

Supplementary Material

Genome-wide association study of brain amyloid deposition as measured by Pittsburgh Compound-B (PiB)-PET imaging

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Supplementary Text

Sample description

All subjects with PiB-PET data were European-Americans and derived from three sites: University of Pittsburgh (PITT), Washington University (WU) and Indiana University (IU) combined with the initial phase of the multicenter ADNI PiB-PET add-on study (here they are referred to as ADNI/IU). All subjects provided informed consent and all studies were approved by their local Institutional Review Boards. The summary statistics of these samples are included in Supplementary Table S1.

The PITT sample comprised a total of 361 subjects with age 36 to 97 years (mean age=78.3±10.1) and they were derived from the Ginkgo Evaluation of Memory Study (GEMS) imaging sub-study¹, healthy aging study² or the PITT-Alzheimer's Disease Research Center (ADRC). The WU sample consisted of 495 Subjects with age 37 to 88 years (mean age=65.8±9.8) and they were recruited as part of the WU-Knight ADRC in St. Louis.³ A total of 127 subjects with age 55 to 88 years (mean age=73.8±7.6) were collected as part of the ADNI and the Indiana Memory and Aging Study.⁴⁻⁷

Genotyping, imputation and quality control

The genotyping platforms used for each study sample are listed in Supplementary Table S1. Imputation of non-genotyped single-nucleotide polymorphisms (SNPs) was performed with IMPUTE2⁸ using the 1000 Genomes Project⁹ Phase III (May 2013 release) data as the reference panel for PITT and Phase I (November 2010 release) data for WU and ADNI/IU datasets. In the PITT sample, SNPs with the imputation info score <0.5, the minor allele frequency (MAF) <0.01, $P < 1E-06$ in the Hardy Weinberg equilibrium test and the missing rate >5% were removed as well as the insertions and deletions were excluded. After quality control measures, 361 subjects and ~7 million genotyped and imputed SNPs were included in the GWAS analysis. Genetic association analysis was conducted using linear regression under an additive genetic model,

adjusting for age, gender, diagnosis, and first four principal components (PCs) calculated using smartPCA.¹⁰

As part of quality control steps in the WU sample, SNPs with minor allele frequency <1%, call rates <98%, Hardy–Weinberg equilibrium $P > 1E-06$ and individuals with >2% missing genotypes were removed from the analysis. The quality control SNP post imputation were as follows: MAF<1%, call rates <95%, Hardy–Weinberg equilibrium $P > 1E-06$ and $r^2 \leq 0.3$. Pairwise genome-wide estimates of proportion identity-by-descent were used to find duplicate and related individuals which were eliminated from the analysis. 495 subjects and ~14 million SNPs were included in the association test. Association testing was conducted using linear regression under an additive genetic model, adjusting for age, gender, diagnosis, and first two PCs calculated using PLINK v1.9 (<http://www.cog-genomics.org/plink2>) to confirm ethnicity of each sample.

In the ADNI/IU sample, SNPs with the imputation info score ≤ 0.5 , MAF<0.01, and $P < 1E-06$ in the Hardy Weinberg equilibrium test were removed as well as the insertions and deletions. After performing the quality control, 127 subjects and ~8 million SNPs were used in the statistical analysis. Association analysis was performed using linear regression adjusted for age, gender, diagnosis and first three PCs.

Functional analyses

To evaluate the biological significance of PiB-associated signals, we conducted five different analyses: differential gene expression in AD versus non-AD in relevant tissues, brain gene expression, expression quantitative trait loci (eQTL) analyses, summary-data-based Mendelian randomization (SMR) analyses to test for pleiotropic association between gene expression and PiB, and pathway analyses.

Differentially expressed genes: We searched for differentially expressed genes from the target gene list using gene expression data from AlzBase.¹¹ AlzBase (<http://alz.big.ac.cn/alzBase/>)

includes transcription data from brain and blood from aging, non-dementia, mild cognitive impairment, early stage AD and late stage AD.

Human brain gene expression: We evaluated the expression level of all target genes in human brain tissues from the Barres Human and Mouse Brain RNA-Seq Resource^{12, 13} (<http://www.brainrnaseq.org/>), and listed the corresponding cell types with expressed genes.

Expression quantitative trait loci (eQTL) analysis: To identify potential functional risk genes at each associated locus, we first identified variants in LD ($R^2 \geq 0.5$) with the top SNPs for the 16 associated loci in **Table 2**. The SNIIPA website (<https://snipa.helmholtz-muenchen.de/snipa3/>) was used to search for variants in LD, using the 1000 Genomes, Phase 3v5 variant set for the European population. The list of variants was searched for genes functionally linked via eQTLs to our expanded list of variants. The GTEx¹⁴ database was searched for eQTL associations in various brain tissues and whole blood.

Summary-data-based Mendelian randomization (SMR) analysis: To test if the genetic effect on PiB is mediated by gene expression in specific tissues, we performed SMR analyses to test for pleiotropic association between the expression level of a gene and PiB using summary-level data from GWAS and eQTL studies.¹⁵

Pathway analyses: Pathway analyses were performed with MAGMA,¹⁶ which performs SNP-wise gene analysis of summary statistics with correction for LD between variants and genes to test whether sets of genes are jointly associated with a phenotype (i.e. PiB), compared to other genes across the genome. Adaptive permutation was used to produce an empirical p-value and FDR. Gene-sets used in the analyses were from GO,^{17, 18} KEGG,^{19, 20} REACTOME,^{21, 22} and BIOCARTA pathways.

Data Availability

Upon publication, data will be submitted to the National Institute on Aging Genetics of Alzheimer's Disease (NIAGADS) data repository.

Association analysis of known non-APOE AD risk loci with amyloid burden

Although none of the known AD susceptibility loci, other than *APOE*, showed significant association at $P < 1E-05$, we examined the top IGAP genome-wide significant SNPs (Supplementary Table S3.1) and the associated gene regions (Supplementary Table S3.2) in relation to amyloid burden. Only one IGAP variant, *HLA-DRB1,HLA-DQA1/rs2760980*; $P=0.0093$, was associated with global PiB retention at $P < 0.05$. This is a proxy for the top *HLA-DRB1,HLA-DQA1/rs9271192* SNP that was not present in our dataset. The regional analysis of these loci found nominally significance SNPs at $P < 0.05$ in all but 4 loci (*CR1, PTK2B, PICALM, SORL1*) and 8 regions had top SNPs with $P < 0.01$ (Supplementary Table S3.2).

Association of amyloid loci with AD risk

To test if the suggestive non-*APOE* amyloid loci listed in **Table 2** are also associated with AD risk, we examined their associations in our PITT-ADRC case-control sample of >2,200 subjects.²³ Two top amyloid-associated SNPs showed association with AD risk at $P < 0.05$ (Supplementary Table S4.1): one is located on chromosome 4 in *CYP4V2/rs7377304* ($P=0.017$) and the other on chromosome 21 near *ICOSLG/rs55708341* ($P=0.0136$). When we examined additional A β -associated SNPs having $P < 0.05$ in each region with AD risk, multiple SNPs with $P < 0.05$ were found in 13 of 15 loci and 10 of them showed odds ratios and beta-values in the same directions (Supplementary Table S4.2), indicating that our suggestive A β -associated loci are also associated with AD risk.

Supplementary Tables

Table S1. Summary of characteristics of participants from the University of Pittsburgh (PITT), Washington University (WU), and the Alzheimer's disease Neuroimaging Initiative (ADNI) and the Indiana Memory and Aging Study (ADNI/IU) included in the meta-analysis

	PITT (n=361)	WU (n=495)	ADNI/IU (n=127)
Age in years (mean \pm standard deviation)	78.3 \pm 10.1	65.6 \pm 9.8	73.8 \pm 7.6
Male gender (n, %)	197(54.6)	205(41.4)	74(58.3)
PiB (mean \pm standard deviation)	1.9 \pm 0.6*	0.2 \pm 0.3**	1.6 \pm 0.4*
Clinical diagnosis of probable Alzheimer disease (n, %)	43(11.9)	76(15.4)	32(25.2)
Genotyping platform	Illumina Omni Quad Chip; Omni2.5 Chip	Illumina 610; Omniexpress chip	Human610-Quad BeadChip; HumanOmni Express BeadChip

*Standardized Uptake Volume Ratio (SUVR)

**Binding Potential (BP)

Table S2. SNPs achieving genome-wide significance ($P < 5E-08$) in the meta-analysis

SNP	Chr	Position	A1	A2	Gene	Region	PITT			WU			ADNI/IU			Meta	
							MAF	Beta	P-value	MAF	Beta	P-value	MAF	Beta	P-value	Beta	P-value
rs429358	19	45411941	C	T	APOE	exonic	0.20	0.35	5.20E-12	0.21	0.16	5.36E-16	0.28	0.19	7.88E-05	0.18	9.09E-30
rs12721051	19	45422160	G	C	APOC1	intronic	0.22	0.31	9.04E-10	0.24	0.12	7.13E-11	0.30	0.14	1.55E-03	0.14	2.60E-21
rs4420638	19	45422946	G	A	APOC1	downstream	0.22	0.31	1.41E-09	0.25	0.11	1.34E-10	0.30	0.14	1.55E-03	0.14	7.31E-21
rs56131196	19	45422846	A	G	APOC1	downstream	0.22	0.31	1.34E-09	0.25	0.11	2.84E-10	0.30	0.14	1.55E-03	0.14	1.45E-20
rs6857	19	45392254	T	C	PVRL2	UTR3	0.23	0.29	8.77E-09	0.20	0.13	4.42E-11	0.27	0.16	1.71E-03	0.15	1.70E-20
rs10414043	19	45415713	A	G	APOE,APOC1	intergenic	0.16	0.33	3.57E-09	0.17	0.13	9.15E-11	0.22	0.16	2.67E-03	0.15	2.24E-20
rs769449	19	45410002	A	G	APOE	intronic	0.16	0.32	1.36E-08	0.15	0.13	5.90E-11	0.22	0.16	3.27E-03	0.15	6.04E-20
rs7256200	19	45415935	T	G	APOE,APOC1	intergenic	0.16	0.32	1.77E-08	0.17	0.13	2.88E-11	0.21	0.15	8.82E-03	0.15	1.43E-19
rs2075650	19	45395619	G	A	TOMM40	intronic	0.20	0.24	2.81E-06	0.17	0.12	9.31E-10	0.22	0.13	1.98E-02	0.13	1.06E-15
rs34404554	19	45395909	G	C	TOMM40	intronic	0.20	0.24	2.37E-06	0.16	0.11	2.10E-09	0.22	0.13	1.98E-02	0.13	1.92E-15
rs11556505	19	45396144	T	C	TOMM40	exonic	0.20	0.24	2.37E-06	0.17	0.11	2.23E-09	0.22	0.13	1.98E-02	0.13	2.03E-15
rs12721046	19	45421254	A	G	APOC1	intronic	0.19	0.26	1.24E-06	0.19	0.11	1.50E-08	0.24	0.11	2.57E-02	0.13	1.01E-14
rs438811	19	45416741	T	C	APOE,APOC1	intergenic	0.26	0.21	1.45E-05	0.30	0.09	7.89E-08	0.32	0.13	2.31E-03	0.11	5.30E-14
rs71352238	19	45394336	C	T	TOMM40	upstream	0.20	0.23	7.82E-06	0.16	0.11	2.22E-08	0.22	0.13	1.98E-02	0.12	5.70E-14
rs483082	19	45416178	T	G	APOE,APOC1	intergenic	0.26	0.21	1.45E-05	0.29	0.09	1.58E-07	0.32	0.13	2.31E-03	0.11	1.02E-13
rs5117	19	45418790	C	T	APOC1	intronic	0.26	0.22	7.03E-06	0.28	0.08	1.17E-06	0.32	0.14	1.77E-03	0.10	2.65E-13
rs59007384	19	45396665	T	G	TOMM40	intronic	0.26	0.21	1.20E-05	0.25	0.09	1.71E-07	0.30	0.12	9.68E-03	0.11	3.31E-13
rs34342646	19	45388130	A	G	PVRL2	intronic	0.21	0.23	8.92E-06	0.13	0.17	1.86E-07	0.23	0.11	3.47E-02	0.17	2.05E-12
rs12972156	19	45387459	G	C	PVRL2	intronic	0.19	0.23	1.51E-05	0.13	0.17	1.86E-07	0.23	0.11	3.47E-02	0.17	3.52E-12
rs12972970	19	45387596	A	G	PVRL2	intronic	0.20	0.23	1.58E-05	0.13	0.17	1.86E-07	0.23	0.11	3.47E-02	0.17	3.71E-12
rs157582	19	45396219	T	C	TOMM40	intronic	0.27	0.20	2.91E-05	0.28	0.09	9.19E-07	0.31	0.11	2.29E-02	0.10	8.92E-12
rs157581	19	45395714	C	T	TOMM40	exonic	0.27	0.20	3.60E-05	0.28	0.09	7.42E-07	0.31	0.11	2.29E-02	0.10	9.19E-12
rs283815	19	45390333	G	A	PVRL2	intronic	0.27	0.21	1.41E-05	0.23	0.15	8.86E-06	0.31	0.11	2.29E-02	0.15	9.15E-11
rs34095326	19	45395844	A	G	TOMM40	intronic	0.17	0.19	5.59E-04	0.11	0.12	9.67E-08	0.17	0.09	1.36E-01	0.12	1.50E-10
rs184017	19	45394969	G	T	TOMM40	intronic	0.27	0.20	2.55E-05	0.24	0.15	2.34E-05	0.31	0.11	2.29E-02	0.15	3.43E-10
rs10119	19	45406673	A	G	TOMM40	UTR3	0.32	0.14	3.39E-03	0.31	0.16	4.50E-07	0.37	0.14	9.84E-04	0.15	4.31E-10
rs75627662	19	45413576	T	C	APOE	downstream	0.23	0.14	3.49E-03	0.23	0.07	3.28E-05	0.26	0.10	2.34E-02	0.08	3.58E-08

A1: minor allele; A2: major allele.

Table S3.1. Association of top IGAP SNPs with PiB-PET

IGAP Locus/SNP	Chr	IGAP <i>P</i>-value	Meta PiB <i>P</i>-value
<i>CR1</i> /rs6656401	1	5.70E-24	0.7552
<i>BIN1</i> /rs10200967*	2	2.24E-35	0.5425
<i>INPP5D</i> /rs35349669	2	3.20E-08	0.05966
<i>CASS4</i> /rs7274581	5	2.50E-08	0.2891
<i>MEF2C</i> /rs190982	5	3.20E-08	0.9975
<i>CD2AP</i> /rs10948363	6	5.20E-11	0.7107
<i>HLA-DRB5,HLA-DRB1</i> /rs2760980*	6	4.03E-51	0.009257
<i>EPHA1</i> /rs11771145	7	1.10E-13	0.1628
<i>NME8</i> /rs2718058	7	4.80E-09	0.2263
<i>SORL1</i> /rs11218343	7	9.70E-15	0.1851
<i>ZCWPW1</i> /rs1476679	7	5.60E-10	0.5949
<i>CLU</i> /rs17057043*	8	2.13E-20	0.5606
<i>PTK2B</i> /rs28834970	8	7.40E-14	0.4002
<i>CELF1</i> /rs10838725	11	1.10E-08	0.07309
<i>MS4A6A</i> /rs983392	11	6.10E-16	0.8271
<i>PICALM</i> /rs10792832	11	9.30E-26	0.1104
<i>FERMT2</i> /rs17125944	14	7.90E-09	0.2323
<i>SLC24A4,RIN3</i> /rs10498633	14	5.50E-09	0.2475
<i>ABCA7</i> /rs4147929	19	1.10E-15	0.3858

*Proxy SNP for the top IGAP SNP

Table S3.2. Regional association of IGAP loci with PiB-PET

IGAP Locus	Start BP	End BP	Total SNPs in the region	# of SNPs <0.05	Top SNP in the region	Chr	Position	A1	A2	Beta	P-value
<i>CR1</i>	207669924	207814835	142	0	<i>CR1</i> /rs7542494	1	207809744	A	G	-0.04	0.0684
<i>BIN1</i>	127806605	127864546	189	5	<i>BIN1</i> /rs17014818	2	127810697	T	C	-0.03	0.0325
<i>INPP5D</i>	233743532	234115739	824	30	<i>INPP5D</i> /rs12052961	2	234076434	A	G	-0.04	0.0043
<i>MEF2C</i>	87963600	88199223	238	1	<i>MEF2C-AS1</i> /rs13159808	5	88194669	A	T	0.03	0.0290
<i>HLA-DRB5/HLA-DRB1</i>	32261252	32826450	3780	128	<i>HLA-DQB1</i> /rs28746853	6	32634646	C	T	0.04	0.0022
<i>CD2AP</i>	47445789	47688606	646	9	<i>GPR111</i> /rs7764134	6	47655330	A	T	0.03	0.0104
<i>NME8</i>	37780799	37939840	439	52	<i>NME8</i> /rs1823519	7	37915816	A	C	0.06	0.0065
<i>ZCWPW1</i>	99488543	100200674	794	10	<i>AZGP1P1</i> /rs10953293	7	99579032	G	A	-0.06	0.0073
<i>EPHA1</i>	143014244	143218545	408	4	<i>CLCN1,FAM131B</i> /rs7806322	7	143049965	T	C	-0.06	0.0188
<i>PTK2B</i>	27094615	27402132	652	0	<i>PTK2B</i> /rs35575787	8	27187520	T	G	-0.04	0.0547
<i>CLU</i>	27183710	27695123	1289	1	<i>EPHX2,CLU</i> /rs1532275	8	27424988	A	G	0.06	0.0496
<i>CELF1</i>	47186424	47868853	907	98	<i>DDB2</i> /rs2291120	11	47237680	C	T	0.12	0.0010
<i>MS4A6A</i>	59807796	60108278	631	13	<i>MS4A6A,MS4A4A</i> /rs11230208	11	60008547	A	C	0.06	0.0107
<i>PICALM</i>	85566157	85779310	486	0	<i>PICALM</i> /rs7951357	11	85762557	G	A	0.04	0.0552
<i>SORL1</i>	121328954	121502894	190	0	<i>SORL1</i> /rs17245976	11	121365720	T	G	-0.04	0.0944
<i>FERMT2</i>	53109716	53417538	427	78	<i>STYX</i> /rs10483618	14	53203590	C	T	0.08	0.0016
<i>SLC24A4</i>	92791068	93153606	1005	60	<i>SLC24A4</i> /rs72695119	14	92838693	A	G	0.09	0.0060
<i>ABCA7</i>	841398	1275987	680	44	<i>PRTN3</i> /rs629631	19	846041	T	C	0.11	0.0012
<i>CASS4</i>	54968038	55111371	241	2	<i>CASS4</i> /rs6127744	20	54986274	T	G	0.06	0.0278

Table S4.1. Association of top non-*APOE* PiB-PET variants with AD risk in a case-control sample of >2,200 subjects (Kamboh et al. *Mol Psychiatry* 2012; 2:e117)

Top PiB-PET Locus/SNP	Odds Ratio	P-value
<i>ADCY8, EFR3A</i> /rs13260032	1.050	0.4419
<i>RAP2B, C3orf79</i> /rs4680057	0.995	0.9258
<i>DAPK2</i> /rs12908891	1.118	0.07431
<i>CYP4V2</i> /rs7377304	0.862	0.01727
<i>C21orf33, ICOSLG</i> /rs55708341	1.206	0.01365
<i>LINC00971</i> /rs9831119	0.918	0.3492
<i>SLITRK1</i> /rs9531483	0.985	0.8269
<i>C2orf80, IDH1</i> /rs6722000	1.001	0.8912
<i>MAGEF1, LOC101928992</i> /rs11923588	0.924	0.5286
<i>DTHD, MIR4801</i> /rs66837203	1.204	0.1694
<i>HTN1</i> /rs200028958	0.907	0.3367
<i>HSD17B6, SDR9C7</i> /rs4526799	1.002	0.9728
<i>ELTD1, LPHN2</i> /rs17105538	1.176	0.06483
<i>LINC01250</i> /rs62121100	1.053	0.5476
<i>KCNF, FLJ33534</i> /rs1809136	0.865	0.2300

Table S4.2. Regional association of top non-*APOE* PiB-PET loci with AD risk in a case-control maple of >2,200 subjects (Kamboh et al. *Mol Psychiatry* 2012; 2:e117). For comparison PiB *P* and beta values are also given for the top corresponding AD risk SNP

Association of PiB-PET gene regions with AD risk												
PiB-PET Locus	Chr	Region Start	Region End	Total PiB SNPs	PiB SNPs <0.05	AD SNPs <0.05	Top AD Risk SNP in the region	A1 from PiB	AD risk Odds Ratio	<i>P</i> for AD Risk	Beta for PiB	<i>P</i> for PiB
<i>ADCY8, EFR3A</i>	8	131951455	132951455	2290	303	110	<i>ADCY8, EFR3A</i> /rs9693785	C	0.7272	0.0004175	-0.056907	0.007005
<i>RAP2B, C3orf79</i>	3	152596985	153596985	2377	359	11	<i>C3orf79, ARHGEF26-AS1</i> /rs7649472	G	1.156	0.02487	0.024879	0.04522
<i>DAPK2</i>	15	63736441	64736441	1626	165	11	<i>DAPK2</i> /rs1380843	A	0.8621	0.02232	-0.053325	0.005655
<i>CYP4V2</i>	4	186629780	187629780	2445	177	13	<i>CYP4V2</i> /rs1053094	A	1.1763	0.009745	0.058916	0.002189
<i>C21orf33, ICOSLG</i>	21	45127581	46127581	2199	227	73	<i>C21orf33, ICOSLG</i> /rs2070554	T	1.237	0.00879	0.037261	0.002774
<i>LINC00971</i>	3	84212077	85212077	2480	657	1	<i>CADM2</i> /rs13075478	T	1.152	0.02369	0.028393	0.02801
<i>SLITRK1</i>	13	83744873	84744873	1677	312	6	<i>SLITRK1</i> /rs9602135	G	0.7734	0.01895	0.042266	0.0297
<i>C2orf80, IDH1</i>	2	208575957	209575957	1562	188	0	<i>C2orf80, IDH1</i> /rs711418664	A	0.8554	0.06475	0.058783	0.00121
<i>MAGEF1, LOC101928992</i>	3	183959667	184959667	1774	72	1	<i>EIF4G1</i> /rs9846954	T	1.164	0.03531	-0.034909	0.04058
<i>DTHD, MIR4801</i>	4	36397136	37397136	3117	91	4	<i>DTHD1, MIR4801</i> /rs1319729	G	1.321	0.008938	0.039352	0.002278
<i>HTN1</i>	4	70423661	71423661	3151	465	42	<i>HTN1</i> /rs6854359	A	1.176	0.01454	-0.038333	0.00506
<i>HSD17B6, SDR9C7</i>	12	56780586	57780586	1132	95	0	<i>HSD17B6, SDR9C7</i> /rs1846400	A	0.9274	0.2208	-0.028111	0.0117
<i>ELTD1, LPHN2</i>	1	80815043	81815043	2130	159	11	<i>ELTD1, LPHN2</i> /rs10874177	C	1.2	0.008051	0.041764	0.002923
<i>LINC01250</i>	2	2593952	3593952	2434	267	7	<i>MYT1L, LINC01250</i> /rs12617695	T	1.447	0.002762	0.062219	0.04794
<i>KCNF, FLJ33534</i>	2	10652180	11652180	2394	209	10	<i>KCNF1, FLJ33534</i> /rs7556946	C	1.507	0.004408	-0.102457	0.04779

Table S5. The eQTL and SMR P-values for the top non-APOE region SNPs from Table 1

Tissue	Chr	Gene	Probe_bp	SNP	SNP_bp	A1	A2	Freq	p_GWAS	p_eQTL	p_SMR
Brain Amygdala	8	ADCY8	131923609	rs13260032	132451455	C	A	0.43	4.87E-07	1.54E-02	3.27E-02
Brain Frontal Cortex BA9	8	ADCY8	131923609	rs13260032	132451455	C	A	0.43	4.87E-07	4.75E-02	6.96E-02
Brain Putamen basal ganglia	8	ADCY8	131923609	rs13260032	132451455	C	A	0.43	4.87E-07	2.86E-02	4.88E-02
Brain Spinal cord cervical c-1	8	ADCY8	131923609	rs13260032	132451455	C	A	0.43	4.87E-07	1.77E-02	3.57E-02
Brain Anterior cingulate cortex BA24	3	RP11-38P22.2	152558203	rs4680057	153096985	A	G	0.44	9.69E-07	2.43E-02	4.72E-02
Brain Hippocampus	3	RP11-38P22.2	152558203	rs4680057	153096985	A	G	0.44	9.69E-07	1.58E-02	3.64E-02
Brain Nucleus accumbens basal ganglia	3	RAP2B	152883147	rs4680057	153096985	A	G	0.44	9.69E-07	2.00E-02	4.19E-02
Brain Spinal cord cervical c-1	3	RP11-23D24.2	153400349	rs4680057	153096985	A	G	0.44	9.69E-07	1.51E-02	3.54E-02
Whole Blood	3	ARHGEF26	153907204	rs4680057	153096985	A	G	0.44	9.69E-07	1.31E-03	1.07E-02
Brain Amygdala	15	RAB8B	63520824	rs12908891	64236441	A	G	0.52	1.39E-06	1.98E-02	3.51E-02
Brain Anterior cingulate cortex BA24	15	HERC1	64013479	rs12908891	64236441	A	G	0.52	1.39E-06	7.02E-05	1.94E-03
Brain Anterior cingulate cortex BA24	15	DAPK2	64281733	rs12908891	64236441	A	G	0.52	1.39E-06	1.40E-02	2.77E-02
Brain Cerebellar Hemisphere	15	ANKDD1A	65227571	rs12908891	64236441	A	G	0.52	1.39E-06	3.20E-02	4.90E-02
Brain Cerebellum	15	RP11-244F12.3	63339909	rs12908891	64236441	A	G	0.52	1.39E-06	4.94E-02	6.77E-02
Brain Cerebellum	15	LACTB	63424129	rs12908891	64236441	A	G	0.52	1.39E-06	2.10E-02	3.64E-02
Brain Cerebellum	15	CA12	63643968	rs12908891	64236441	A	G	0.52	1.39E-06	2.44E-02	4.04E-02
Brain Cerebellum	15	USP3-AS1	63864970	rs12908891	64236441	A	G	0.52	1.39E-06	4.85E-02	6.69E-02
Brain Cerebellum	15	DAPK2	64281733	rs12908891	64236441	A	G	0.52	1.39E-06	1.95E-03	8.63E-03
Brain Frontal Cortex BA9	15	AC100830.3	65002624	rs12908891	64236441	A	G	0.52	1.39E-06	1.67E-02	3.12E-02
Brain Frontal Cortex BA9	15	PLEKH02	65147147	rs12908891	64236441	A	G	0.52	1.39E-06	4.73E-02	6.56E-02
Brain Hippocampus	15	FBXL22	63892089	rs12908891	64236441	A	G	0.52	1.39E-06	4.97E-02	6.81E-02
Brain Hippocampus	15	AC100830.4	64987516	rs12908891	64236441	A	G	0.52	1.39E-06	4.44E-02	6.25E-02
Brain Nucleus accumbens basal ganglia	15	RP11-244F12.3	63339909	rs12908891	64236441	A	G	0.52	1.39E-06	3.96E-02	5.74E-02
Brain Nucleus accumbens basal ganglia	15	USP3-AS1	63864970	rs12908891	64236441	A	G	0.52	1.39E-06	7.63E-03	1.88E-02
Brain Nucleus accumbens basal ganglia	15	SNX22	64446798	rs12908891	64236441	A	G	0.52	1.39E-06	3.18E-02	4.89E-02
Brain Putamen basal ganglia	15	TPM1	63349472	rs12908891	64236441	A	G	0.52	1.39E-06	3.55E-02	5.29E-02
Brain Putamen basal ganglia	15	SNX22	64446798	rs12908891	64236441	A	G	0.52	1.39E-06	4.62E-03	1.39E-02
Brain Putamen basal ganglia	15	TRIP4	64713724	rs12908891	64236441	A	G	0.52	1.39E-06	2.45E-02	4.06E-02
Brain Putamen basal ganglia	15	RBPMS2	65049938	rs12908891	64236441	A	G	0.52	1.39E-06	4.15E-02	5.94E-02
Brain Spinal cord cervical c-1	15	RAB8B	63520824	rs12908891	64236441	A	G	0.52	1.39E-06	4.81E-02	6.64E-02
Brain Spinal cord cervical c-1	15	FBXL22	63892089	rs12908891	64236441	A	G	0.52	1.39E-06	1.29E-02	2.63E-02
Brain Spinal cord cervical c-1	15	TRIP4	64713724	rs12908891	64236441	A	G	0.52	1.39E-06	4.60E-02	6.42E-02
Brain Substantia nigra	15	FBXL22	63892089	rs12908891	64236441	A	G	0.52	1.39E-06	2.05E-02	3.58E-02
Whole Blood	15	TPM1	63349472	rs12908891	64236441	A	G	0.52	1.39E-06	2.66E-02	4.30E-02
Whole Blood	15	KIAA0101	64668539	rs12908891	64236441	A	G	0.52	1.39E-06	1.86E-02	3.35E-02
Brain Amygdala	4	KIAA1430	186105738	rs7377304	187129780	G	T	0.45	2.46E-06	2.21E-02	3.88E-02
Brain Anterior cingulate cortex BA24	4	SORBS2	186692202	rs7377304	187129780	G	T	0.45	2.46E-06	3.88E-02	5.77E-02
Brain Anterior cingulate cortex BA24	4	FAM149A	187059697	rs7377304	187129780	G	T	0.45	2.46E-06	1.35E-02	2.81E-02
Brain Anterior cingulate cortex BA24	4	F11	187198967	rs7377304	187129780	G	T	0.45	2.46E-06	8.33E-03	2.08E-02
Brain Anterior cingulate cortex BA24	4	MTNR1A	187465765	rs7377304	187129780	G	T	0.45	2.46E-06	1.51E-02	3.02E-02
Brain Caudate basal ganglia	4	CYP4V2	187123642	rs7377304	187129780	G	T	0.45	2.46E-06	1.48E-02	2.97E-02
Brain Caudate basal ganglia	4	F11	187198967	rs7377304	187129780	G	T	0.45	2.46E-06	2.71E-02	4.47E-02
Brain Cerebellar Hemisphere	4	C4orf47	186359187	rs7377304	187129780	G	T	0.45	2.46E-06	2.02E-02	3.66E-02
Brain Cerebellum	4	UFSP2	186333916	rs7377304	187129780	G	T	0.45	2.46E-06	4.55E-02	6.48E-02
Brain Cerebellum	4	PDLIM3	186439808	rs7377304	187129780	G	T	0.45	2.46E-06	7.07E-03	1.88E-02
Brain Cerebellum	4	ORAOV1P1	187092214	rs7377304	187129780	G	T	0.45	2.46E-06	2.97E-02	4.77E-02
Brain Cortex	4	F11	187198967	rs7377304	187129780	G	T	0.45	2.46E-06	1.10E-05	1.19E-03
Brain Frontal Cortex BA9	4	RP11-714G18.1	186302025	rs7377304	187129780	G	T	0.45	2.46E-06	2.27E-02	3.96E-02
Brain Frontal Cortex BA9	4	F11	187198967	rs7377304	187129780	G	T	0.45	2.46E-06	4.91E-02	6.87E-02
Brain Hippocampus	4	F11	187198967	rs7377304	187129780	G	T	0.45	2.46E-06	2.85E-04	3.80E-03
Brain Nucleus accumbens basal ganglia	4	CYP4V2	187123642	rs7377304	187129780	G	T	0.45	2.46E-06	2.81E-02	4.58E-02
Brain Putamen basal ganglia	4	F11	187198967	rs7377304	187129780	G	T	0.45	2.46E-06	5.04E-03	1.55E-02
Brain Putamen basal ganglia	4	FAT1	187578406	rs7377304	187129780	G	T	0.45	2.46E-06	1.06E-02	2.40E-02
Brain Spinal cord cervical c-1	4	TLR3	186999764	rs7377304	187129780	G	T	0.45	2.46E-06	4.35E-02	6.27E-02
Brain Substantia nigra	4	F11	187198967	rs7377304	187129780	G	T	0.45	2.46E-06	1.19E-02	2.59E-02
Whole Blood	4	UFSP2	186333916	rs7377304	187129780	G	T	0.45	2.46E-06	3.65E-04	4.22E-03
Brain Amygdala	21	AP001053.11	45229043	rs55708341	45627581	T	A	0.2	2.51E-06	4.54E-02	7.10E-02
Brain Anterior cingulate cortex BA24	21	CSTB	45194359	rs55708341	45627581	T	A	0.2	2.51E-06	3.97E-02	6.49E-02
Brain Anterior cingulate cortex BA24	21	RRP1	45217284	rs55708341	45627581	T	A	0.2	2.51E-06	8.64E-03	2.61E-02
Brain Caudate basal ganglia	21	TRAPPC10	45479316	rs55708341	45627581	T	A	0.2	2.51E-06	2.90E-02	5.29E-02
Brain Caudate basal ganglia	21	UBE2G2	46205444	rs55708341	45627581	T	A	0.2	2.51E-06	3.66E-02	6.15E-02
Brain Cerebellar Hemisphere	21	RRP1B	45097693	rs55708341	45627581	T	A	0.2	2.51E-06	2.72E-02	5.08E-02
Brain Cerebellar Hemisphere	21	CSTB	45194359	rs55708341	45627581	T	A	0.2	2.51E-06	4.25E-02	6.79E-02
Brain Cerebellar Hemisphere	21	AP001055.6	45579291	rs55708341	45627581	T	A	0.2	2.51E-06	1.11E-02	2.99E-02
Brain Cerebellar Hemisphere	21	AP001058.3	45626845	rs55708341	45627581	T	A	0.2	2.51E-06	3.48E-02	5.95E-02
Brain Cerebellum	21	C21orf67	46356278	rs55708341	45627581	T	A	0.2	2.51E-06	2.07E-02	4.29E-02
Brain Cortex	21	LL21NC02-1C16.1	46349810	rs55708341	45627581	T	A	0.2	2.51E-06	7.94E-03	2.50E-02
Brain Frontal Cortex BA9	21	LINC00313	44890694	rs55708341	45627581	T	A	0.2	2.51E-06	4.70E-02	7.27E-02
Brain Frontal Cortex BA9	21	HSF2BP	45014223	rs55708341	45627581	T	A	0.2	2.51E-06	4.84E-02	7.42E-02

Brain Frontal Cortex BA9	21	CSTB	45194359	rs55708341	45627581	T	A	0.2	2.51E-06	5.21E-03	2.02E-02
Brain Frontal Cortex BA9	21	AP001058.3	45626845	rs55708341	45627581	T	A	0.2	2.51E-06	6.86E-04	8.38E-03
Brain Hippocampus	21	LL21NC02-1C16.2	46356543	rs55708341	45627581	T	A	0.2	2.51E-06	2.38E-02	4.67E-02
Brain Hypothalamus	21	HSF2BP	45014223	rs55708341	45627581	T	A	0.2	2.51E-06	3.71E-02	6.20E-02
Brain Hypothalamus	21	CSTB	45194359	rs55708341	45627581	T	A	0.2	2.51E-06	1.83E-02	3.98E-02
Brain Hypothalamus	21	AP001065.7	45891105	rs55708341	45627581	T	A	0.2	2.51E-06	3.73E-02	6.23E-02
Brain Nucleus accumbens basal ganglia	21	AP001058.3	45626845	rs55708341	45627581	T	A	0.2	2.51E-06	4.65E-02	7.22E-02
Brain Nucleus accumbens basal ganglia	21	ICOSLG	45651861	rs55708341	45627581	T	A	0.2	2.51E-06	4.79E-02	7.37E-02
Brain Nucleus accumbens basal ganglia	21	LRR3	45877054	rs55708341	45627581	T	A	0.2	2.51E-06	3.77E-02	6.27E-02
Brain Nucleus accumbens basal ganglia	21	C21orf90	45941467	rs55708341	45627581	T	A	0.2	2.51E-06	1.11E-02	2.99E-02
Brain Putamen basal ganglia	21	SUMO3	46232113	rs55708341	45627581	T	A	0.2	2.51E-06	3.26E-02	5.71E-02
Brain Substantia nigra	21	AP001056.1	45595854	rs55708341	45627581	T	A	0.2	2.51E-06	4.07E-02	6.60E-02
Whole Blood	21	RRP1B	45097693	rs55708341	45627581	T	A	0.2	2.51E-06	4.30E-02	6.84E-02
Brain Amygdala	3	CADM2	85565855	rs9831119	84712077	C	T	0.13	2.98E-06	1.50E-03	9.29E-03
Brain Cortex	3	CADM2	85565855	rs9831119	84712077	C	T	0.13	2.98E-06	2.43E-02	4.37E-02
Brain Anterior cingulate cortex BA24	2	AC096772.6	208686753	rs6722000	209075957	G	A	0.21	4.96E-06	7.00E-03	2.15E-02
Brain Caudate basal ganglia	2	CREB1	208431337	rs6722000	209075957	G	A	0.21	4.96E-06	2.49E-02	4.57E-02
Brain Cerebellum	2	C2orf80	209042432	rs6722000	209075957	G	A	0.21	4.96E-06	6.70E-03	2.10E-02
Brain Cerebellum	2	PIKFYVE	209177233	rs6722000	209075957	G	A	0.21	4.96E-06	2.27E-02	4.31E-02
Brain Cortex	2	IDH1-AS1	209120438	rs6722000	209075957	G	A	0.21	4.96E-06	4.81E-03	1.76E-02
Brain Hippocampus	2	IDH1-AS1	209120438	rs6722000	209075957	G	A	0.21	4.96E-06	1.65E-02	3.54E-02
Brain Hypothalamus	2	PTH2R	209471832	rs6722000	209075957	G	A	0.21	4.96E-06	3.53E-02	5.77E-02
Brain Substantia nigra	2	CNNYL1	208601413	rs6722000	209075957	G	A	0.21	4.96E-06	4.92E-02	7.26E-02
Brain Substantia nigra	2	CRYGEP	208975096	rs6722000	209075957	G	A	0.21	4.96E-06	4.90E-02	7.24E-02
Whole Blood	2	AC007879.2	208076115	rs6722000	209075957	G	A	0.21	4.96E-06	4.39E-02	6.70E-02
Whole Blood	2	PIKFYVE	209177233	rs6722000	209075957	G	A	0.21	4.96E-06	1.08E-02	2.75E-02
Brain Amygdala	3	YEATS2-AS1	183526253	rs11923588	184459667	T	C	0.06	5.66E-06	7.92E-03	2.02E-02
Brain Amygdala	3	PARL	183574934	rs11923588	184459667	T	C	0.06	5.66E-06	1.56E-02	3.08E-02
Brain Amygdala	3	ABCC5	183686762	rs11923588	184459667	T	C	0.06	5.66E-06	3.63E-03	1.29E-02
Brain Amygdala	3	CAMK2N2	183978312	rs11923588	184459667	T	C	0.06	5.66E-06	2.62E-02	4.37E-02
Brain Amygdala	3	VPS8	184650166	rs11923588	184459667	T	C	0.06	5.66E-06	2.94E-02	4.74E-02
Brain Anterior cingulate cortex BA24	3	YEATS2-AS1	183526253	rs11923588	184459667	T	C	0.06	5.66E-06	1.68E-02	3.23E-02
Brain Anterior cingulate cortex BA24	3	ABCC5	183686762	rs11923588	184459667	T	C	0.06	5.66E-06	8.10E-03	2.05E-02
Brain Anterior cingulate cortex BA24	3	VPS8	184650166	rs11923588	184459667	T	C	0.06	5.66E-06	1.96E-02	3.59E-02
Brain Caudate basal ganglia	3	YEATS2-AS1	183526253	rs11923588	184459667	T	C	0.06	5.66E-06	4.74E-02	6.69E-02
Brain Caudate basal ganglia	3	FAM131A	184058843	rs11923588	184459667	T	C	0.06	5.66E-06	3.06E-02	4.87E-02
Brain Caudate basal ganglia	3	SENP2	185325811	rs11923588	184459667	T	C	0.06	5.66E-06	1.91E-02	3.53E-02
Brain Cerebellar Hemisphere	3	HSP90AA5P	183834413	rs11923588	184459667	T	C	0.06	5.66E-06	2.43E-02	4.14E-02
Brain Cerebellar Hemisphere	3	RP11-329B9.5	184460839	rs11923588	184459667	T	C	0.06	5.66E-06	1.48E-02	2.98E-02
Brain Cerebellum	3	CAMK2N2	183978312	rs11923588	184459667	T	C	0.06	5.66E-06	1.98E-02	3.61E-02
Brain Hippocampus	3	RP11-329B9.4	184454300	rs11923588	184459667	T	C	0.06	5.66E-06	3.38E-02	5.23E-02
Brain Nucleus accumbens basal ganglia	3	AP2M1	183897178	rs11923588	184459667	T	C	0.06	5.66E-06	3.05E-02	4.86E-02
Brain Putamen basal ganglia	3	RP11-778D9.12	183852416	rs11923588	184459667	T	C	0.06	5.66E-06	4.80E-02	6.75E-02
Brain Putamen basal ganglia	3	EPHB3	184289884	rs11923588	184459667	T	C	0.06	5.66E-06	4.75E-02	6.70E-02
Brain Spinal cord cervical c-1	3	CAMK2N2	183978312	rs11923588	184459667	T	C	0.06	5.66E-06	4.73E-02	6.68E-02
Brain Substantia nigra	3	CAMK2N2	183978312	rs11923588	184459667	T	C	0.06	5.66E-06	4.15E-02	6.07E-02
Brain Substantia nigra	3	LIPH	185247225	rs11923588	184459667	T	C	0.06	5.66E-06	3.57E-02	5.43E-02
Whole Blood	3	CHRD	184102739	rs11923588	184459667	T	C	0.06	5.66E-06	3.51E-02	5.37E-02
Brain Cerebellum	4	DTHD1	36315311	rs66837203	36897136	T	C	0.07	6.03E-06	1.20E-02	2.98E-02
Brain Hypothalamus	4	ARAP2	36097987	rs66837203	36897136	T	C	0.07	6.03E-06	2.68E-03	1.36E-02
Brain Putamen basal ganglia	4	ARAP2	36097987	rs66837203	36897136	T	C	0.07	6.03E-06	4.88E-02	7.29E-02
Brain Putamen basal ganglia	4	RP11-431M7.3	36260790	rs66837203	36897136	T	C	0.07	6.03E-06	1.57E-02	3.49E-02
Brain Substantia nigra	4	RP11-431M7.3	36260790	rs66837203	36897136	T	C	0.07	6.03E-06	2.53E-02	4.69E-02
Brain Cerebellar Hemisphere	4	RP11-46J23.1	71569836	rs200028958	70923661	A	G	0.1	6.25E-06	2.90E-02	5.35E-02
Brain Hypothalamus	4	UTP3	71555231	rs200028958	70923661	A	G	0.1	6.25E-06	1.41E-02	3.49E-02
Brain Hypothalamus	4	RUFY3	71621775	rs200028958	70923661	A	G	0.1	6.25E-06	2.78E-02	5.21E-02
Brain Hypothalamus	4	DCK	71877443	rs200028958	70923661	A	G	0.1	6.25E-06	1.25E-02	3.26E-02
Whole Blood	4	GRSF1	71693580	rs200028958	70923661	A	G	0.1	6.25E-06	6.40E-03	2.29E-02
Brain Amygdala	12	ERBB3	56485465	rs4526799	57280586	T	C	0.34	7.26E-06	3.43E-02	6.91E-02
Brain Amygdala	12	ATP5B	57035878	rs4526799	57280586	T	C	0.34	7.26E-06	1.95E-02	5.10E-02
Brain Amygdala	12	PRIM1	57135785	rs4526799	57280586	T	C	0.34	7.26E-06	4.71E-03	2.70E-02
Brain Amygdala	12	AC025165.8	58008874	rs4526799	57280586	T	C	0.34	7.26E-06	2.87E-02	6.25E-02
Brain Amygdala	12	TSPAN31	58138756	rs4526799	57280586	T	C	0.34	7.26E-06	4.57E-02	8.16E-02
Brain Amygdala	12	AVIL	58201929	rs4526799	57280586	T	C	0.34	7.26E-06	2.48E-03	2.13E-02
Brain Anterior cingulate cortex BA24	12	MYL6	56554355	rs4526799	57280586	T	C	0.34	7.26E-06	2.10E-02	5.30E-02
Brain Anterior cingulate cortex BA24	12	CNPY2	56706816	rs4526799	57280586	T	C	0.34	7.26E-06	4.40E-02	7.98E-02
Brain Anterior cingulate cortex BA24	12	BAZZA	57009990	rs4526799	57280586	T	C	0.34	7.26E-06	2.80E-02	6.17E-02
Brain Anterior cingulate cortex BA24	12	TMEM194A	57465636	rs4526799	57280586	T	C	0.34	7.26E-06	9.25E-04	1.54E-02
Brain Anterior cingulate cortex BA24	12	INHBE	57849584	rs4526799	57280586	T	C	0.34	7.26E-06	1.93E-03	1.95E-02
Brain Anterior cingulate cortex BA24	12	RP11-571M6.17	58197909	rs4526799	57280586	T	C	0.34	7.26E-06	4.87E-02	8.48E-02
Brain Anterior cingulate cortex BA24	12	AVIL	58201929	rs4526799	57280586	T	C	0.34	7.26E-06	1.68E-02	4.73E-02
Brain Caudate basal ganglia	12	PA2G4	56502897	rs4526799	57280586	T	C	0.34	7.26E-06	1.56E-02	4.56E-02

Brain Caudate basal ganglia	12	COQ10A	56662696	rs4526799	57280586	T	C	0.34	7.26E-06	2.82E-02	6.19E-02
Brain Caudate basal ganglia	12	IL23A	56733428	rs4526799	57280586	T	C	0.34	7.26E-06	1.34E-02	4.24E-02
Brain Caudate basal ganglia	12	RP11-74M13.4	57242410	rs4526799	57280586	T	C	0.34	7.26E-06	1.97E-02	5.12E-02
Brain Caudate basal ganglia	12	MYO1A	57433641	rs4526799	57280586	T	C	0.34	7.26E-06	1.86E-02	4.97E-02
Brain Cerebellar Hemisphere	12	PMEL	56357495	rs4526799	57280586	T	C	0.34	7.26E-06	9.90E-03	3.69E-02
Brain Cerebellar Hemisphere	12	RP11-603J24.7	56374517	rs4526799	57280586	T	C	0.34	7.26E-06	9.33E-03	3.59E-02
Brain Cerebellar Hemisphere	12	MYL6	56554355	rs4526799	57280586	T	C	0.34	7.26E-06	1.40E-02	4.33E-02
Brain Cerebellar Hemisphere	12	METTL21B	58170856	rs4526799	57280586	T	C	0.34	7.26E-06	4.24E-02	7.81E-02
Brain Cerebellum	12	RPS26	56436876	rs4526799	57280586	T	C	0.34	7.26E-06	2.88E-02	6.27E-02
Brain Cerebellum	12	CS	56679829	rs4526799	57280586	T	C	0.34	7.26E-06	3.16E-02	6.59E-02
Brain Cerebellum	12	MIP	56853054	rs4526799	57280586	T	C	0.34	7.26E-06	4.42E-02	8.00E-02
Brain Cerebellum	12	PTGES3	57069643	rs4526799	57280586	T	C	0.34	7.26E-06	3.11E-02	6.53E-02
Brain Cerebellum	12	RDH16	57349188	rs4526799	57280586	T	C	0.34	7.26E-06	2.13E-02	5.34E-02
Brain Cortex	12	WIBG	56310770	rs4526799	57280586	T	C	0.34	7.26E-06	3.72E-02	7.24E-02
Brain Cortex	12	PMEL	56357495	rs4526799	57280586	T	C	0.34	7.26E-06	2.36E-03	2.09E-02
Brain Cortex	12	STAC3	57641106	rs4526799	57280586	T	C	0.34	7.26E-06	4.54E-02	8.12E-02
Brain Frontal Cortex BA9	12	IKZF4	56416831	rs4526799	57280586	T	C	0.34	7.26E-06	2.60E-02	5.92E-02
Brain Frontal Cortex BA9	12	COQ10A	56662696	rs4526799	57280586	T	C	0.34	7.26E-06	4.08E-02	7.63E-02
Brain Frontal Cortex BA9	12	RP11-977G19.11	56701259	rs4526799	57280586	T	C	0.34	7.26E-06	1.96E-02	5.11E-02
Brain Hippocampus	12	RAB5B	56378093	rs4526799	57280586	T	C	0.34	7.26E-06	2.48E-02	5.78E-02
Brain Hippocampus	12	RNF41	56607001	rs4526799	57280586	T	C	0.34	7.26E-06	2.32E-02	5.58E-02
Brain Hippocampus	12	ANKRD52	56641903	rs4526799	57280586	T	C	0.34	7.26E-06	3.06E-02	6.47E-02
Brain Hippocampus	12	ZBTB39	57396424	rs4526799	57280586	T	C	0.34	7.26E-06	4.04E-02	7.58E-02
Brain Hippocampus	12	METTL1	58164318	rs4526799	57280586	T	C	0.34	7.26E-06	8.61E-03	3.47E-02
Brain Hypothalamus	12	PTGES3	57069643	rs4526799	57280586	T	C	0.34	7.26E-06	1.05E-02	3.79E-02
Brain Nucleus accumbens basal ganglia	12	RNF41	56607001	rs4526799	57280586	T	C	0.34	7.26E-06	4.91E-02	8.53E-02
Brain Nucleus accumbens basal ganglia	12	BAZZA	57009990	rs4526799	57280586	T	C	0.34	7.26E-06	3.20E-02	6.64E-02
Brain Putamen basal ganglia	12	WIBG	56310770	rs4526799	57280586	T	C	0.34	7.26E-06	3.45E-02	6.93E-02
Brain Putamen basal ganglia	12	CDK2	56363560	rs4526799	57280586	T	C	0.34	7.26E-06	1.90E-02	5.03E-02
Brain Putamen basal ganglia	12	RPS26	56436876	rs4526799	57280586	T	C	0.34	7.26E-06	1.38E-02	4.30E-02
Brain Putamen basal ganglia	12	MYL6B	56548905	rs4526799	57280586	T	C	0.34	7.26E-06	1.59E-02	4.60E-02
Brain Putamen basal ganglia	12	NABP2	56619718	rs4526799	57280586	T	C	0.34	7.26E-06	3.66E-02	7.16E-02
Brain Putamen basal ganglia	12	CS	56679829	rs4526799	57280586	T	C	0.34	7.26E-06	3.12E-02	6.55E-02
Brain Putamen basal ganglia	12	RP11-977G19.11	56701259	rs4526799	57280586	T	C	0.34	7.26E-06	3.55E-02	7.04E-02
Brain Putamen basal ganglia	12	IL23A	56733428	rs4526799	57280586	T	C	0.34	7.26E-06	1.97E-02	5.13E-02
Brain Putamen basal ganglia	12	NAB2	57485933	rs4526799	57280586	T	C	0.34	7.26E-06	7.23E-03	3.22E-02
Brain Putamen basal ganglia	12	INHBE	57849584	rs4526799	57280586	T	C	0.34	7.26E-06	3.79E-02	7.31E-02
Brain Putamen basal ganglia	12	AVIL	58201929	rs4526799	57280586	T	C	0.34	7.26E-06	2.01E-02	5.18E-02
Brain Spinal cord cervical c-1	12	ESYT1	56530147	rs4526799	57280586	T	C	0.34	7.26E-06	4.85E-02	8.46E-02
Brain Spinal cord cervical c-1	12	TAC3	57413225	rs4526799	57280586	T	C	0.34	7.26E-06	3.04E-02	6.46E-02
Brain Substantia nigra	12	RP11-603J24.7	56374517	rs4526799	57280586	T	C	0.34	7.26E-06	3.56E-02	7.06E-02
Brain Substantia nigra	12	MYL6	56554355	rs4526799	57280586	T	C	0.34	7.26E-06	3.69E-02	7.20E-02
Brain Substantia nigra	12	RP11-153M3.1	56905636	rs4526799	57280586	T	C	0.34	7.26E-06	4.31E-02	7.88E-02
Brain Substantia nigra	12	CYP27B1	58158578	rs4526799	57280586	T	C	0.34	7.26E-06	4.56E-02	8.15E-02
Whole Blood	12	RP11-977G19.11	56701259	rs4526799	57280586	T	C	0.34	7.26E-06	1.21E-02	4.04E-02
Whole Blood	12	STAT2	56744645	rs4526799	57280586	T	C	0.34	7.26E-06	3.25E-02	6.69E-02
Whole Blood	12	GLS2	56873481	rs4526799	57280586	T	C	0.34	7.26E-06	1.06E-02	3.80E-02
Whole Blood	12	NAB2	57485933	rs4526799	57280586	T	C	0.34	7.26E-06	7.08E-03	3.19E-02
Whole Blood	12	KIF5A	57962098	rs4526799	57280586	T	C	0.34	7.26E-06	5.09E-03	2.79E-02
Whole Blood	12	RP11-571M6.8	58118261	rs4526799	57280586	T	C	0.34	7.26E-06	4.56E-02	8.15E-02
Whole Blood	12	AGAP2	58127694	rs4526799	57280586	T	C	0.34	7.26E-06	1.48E-02	4.45E-02
Brain Amygdala	1	MED28P8	82023161	rs17105538	81315043	G	A	0.15	7.66E-06	2.23E-02	4.19E-02
Brain Hippocampus	1	LPHN2	82114982	rs17105538	81315043	G	A	0.15	7.66E-06	1.48E-02	3.23E-02
Brain Substantia nigra	1	LPHN2	82114982	rs17105538	81315043	G	A	0.15	7.66E-06	3.79E-02	5.98E-02
Brain Amygdala	2	RNASEH1	3599232	rs62121100	3093952	G	T	0.18	8.44E-06	1.76E-02	4.34E-02
Brain Cerebellar Hemisphere	2	RNASEH1	3599232	rs62121100	3093952	G	T	0.18	8.44E-06	4.98E-02	8.07E-02
Brain Cerebellar Hemisphere	2	ALLC	3727979	rs62121100	3093952	G	T	0.18	8.44E-06	4.90E-02	7.98E-02
Brain Cerebellum	2	RP11-1293J14.1	3500929	rs62121100	3093952	G	T	0.18	8.44E-06	8.66E-03	3.03E-02
Brain Cortex	2	TSSC1	3287174	rs62121100	3093952	G	T	0.18	8.44E-06	3.99E-02	7.00E-02
Brain Cortex	2	RPS7	3625652	rs62121100	3093952	G	T	0.18	8.44E-06	7.25E-03	2.78E-02
Brain Frontal Cortex BA9	2	TRAPPC12	3436155	rs62121100	3093952	G	T	0.18	8.44E-06	2.53E-02	5.32E-02
Brain Hippocampus	2	MYT1L	2063958	rs62121100	3093952	G	T	0.18	8.44E-06	3.86E-02	6.86E-02
Brain Hippocampus	2	RP11-1293J14.1	3500929	rs62121100	3093952	G	T	0.18	8.44E-06	1.11E-02	3.42E-02
Brain Nucleus accumbens basal ganglia	2	TSSC1-IT1	3303674	rs62121100	3093952	G	T	0.18	8.44E-06	1.98E-02	4.64E-02
Brain Nucleus accumbens basal ganglia	2	RP11-1293J14.1	3500929	rs62121100	3093952	G	T	0.18	8.44E-06	4.22E-02	7.26E-02
Brain Nucleus accumbens basal ganglia	2	AC142528.1	3525007	rs62121100	3093952	G	T	0.18	8.44E-06	3.56E-02	6.53E-02
Brain Spinal cord cervical c-1	2	AC142528.1	3525007	rs62121100	3093952	G	T	0.18	8.44E-06	3.75E-02	6.74E-02
Brain Substantia nigra	2	TMSB4XP2	3665242	rs62121100	3093952	G	T	0.18	8.44E-06	2.51E-02	5.30E-02

Brain Amygdala	2	<i>NOL10</i>	10770496	rs1809136	11152180	C	G	0.93	9.99E-06	1.71E-02	3.85E-02
Brain Amygdala	2	<i>RP11-791G15.2</i>	10909092	rs1809136	11152180	C	G	0.93	9.99E-06	2.43E-02	4.75E-02
Brain Amygdala	2	<i>PDIA6</i>	10952755	rs1809136	11152180	C	G	0.93	9.99E-06	4.29E-02	6.86E-02
Brain Amygdala	2	<i>E2F6</i>	11595399	rs1809136	11152180	C	G	0.93	9.99E-06	6.29E-04	8.21E-03
Brain Amygdala	2	<i>GREB1</i>	11728578	rs1809136	11152180	C	G	0.93	9.99E-06	1.31E-02	3.31E-02
Brain Caudate basal ganglia	2	<i>RN7SL832P</i>	10831347	rs1809136	11152180	C	G	0.93	9.99E-06	1.66E-02	3.78E-02
Brain Cerebellar Hemisphere	2	<i>RP11-254F7.2</i>	10180004	rs1809136	11152180	C	G	0.93	9.99E-06	3.36E-03	1.65E-02
Brain Cerebellar Hemisphere	2	<i>C2orf50</i>	11280047	rs1809136	11152180	C	G	0.93	9.99E-06	1.71E-02	3.85E-02
Brain Cortex	2	<i>AC007249.3</i>	10594061	rs1809136	11152180	C	G	0.93	9.99E-06	3.75E-02	6.27E-02
Brain Cortex	2	<i>ROCK2</i>	11404171	rs1809136	11152180	C	G	0.93	9.99E-06	8.31E-03	2.58E-02
Brain Frontal Cortex BA9	2	<i>ATP6V1C2</i>	10893505	rs1809136	11152180	C	G	0.93	9.99E-06	1.64E-02	3.75E-02
Brain Hippocampus	2	<i>CYS1</i>	10208989	rs1809136	11152180	C	G	0.93	9.99E-06	2.82E-02	5.21E-02
Brain Hippocampus	2	<i>ROCK2</i>	11404171	rs1809136	11152180	C	G	0.93	9.99E-06	3.30E-02	5.77E-02
Brain Hippocampus	2	<i>NTSR2</i>	11804297	rs1809136	11152180	C	G	0.93	9.99E-06	2.92E-03	1.54E-02
Brain Hypothalamus	2	<i>ATP6V1C2</i>	10893505	rs1809136	11152180	C	G	0.93	9.99E-06	4.93E-02	7.54E-02
Brain Putamen basal ganglia	2	<i>KCNF1</i>	11053206	rs1809136	11152180	C	G	0.93	9.99E-06	2.97E-02	5.39E-02
Brain Putamen basal ganglia	2	<i>NTSR2</i>	11804297	rs1809136	11152180	C	G	0.93	9.99E-06	1.50E-02	3.56E-02
Brain Spinal_cord_cervical_c-1	2	<i>RRM2</i>	10267000	rs1809136	11152180	C	G	0.93	9.99E-06	2.32E-02	4.62E-02
Brain Substantia nigra	2	<i>ATP6V1C2</i>	10893505	rs1809136	11152180	C	G	0.93	9.99E-06	2.13E-02	4.38E-02
Whole_Blood	2	<i>RP11-245G13.2</i>	11021819	rs1809136	11152180	C	G	0.93	9.99E-06	5.78E-03	2.14E-02

Supplementary Figures

Figure S1. Forest plots of betas (i.e., effect sizes) and 95% confidence interval for the association of the *APOE*/rs429358 SNP with PiB-PET

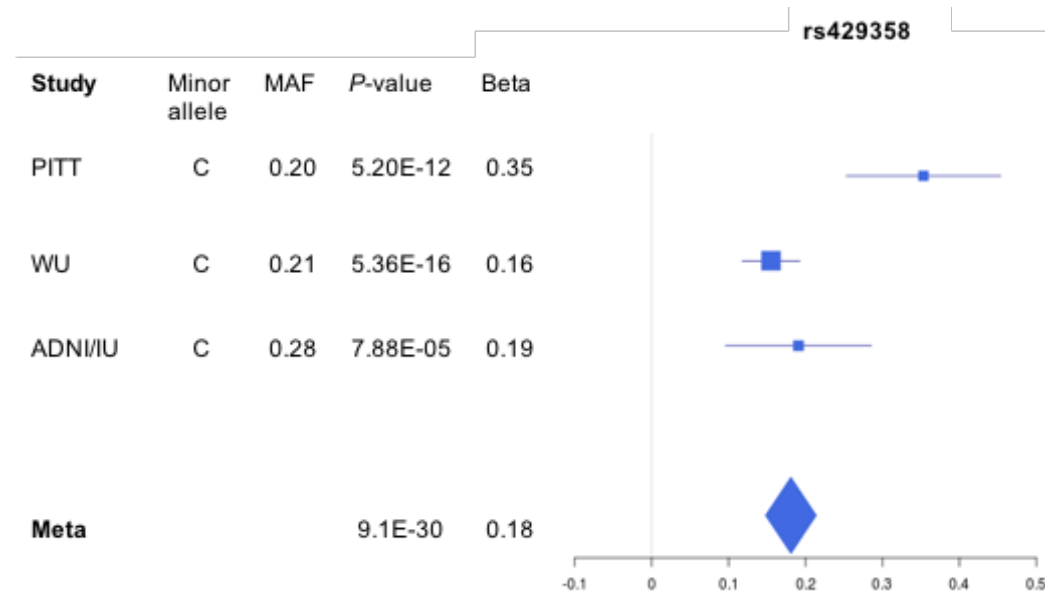


Figure S2. Regional plots of 15 non-*APOE* loci listed as S2a to S2o and they correspond to loci listed in Table 2.

Figure S2.1

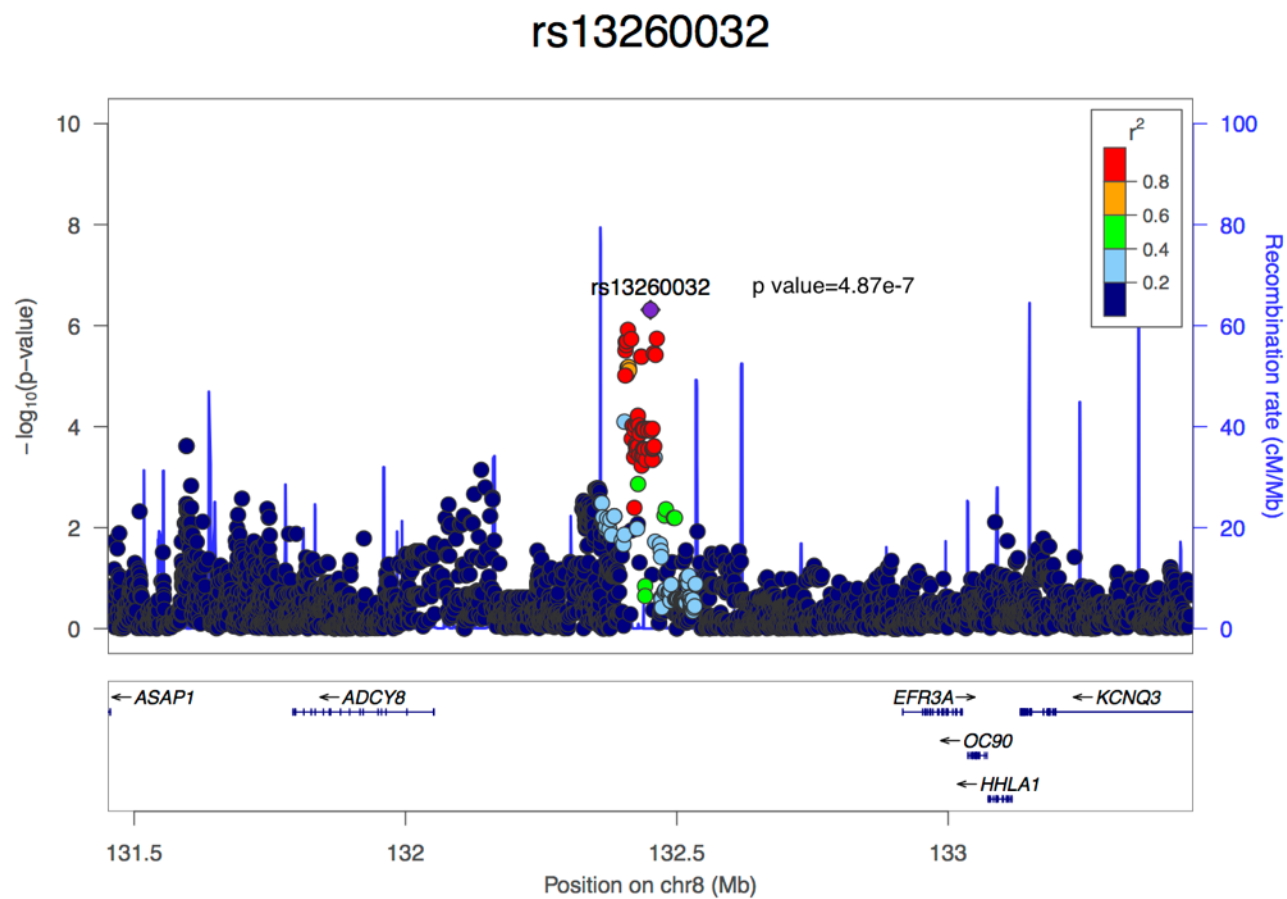


Figure S2.2

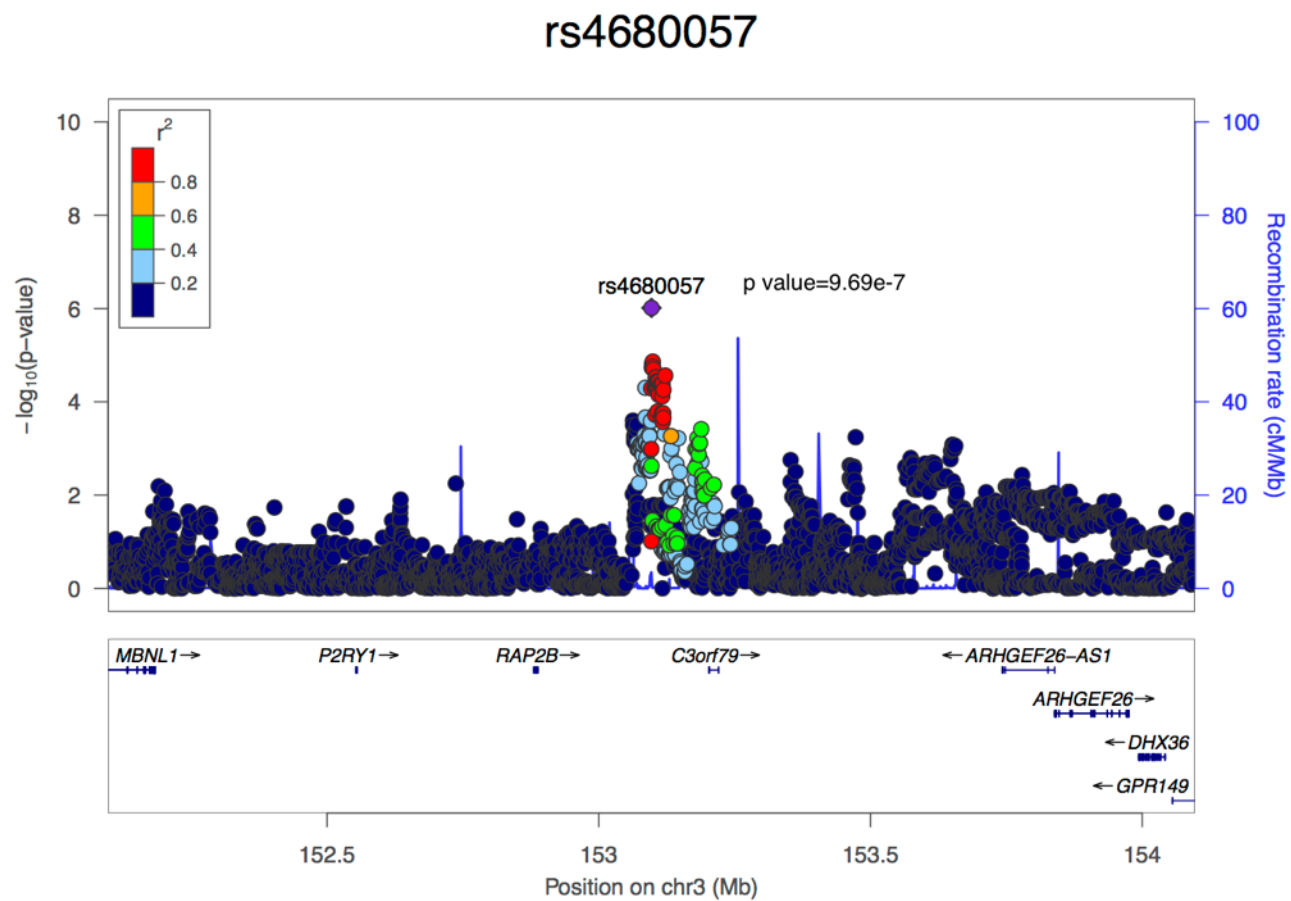


Figure S2.3

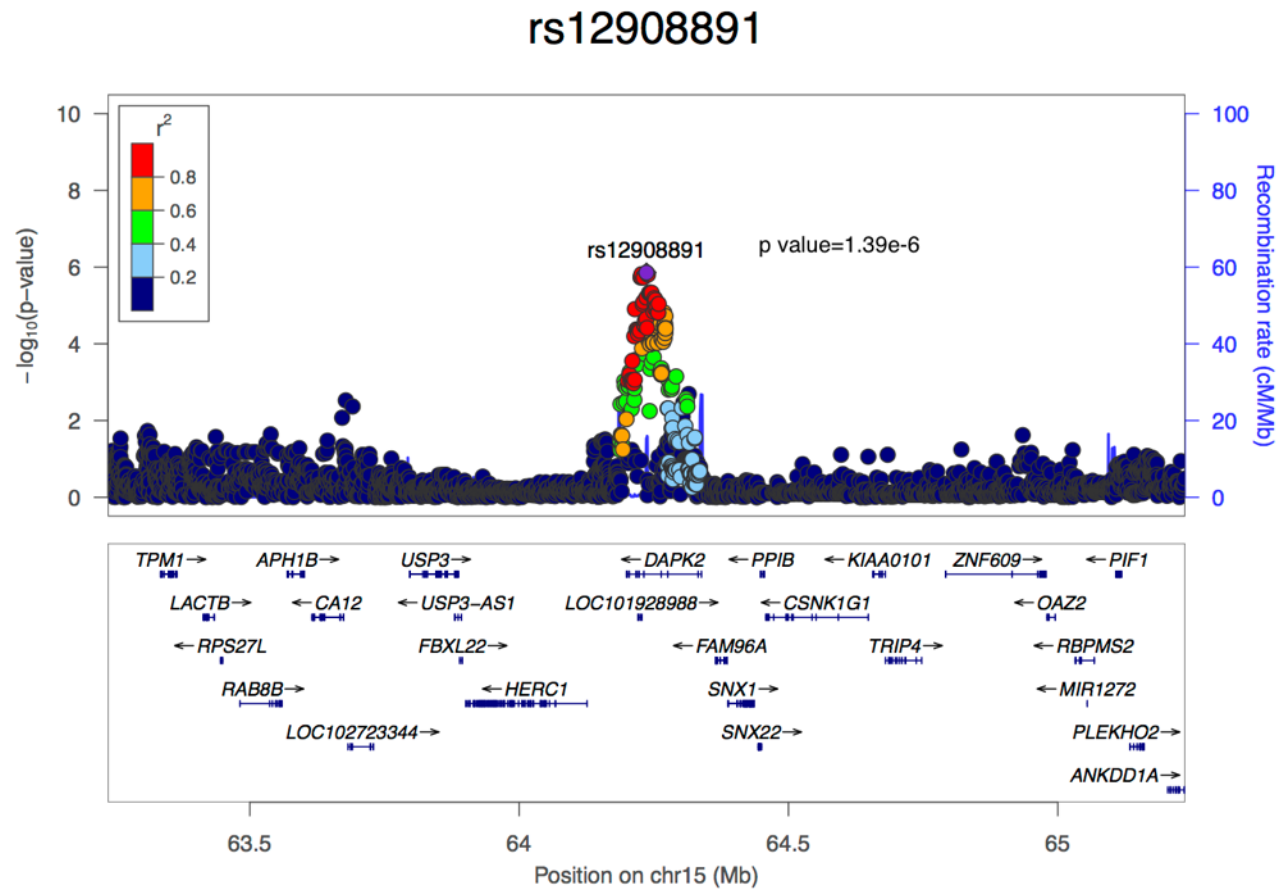


Figure S2.4

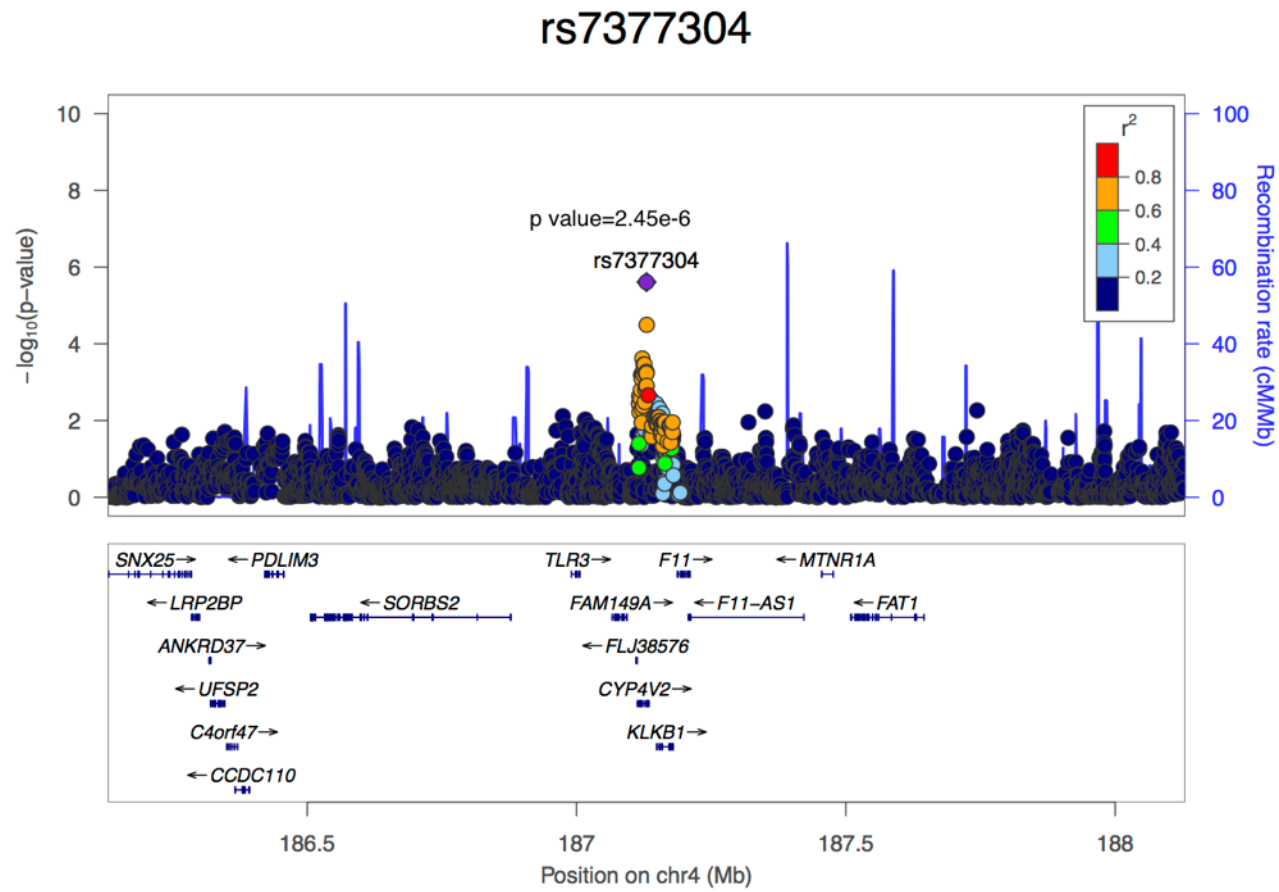


Figure S2.5

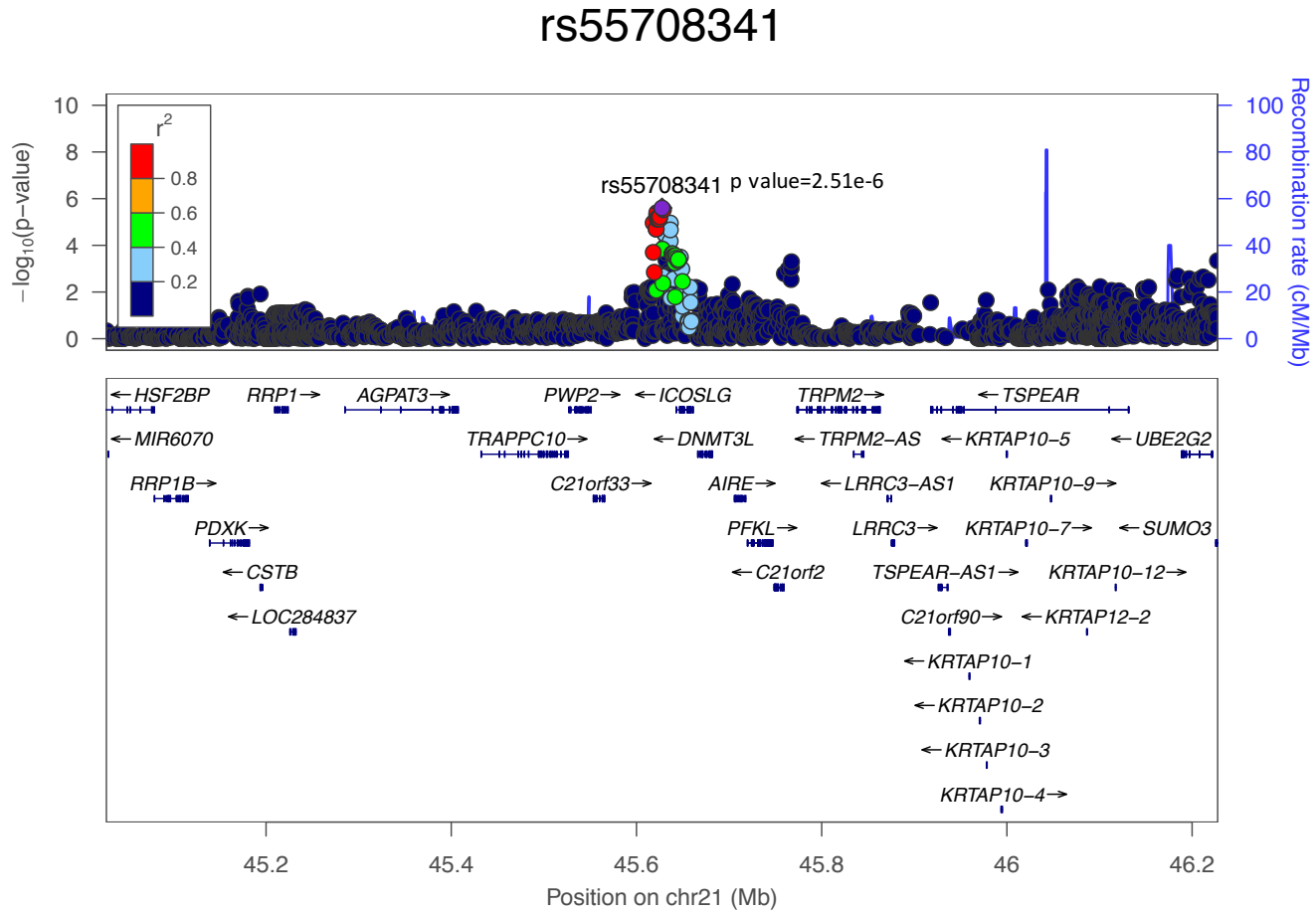


Figure S2.6

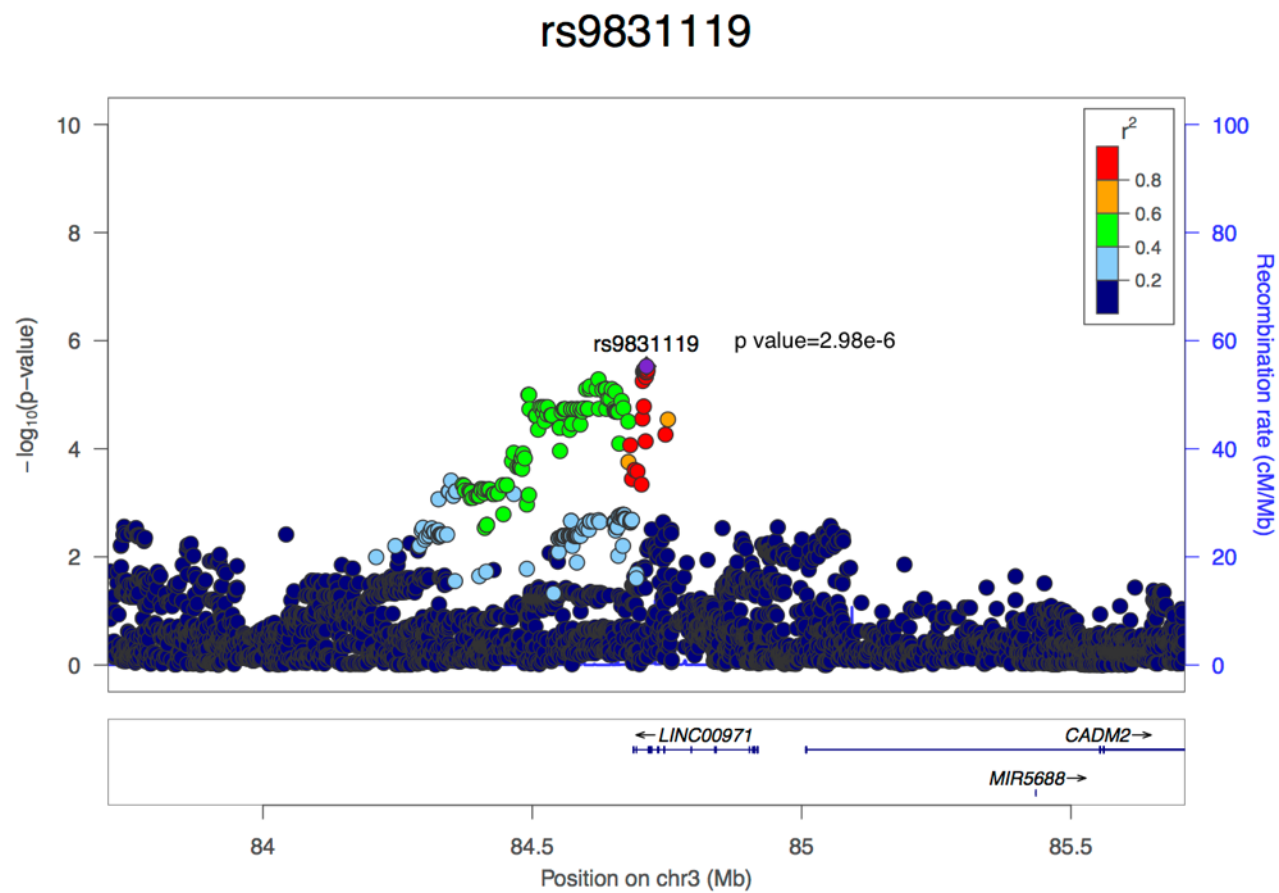


Figure S2.7

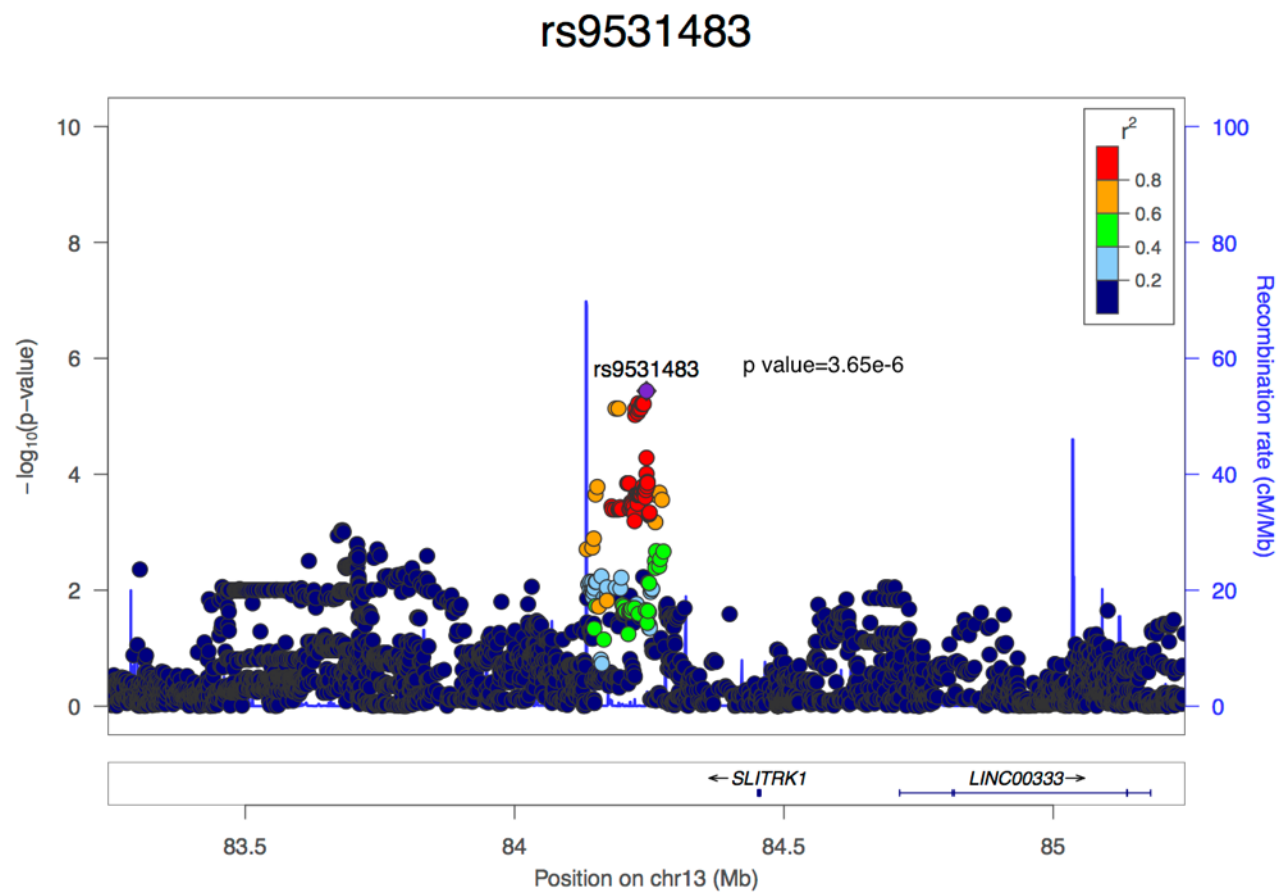


Figure S2.8

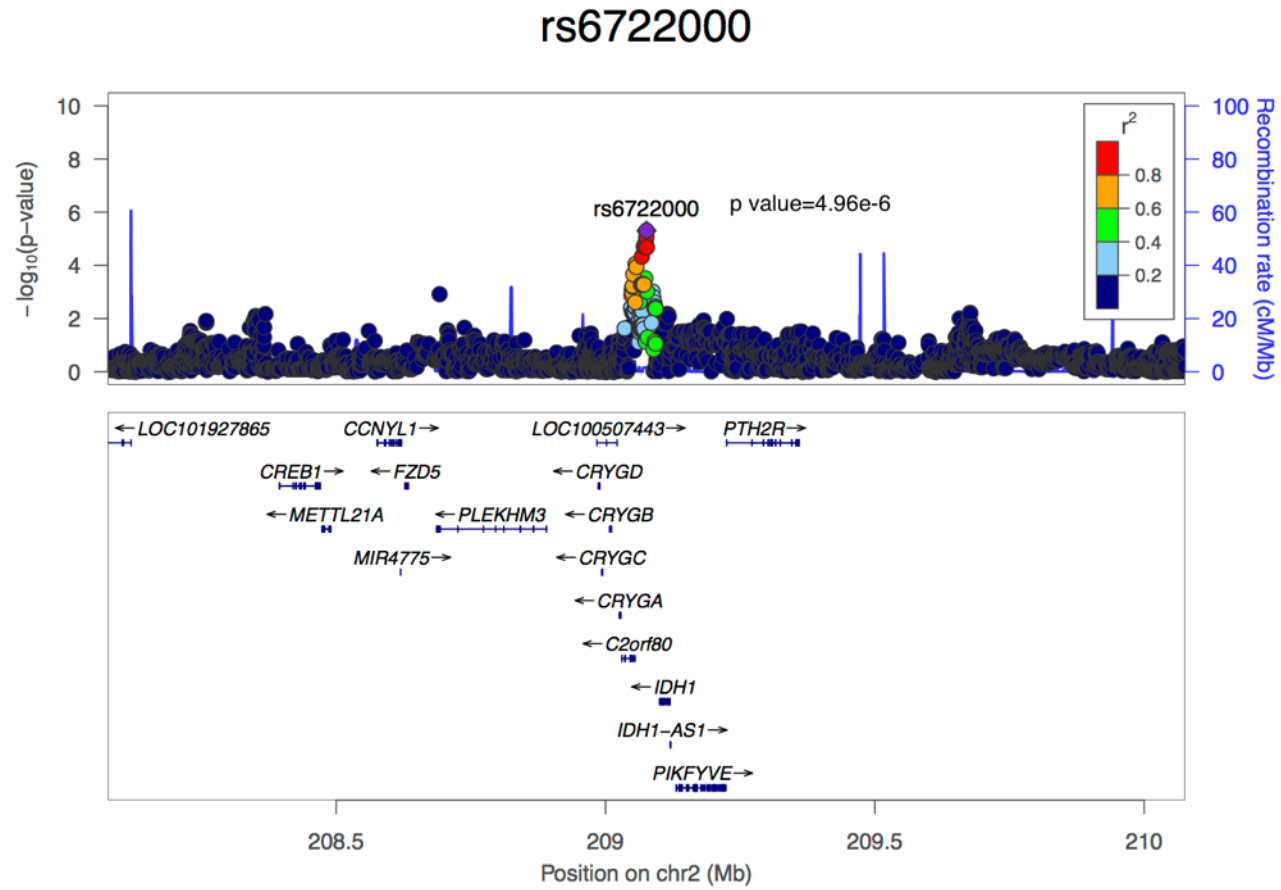


Figure S2.9

rs11923588

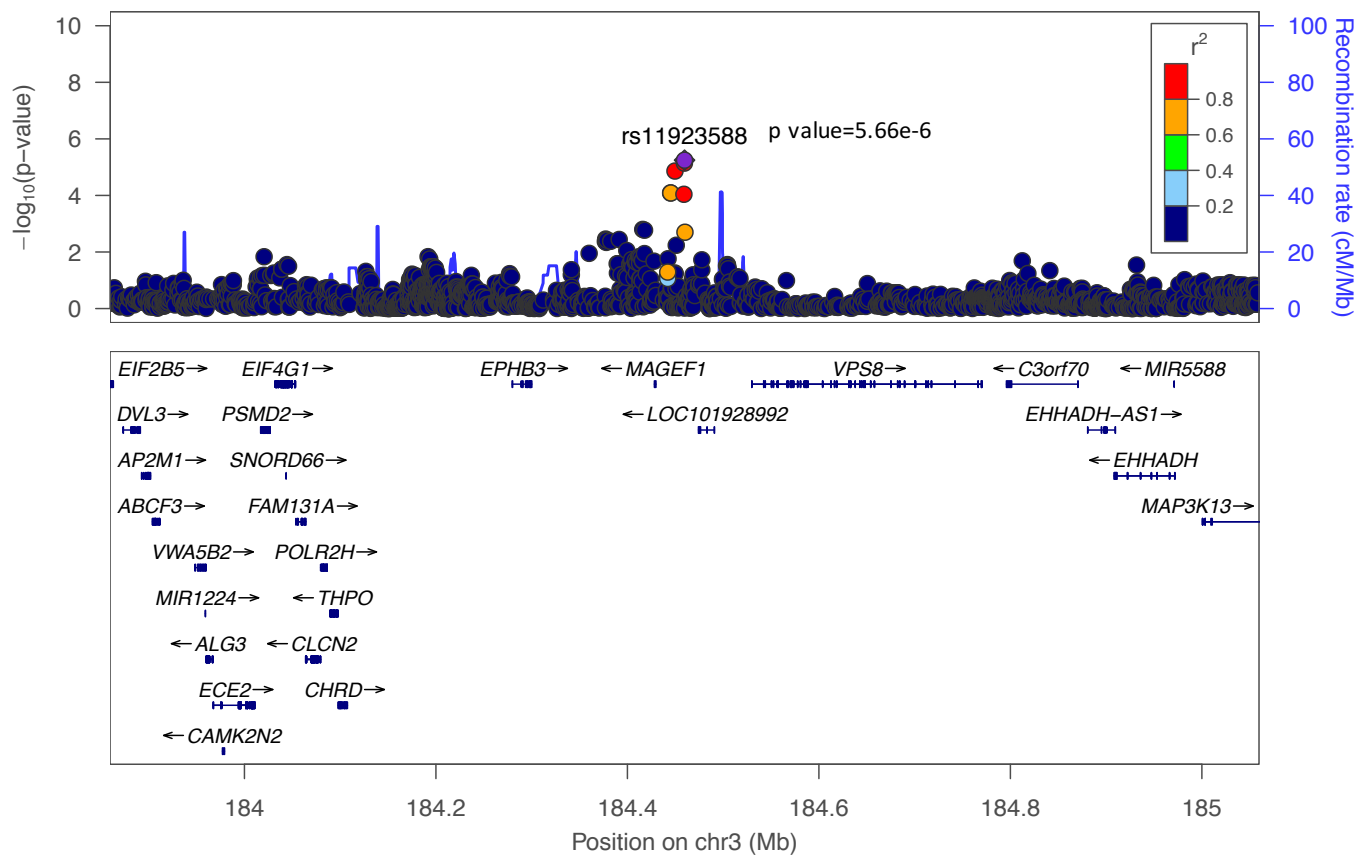


Figure S2.10

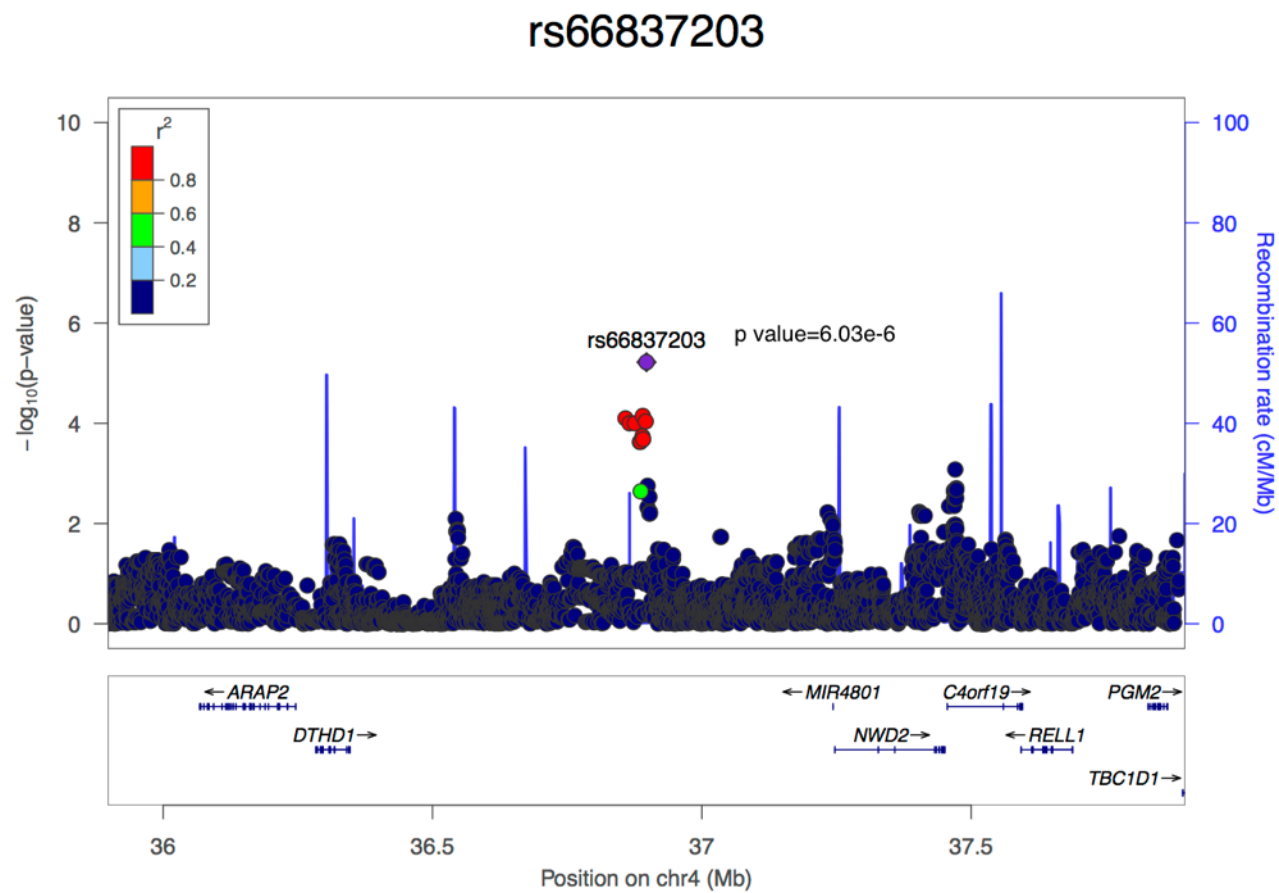


Figure S2.11

rs200028958

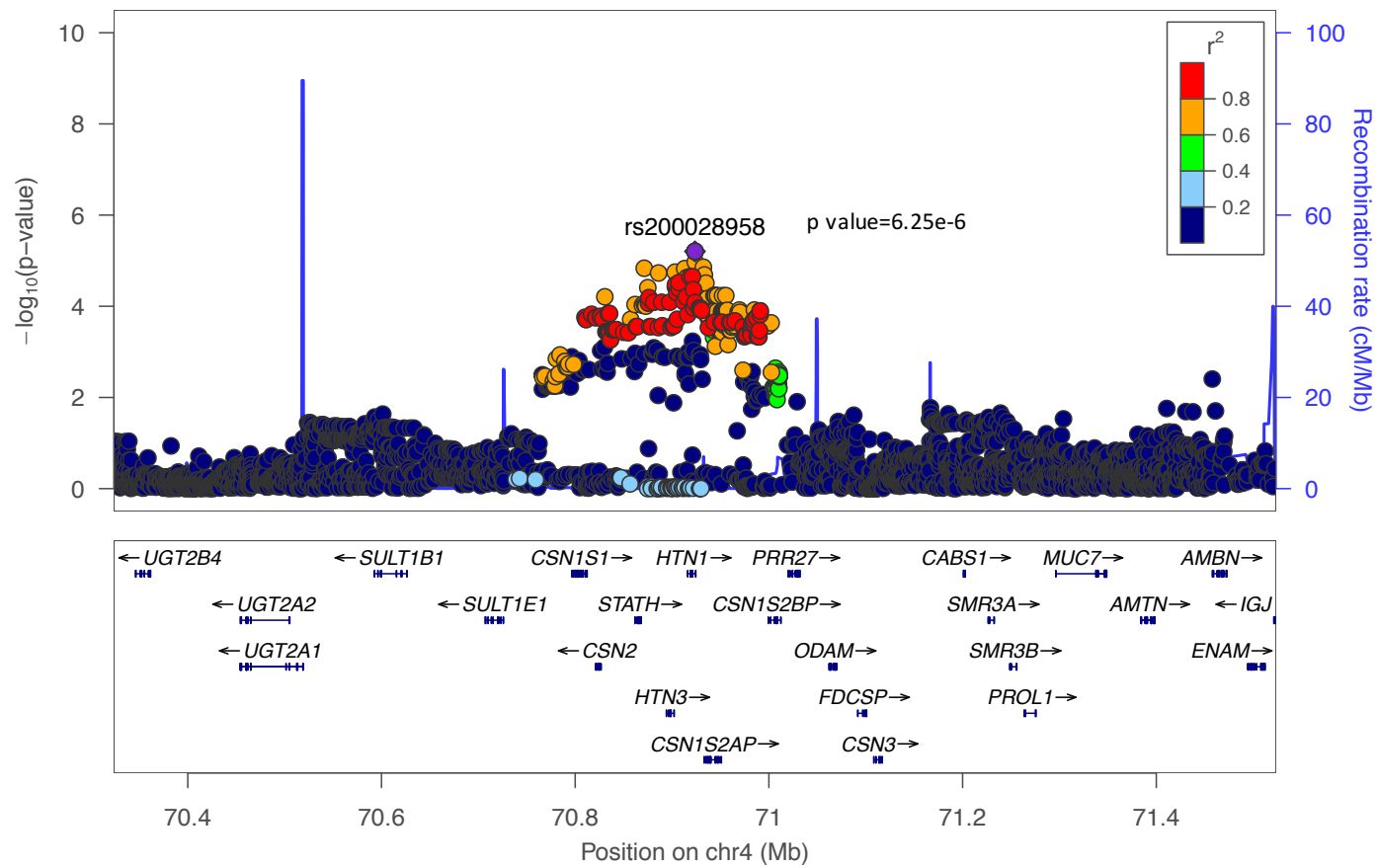


Figure S2.12

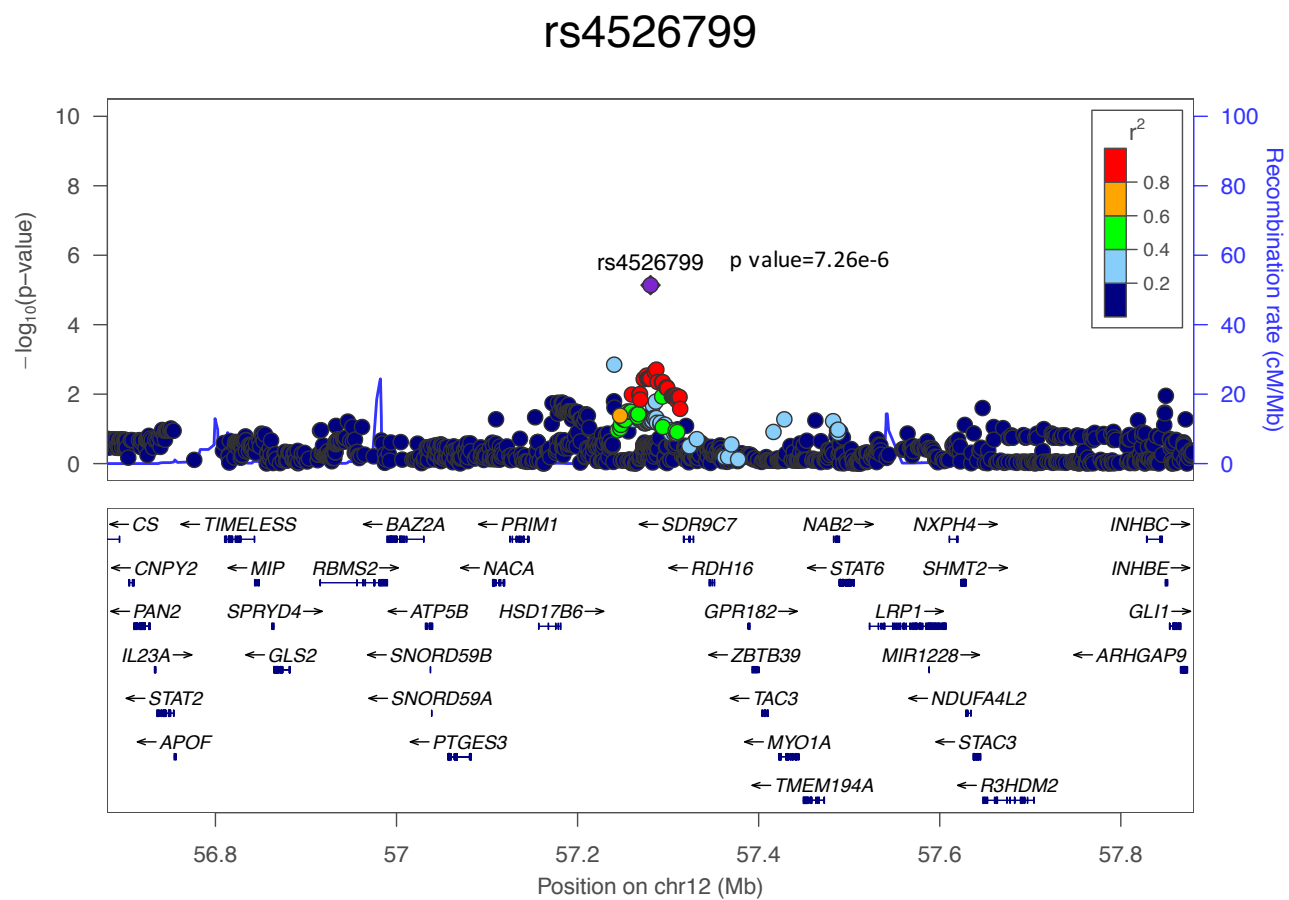


Figure S2.13

rs17105538

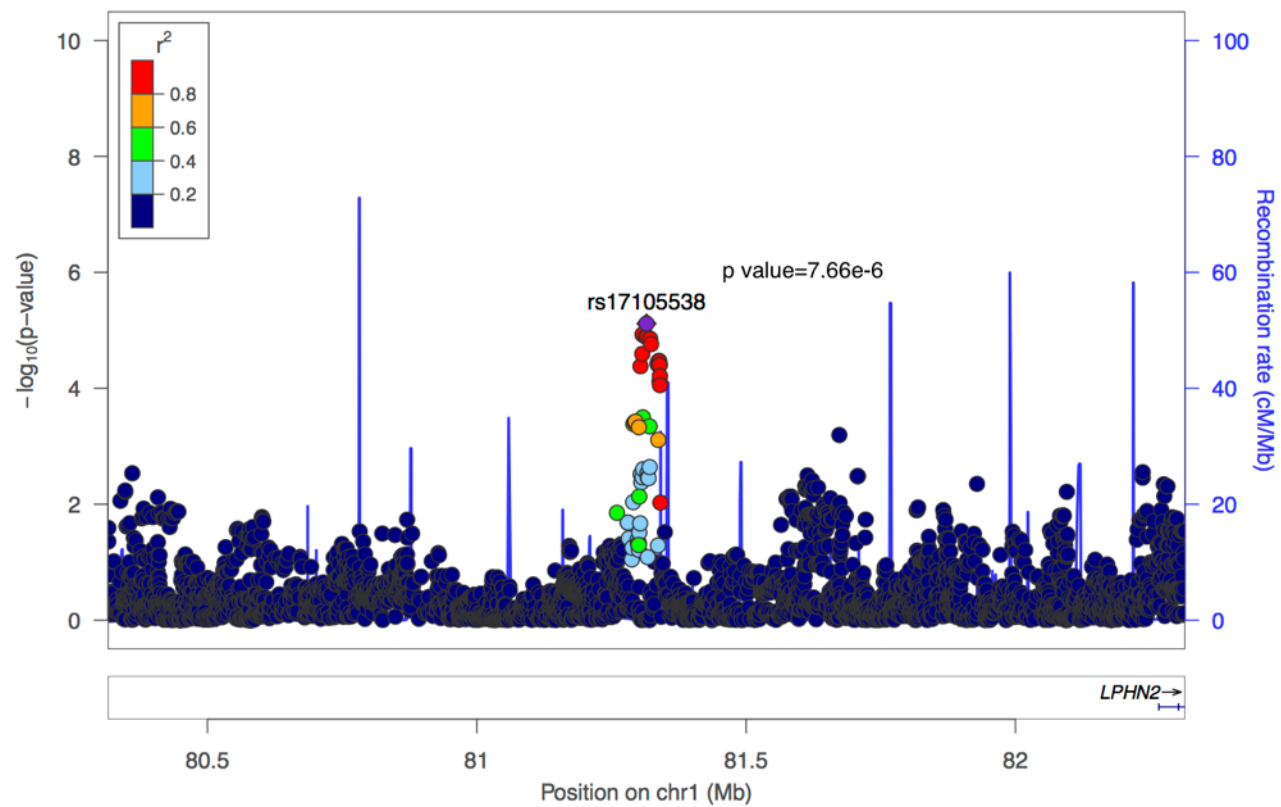


Figure S2.14

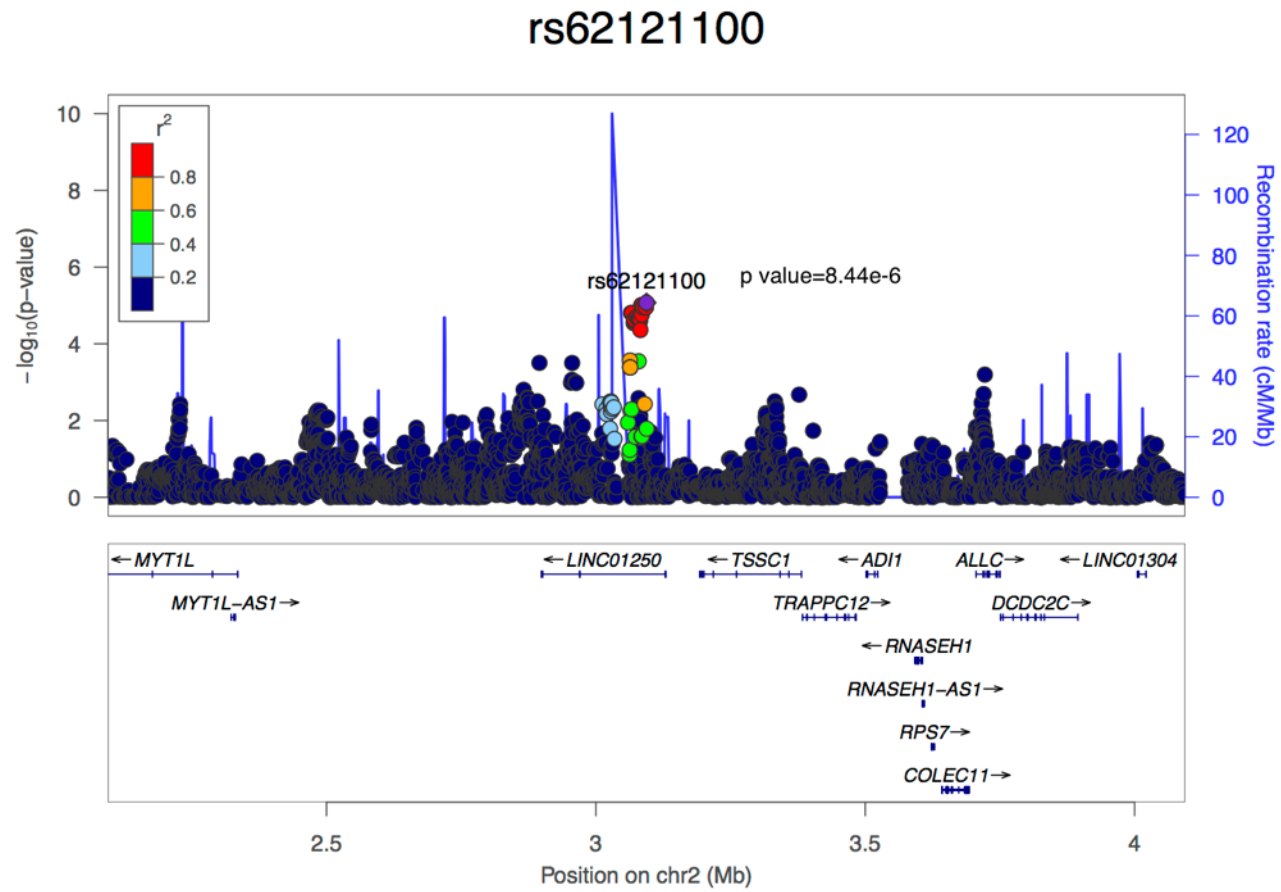
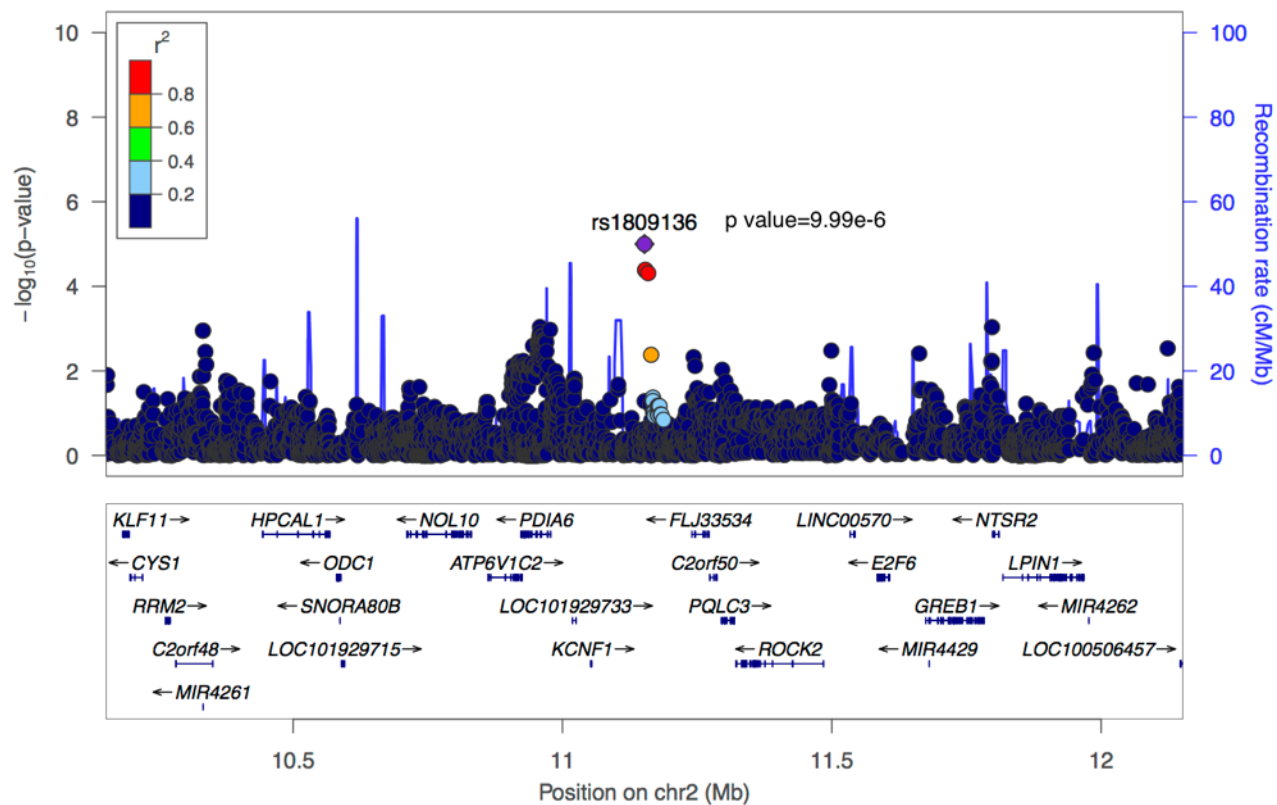


Figure S2.15

rs1809136



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Supplementary References

1. Mathis CA, Kuller LH, Klunk WE, Snitz BE, Price JC, Weissfeld LA *et al.* In vivo assessment of amyloid-beta deposition in nondemented very elderly subjects. *Ann Neurol* 2013; **73**(6): 751-761.
2. Nebes RD, Snitz BE, Cohen AD, Aizenstein HJ, Saxton JA, Halligan EM *et al.* Cognitive aging in persons with minimal amyloid-beta and white matter hyperintensities. *Neuropsychologia* 2013; **51**(11): 2202-2209.
3. Morris JC, Roe CM, Xiong C, Fagan AM, Goate AM, Holtzman DM *et al.* APOE predicts amyloid-beta but not tau Alzheimer pathology in cognitively normal aging. *Ann Neurol* 2010; **67**(1): 122-131.
4. Swaminathan S, Shen L, Risacher SL, Yoder KK, West JD, Kim S *et al.* Amyloid pathway-based candidate gene analysis of [(11)C]PiB-PET in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort. *Brain Imaging Behav* 2012; **6**(1): 1-15.
5. Saykin AJ, Shen L, Yao X, Kim S, Nho K, Risacher SL *et al.* Genetic studies of quantitative MCI and AD phenotypes in ADNI: Progress, opportunities, and plans. *Alzheimers Dement* 2015; **11**(7): 792-814.
6. Jagust WJ, Bandy D, Chen K, Foster NL, Landau SM, Mathis CA *et al.* The Alzheimer's Disease Neuroimaging Initiative positron emission tomography core. *Alzheimers Dement* 2010; **6**(3): 221-229.
7. Deters KD, Risacher SL, Yoder KK, Oblak AL, Unverzagt FW, Murrell JR *et al.* [(11)C]PiB PET in Gerstmann-Straussler-Scheinker disease. *Am J Nucl Med Mol Imaging* 2016; **6**(1): 84-93.
8. Howie BN, Donnelly P, Marchini J. A flexible and accurate genotype imputation method for the next generation of genome-wide association studies. *PLoS Genet* 2009; **5**(6): e1000529.
9. Genomes Project C, Abecasis GR, Altshuler D, Auton A, Brooks LD, Durbin RM *et al.* A map of human genome variation from population-scale sequencing. *Nature* 2010; **467**(7319): 1061-1073.

10. Price AL, Patterson NJ, Plenge RM, Weinblatt ME, Shadick NA, Reich D. Principal components analysis corrects for stratification in genome-wide association studies. *Nat Genet* 2006; **38**(8): 904-909.
11. Bai Z, Han G, Xie B, Wang J, Song F, Peng X *et al.* AlzBase: an Integrative Database for Gene Dysregulation in Alzheimer's Disease. *Mol Neurobiol* 2016; **53**(1): 310-319.
12. Zhang Y, Chen K, Sloan SA, Bennett ML, Scholze AR, O'Keefe S *et al.* An RNA-sequencing transcriptome and splicing database of glia, neurons, and vascular cells of the cerebral cortex. *J Neurosci* 2014; **34**(36): 11929-11947.
13. Zhang Y, Sloan SA, Clarke LE, Caneda C, Plaza CA, Blumenthal PD *et al.* Purification and Characterization of Progenitor and Mature Human Astrocytes Reveals Transcriptional and Functional Differences with Mouse. *Neuron* 2016; **89**(1): 37-53.
14. Consortium GT. The Genotype-Tissue Expression (GTEx) project. *Nat Genet* 2013; **45**(6): 580-585.
15. Zhu Z, Zhang F, Hu H, Bakshi A, Robinson MR, Powell JE *et al.* Integration of summary data from GWAS and eQTL studies predicts complex trait gene targets. *Nat Genet* 2016; **48**(5): 481-487.
16. de Leeuw CA, Mooij JM, Heskes T, Posthuma D. MAGMA: generalized gene-set analysis of GWAS data. *PLoS Comput Biol* 2015; **11**(4): e1004219.
17. Ashburner M, Ball CA, Blake JA, Botstein D, Butler H, Cherry JM *et al.* Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. *Nat Genet* 2000; **25**(1): 25-29.
18. Gene Ontology C. Gene Ontology Consortium: going forward. *Nucleic Acids Res* 2015; **43**(Database issue): D1049-1056.
19. Kanehisa M, Sato Y, Kawashima M, Furumichi M, Tanabe M. KEGG as a reference resource for gene and protein annotation. *Nucleic Acids Res* 2016; **44**(D1): D457-462.
20. Ogata H, Goto S, Sato K, Fujibuchi W, Bono H, Kanehisa M. KEGG: Kyoto Encyclopedia of Genes and Genomes. *Nucleic Acids Res* 1999; **27**(1): 29-34.
21. Fabregat A, Sidiropoulos K, Garapati P, Gillespie M, Hausmann K, Haw R *et al.* The Reactome pathway Knowledgebase. *Nucleic Acids Res* 2016; **44**(D1): D481-487.

22. Croft D, O'Kelly G, Wu G, Haw R, Gillespie M, Matthews L *et al.* Reactome: a database of reactions, pathways and biological processes. *Nucleic Acids Res* 2011; **39**(Database issue): D691-697.
23. Kamboh MI, Demirci FY, Wang X, Minster RL, Carrasquillo MM, Pankratz VS *et al.* Genome-wide association study of Alzheimer's disease. *Transl Psychiatry* 2012; **2**: e117.