1688231	6	rs10826975	12	85749398		rs2395771	6	41264577	TREM1	5.42	0.11	0.25	0.11		
TREM1	ILMN_1688231	6	rs12412964	10	108256422		rs2395771	6	41264577	TREM1	5.92	1.20	1.23	1.69		
TRIM38	ILMN_1697971	6	rs2527180	7	158808416		rs2023447	6	26044369	TRIM38	6.46	0.04	0.91	0.39		
TSPAN14	ILMN_1785060	10	rs968726	17	27194634		rs10748526	10	82273079	TSPAN14	5.01	0.00	0.07	0.18	45.345	
TSPAN32	ILMN_1718621	11	rs10838738	11	47663049	MYBPC3	rs12800998	11	2317951	TSPAN32	5.51					
TSPAN32	ILMN_1718621	11	rs12800998	11	2317951	TSPAN32	rs620607	6	137947208		5.12					
TYMP	ILMN_3223126	22	rs140522	22	50971266	ECGF1	rs1198819	2	238746880		6.34					
TYMP	ILMN_3223126	22	rs470119	22	50966914	ECGF1	rs4783126	16	85147633		6.13					
UBASH3A	ILMN_2338348	21	rs1893592	21	43855067	UBASH3A	rs7201194	16	83600397		5.91	0.59	0.42	0.52		
UBASH3A	ILMN_2338348	21	rs1893592	21	43855067	UBASH3A	rs7512594	1	214514361		6.01	0.48	1.29	1.10		
USP36	ILMN_1697227	17	rs2279308	17	76764981	USP36	rs7225546	17	75151717		5.71	0.03	0.14	0.03	1.643	
VASP	ILMN_1743646	19	rs126426	19	46063167		rs2276470	19	45974668		5.09	0.94	5.14	4.95	0.088	
VNN2	ILMN_1678939	6	rs10435352	7	105252718		rs1883613	6	133077063	VNN2	5.64	0.84	0.15	0.46		
VNN2	ILMN_1678939	6	rs13044386	20	9116155		rs1883613	6	133072650	VNN2	5.44	0.39	0.69	0.57		
VNN2	ILMN_1678939	6	rs134447	22	49927332		rs1883613	6	133072650	VNN2	5.72					
VNN2	ILMN_1678939	6	rs216495	11	16834510		rs1883613	6	133072650	VNN2	5.77	0.33	0.19	0.19		
VNN3	ILMN_1804935	6	rs10278073	7	15162184		rs2267952	6	133067782	VNN3	6.44	0.16	0.74	0.41		
VNN3	ILMN_1804935	6	rs1443946	8	73006453		rs2267952	6	133067782	VNN3	5.74	0.23	0.48	0.31		
VNN3	ILMN_1804935	6	rs348462	9	75547169		rs2267952	6	133067782	VNN3	6.44	0.31	0.17	0.17		
VNN3	ILMN_1804935	6	rs7157055	14	83262064		rs2267952	6	133067782	VNN3	5.82	0.03	0.19	0.04		
VNN3	ILMN_2387680	21	rs2823165	21	16594253		rs2267952	6	133067782	VNN3	6.12	0.73	1.15	1.21		
VNN3	ILMN_2387680	6	rs9596457	13	51692548		rs2267952	6	133067782	VNN3	6.44	0.53	0.54	0.57		
VSTM1	ILMN_1763455	19	rs10500316	19	5453697	VSTM1	rs4552100	18	71024750		5.60	0.53	0.54	0.57		
VSTM1	ILMN_1763455	19	rs10500316	19	5453697	VSTM1	rs7895870	10	123098249		5.71	0.48	0.17	0.26		
VSTM1	ILMN_1763455	19	rs9625870	22	30261219		rs10500316	19	5453697	VSTM1	5.88	0.81	1.38	1.47		
WDR48	ILMN_1721013	3	rs1388935	4	188927822		rs6778963	3	39091812							

**Table S2: Estimation of additive and non-additive variance components from pedigree information** Taken from previous analysis in Powell et al 2013<sup>22</sup>

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

<sup>a</sup> “All” denotes 434 discovery interactions and “Significant” denotes 30 interactions with significant replication *p*-values

<sup>b</sup> Number of tests for concordance

<sup>c</sup> Expected number of concordant cases under the null hypothesis of no interactions

<sup>d</sup> Observed number of concordant cases

<sup>e</sup> The sign of the most significant epistatic variance component in discovery is the same as the corresponding variance component in the replication data.

<sup>f</sup> The largest epistatic variance component in the discovery is the same as in the replication with the same sign in both.

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

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

Interactions <sup>a</sup>	Dataset	<i>n</i> <sup>b</sup>	0 <sup>c</sup>	1 <sup>c</sup>	2 <sup>c</sup>	3 <sup>c</sup>	4 <sup>c</sup>	<i>p</i>
Expected <sup>d</sup>	-	-	0.06	0.25	0.38	0.25	0.06	-
All	EGCUT	434	0.06	0.22	0.41	0.23	0.08	0.194
All	Fehrman	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	$4.72 \times 10^{-4}$
Significant	Fehrman	30	0.03	0.07	0.33	0.27	0.30	$6.69 \times 10^{-4}$
Significant	Combined	60	0.05	0.05	0.32	0.30	0.28	$5.49 \times 10^{-8}$

<sup>a</sup> “All” denotes 434 discovery interactions and “Significant” denotes 30 interactions with significant replication *p*-values.

<sup>b</sup> Number of tests for concordance.

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

<sup>d</sup> Expected proportion of concordant signs under the null hypothesis of no epistasis.

**Table S5: Details on linkage disequilibrium and relative positions of all discovery interactions with SNPs on the same chromosome**

Chr	Gene	SNP 1	SNP 2	Position 1	Position 2	Distance / Mb	R <sup>2</sup>	D'
19	TMEM149	rs807491	rs7254601	36268923	36147315	0.122	0.000	0.001
17	FN3KRP	rs898095	rs9892064	80890638	80827903	0.063	0.063	0.088
21	CSTB	rs9979356	rs3761385	45230974	45198355	0.033	0.041	0.066
3	MBNL1	rs16864367	rs13079208	152234166	152116652	0.118	0.041	0.117
10	ADK	rs2395095	rs10824092	76446305	75929517	0.517	0.013	0.020
11	CTSC	rs7930237	rs556895	88117962	88077479	0.040	0.012	0.045
17	GAA	rs11150847	rs12602462	78153130	78146016	0.007	0.000	0.001
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	rs8092433	rs4890876	74747424	74732087	0.015	0.035	0.053
11	SNORD14A	rs2634462	rs6486334	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	0.060
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	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	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	TRAPP C4	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	TRAPP C5	rs17159840	rs17763599	7758194	2369415	5.389	0.000	0.000
22	PISD	rs715572	rs6518754	33234931	32097775	1.137	0.001	0.003
12	DIP2B	rs871257	rs12427378	117994348	51074199	66.920	0.001	0.001
12	GPR162	rs2272500	rs2707210	79685913	6902002	72.784	0.003	0.005
17	USP36	rs2279308	rs7225546	76794981	75151717	1.643	0.000	0.000