Online supplement to Ming Li, Xiong-jian Luo, *et al*. Impact of a *cis*-associated gene expression SNP on chromosome 20q11.22 on bipolar disorder susceptibility, hippocampal structure and cognitive performance. Br J Psychiatry doi: 10.1192/bjp.bp.114.156976

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Description about discovery eQTL database

The brain eQTL dataset used in this study was reported previously.[1] In brief, human cortex samples were collected from the National Institute of Aging Alzheimer Centers and the Miami Brain Bank and the original subjects met several criteria: (a) self-defined as being ethnically of European descent; (b) had no clinical history of stroke, cerebrovascular disease, Lewy bodies or co-morbidity with neurological disease; (c) were assessed by board certified neurologists who made a determination on their condition; and (d) had an age at death greater than 65 years. After excluding ethnic outliers and samples that were possibly related, a total of 193 independent subjects' samples remained for subsequent analysis.

Genotyping of the 193 cortex samples was conducted using Affymetrix GeneChip Human Mapping 500K Array Set, and mRNA expression measurements were performed using Illumina HumanRefseq-8 Expression BeadChip using standard manufacturer's protocols. The PLINK program was used to carry out as a one-degree-of-freedom allelic test of association, and the associations results were further separated into *cis* and *trans* significantly associated SNP-transcript pair sets. *Cis* SNPs were defined as SNPs within either 1 Mb of the 5' or 3' end of the transcript and within the transcript. Sherlock considers both *cis* and *trans* eQTL SNPs. Detailed information about genotyping and expression profiling as well as statistical methods can be found in the original publication.[1]

Description about non-brain tissue replication eQTL databases

The non-brain tissue eQTL databases were retrieved through Genevar,[2] which have ever been reported by Nica *et al*,[3] Dimas *et al*,[4] and Stranger *et al*[5] In brief, Nica *et al* explored in depth the roles of genetic variation on gene expression in three human tissues: lymphoblastoid cell lines (LCL), skin, and adipose, and the samples (156 LCL, 160 skin, 166 adipose) derived simultaneously from a subset of healthy female twins of the MuTHER resource;[3] Dimas *et al* conducted the genome-wide expression analysis in three types of cells (fibroblast, LCL and T-cell) from 75 Geneva GenCord Caucasian individuals;[4] Stranger *et al* analyzed genome-wide gene expression in LCL from 8 global populations of the HapMap3 project and correlated gene expression levels with HapMap3 SNPs located in cis to the genes. We used the data from the Caucasian samples (N=109) reported by Stranger *et al*[5] In these three datasets, all the statistical analysis between SNPs and gene expression were conducted using Spearman's correlation.

Replication-I sample information (see Table DS1)

Germany II and III sample

Cases for Germany II and III samples were again ascertained from consecutive admissions to the inpatient units of the Department of Psychiatry and Psychotherapy at the University of Bonn and at the Central Institute for Mental Health in Mannheim, University of Heidelberg, as well as at other collaborating psychiatric university hospitals in Germany. DSM-IV lifetime diagnoses of bipolar disorder were assigned using a consensus best-estimate procedure, based on all available information, including structured interviews (SCID-I, SADS-L; Germany III) or semi-structured interviews (AMDP; Germany II), medical records, and the family history method. In addition, the OPCRIT system was used for the detailed polydiagnostic documentation of symptoms.[6]

Controls for Germany II were ascertained from the population-based Heinz Nixdorf Recall Study.[7] Study protocols were reviewed and approved in advance by Institutional Review Boards of the participating institutions. All subjects provided written informed consent. This includes a clause that all data may be shared with collaborating partners such as the PGC. However, consents do not include permission for depositing of de-identified individual GWAS genotype and phenotype data into the NIMH genetics initiative repository, although these data may be used in specific collaborations for studies of neuropsychiatric disorders. All subjects were genotyped using the Illumina platform.

The controls for Germany III were recruited at the Max Planck Institute of Psychiatry in Munich, Germany, and were selected randomly from a Munich-based community sample. They were collected in the course of genetic studies of major depression, and were therefore screened for the presence of anxiety and affective disorders using the Composite International Diagnostic Screener (WHO-CIDI). Only individuals negative for the above-named disorders were included in the sample. All included controls were Caucasian, 93.04% were of German origin. These subjects thus represent a group of healthy individuals with regard to depression and anxiety. The study was approved by the ethics committee of the Ludwig Maximilians University in Munich, Germany, and written informed consent was obtained from all subjects.

Australia sample

Subjects were ascertained through two studies: (a) a bipolar disorder pedigree sample (described in McAuley *et al*)[8] and (b) a specialized Sydney Black Dog Institute bipolar disorder clinic sample (described in Mitchell *et al* 2009).[9] All subjects were interviewed by trained research staff using the DIGS or SCID, using best-estimate DSM-IV diagnoses derived from those instruments, medical records and FIGS. First, for the pedigree sample, only one bipolar disorder subject per family was included in the case sample. Pedigrees were only included in the original genetic study if there was unilineal inheritance, and at least two bipolar disorder subjects including at least one with bipolar I disorder. Subjects were ascertained through clinical presentations to the Mood Disorders Unit at the Prince of Wales Hospital in Sydney, direct referrals from Australian clinicians, and bipolar disorder consumer organizations. Second, for

the clinic sample, subjects comprised consecutive subjects referred by psychiatrists or general practitioners for specialized clinical review. All patients provided written informed consent to participate in this study and the study was approved by the local ethics committee. Patients were included in the BOMA study and genotyped at the Life & Brain Centre in Bonn.

Australia controls were drawn from families participating in the Brisbane Longitudinal Twin Study, an unselected community sample recruited to take part in studies of melanoma risk factors, cognition, and other phenotypes. Subjects were not screened for any phenotype relevant to bipolar disorder. The study was approved by the ethic committee and all proband gave written informed consent. All subjects were genotyped as a single project by deCODE and have been through an extensive QC process including exclusion for non-European ancestry. The sample is overwhelmingly of northern European origin, predominately from the British Isles.

France sample

Patients with bipolar disorder and controls were recruited as part of a large study on genetics of bipolar disorder in France (Paris-Creteil, Bordeaux, Nancy) with a protocol approved by relevant IRBs and with written informed consent. Cases were of French descent for more than three generations and were all been assessed by a well-trained psychiatrist or psychologist with the DIGS[10] and the FIGS. Diagnoses were based on structured interviews supplemented by medical case notes, mood scales and a self-rating questionnaire assessing dimensions. Genotyping of controls were provided by the Centre National de Génotypage (M Lathrop, Evry). Patients and controls were genotyped on the Illumina platform (HumanHap300, HumanHap550, HumanHap 610-quad).

Sweden I sample

SBP Bipolar cases were recruited from St. Göran's Hospital in Stockholm, Sweden. All participants provided written informed consent to participate in a genetic study of bipolar disorder, and the study was approved by the Regional Ethics Committee of Stockholm. Diagnoses were based on physician administered ADE[11] and MINI.[12]

Bipolar disorder cases were identified from the Swedish Bipolar Quality Assurance Registry. Patient information within the registry includes disease sub-classification, psychosis, age at onset, number of manic and depressive episodes, number of hospitalizations and family history. Participants provided written informed consent to participate in a genetic study of psychiatric disease, and the study was approved by the Regional Ethics Committee of Stockholm.

Hospital Discharge Registry (HDR) bipolar cases were identified from the Swedish Hospital Discharge Registry if they a) have at least two admissions with discharge diagnoses of bipolar disorder and b) were born in Sweden or another Nordic country. The register contains a nearly complete record of all individuals hospitalized in Sweden since 1973. Diagnoses were established by an attending physician and were shown to have high sensitivity and specificity.[13] The study was approved by the Regional Ethics Committee of Stockholm. All participants provided written informed consent to participate in genetic studies of psychotic disorders and were interviewed by a research nurse about other medical conditions.

The SBP bipolar disorder cases were recruited from the Stockholm County catchment area. All patients provided written informed consent to participate in a genetic study of bipolar disorder, and the study was approved by the Regional Ethics Committee of Stockholm. Diagnoses were made according to the DSM-IV criteria.

Sweden control samples were obtained from the Swedish Hospital Discharge Registry on the condition they had never received discharge diagnoses of bipolar disorder, schizophrenia and/or schizoaffective disorder.

Sweden II sample

This sample consisted of 1415 patients with bipolar disorder (62.5% female, age ± s.d. = 53 ± 14, bipolar disorder type I =578, bipolar disorder type II= 517, NOS=281, SAB = 39, unknown subtype = 4), and 1271healthy controls (50.3% female, age ± s.d.= 59 ± 11 years). All subjects were unrelated to each other and ethnically Swedish. Patients with bipolar disorder were collected from the Swedish National Quality Assurance Registry for bipolar disorder (BipoläR), to which all patients with a DSM-IV diagnosis of bipolar I, II, NOS, or schizoaffective disorder are considered for registration at the participating clinics.[14] There were no other inclusion or exclusion criteria. Diagnoses were made by the treating physician with longitudinal access to all available clinical information. Controls were also identified from national population registers, and had never received a discharge diagnosis of SCZ or bipolar disorder. Controls were contacted directly in a similar procedure as the cases, gave written informed consent, were interviewed about other medical conditions and visited their family doctor or local hospital laboratory for blood donation. Patients and controls were genotyped on the Illumina Omni Express array, and the genomic inflation factor (lambda) is 1.03.

Iceland sample

The Iceland sample consisted of 541 subjects with bipolar disorder and 34,546 population controls. Patients and controls were Icelandic and were recruited throughout the country. Diagnoses were assigned according to RDC through the use of the SADS-L for 303 subjects. DSM-IV BD diagnoses were obtained through the use of the Composite International Diagnostic Interview (CIDI-Auto) for 82 subjects. In addition, there were 150 subjects with ICD-9 or ICD-10 bipolar disorder diagnoses and nine subjects with DSM-III bipolar disorder diagnoses.

The 34,546 controls were recruited as a part of various genetic programs at deCODE and were not screened for psychiatric disorders. Approval for the study was granted by the National Bioethics Committee of Iceland and the Icelandic Data Protection Authority and written informed consent was obtained for all participants.

Romania sample

All patients were recruited from consecutive hospital admissions and were directly interviewed with the Structured Clinical Interview for DSM-IV-TR-Axis I Disorders - Patient Version (SCID-I, 1994) and the Diagnostic Interview for Genetic Studies (DIGS) version 3.0 (1999). Information provided by medical records and interviews of family members was also used in a best estimate procedure of diagnosis on the basis of DSM-IV-TR criteria. The control sample was population-based, drawn from the same population as the patients, and was screened for major psychiatric disorders. The

ethnicity of the patients and control subjects was determined by genealogical investigation to the grandparental generation. Only the patient sample was previously reported in other collaborative studies.[15-17] The 174 controls were genotyped on Illumina OMNI-Express chips in Bonn, and the patients were also genotyped on Illumina chips (partly on Quad Omni-1).

China sample

The patients who met DSM-IV criteria for bipolar disorder type 1or type 2 were recruited from the Division of Mood Disorders at Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine between November 2006 and October 2010. Each patient was independently interviewed and diagnosed by a consensus of at least two experienced psychiatrists. Diagnoses were further confirmed with an Extensive Clinical Interview and a Structured Clinical Interview for DSM-IV Axis/Disorders, Patient Version (SCID-P) given by a research psychiatrist. Subjects with comorbid diagnosis of other psychiatric disorders or chronic physical illness were excluded in this study to mitigate the potential for compounding factors during our analysis. The Extensive Clinical Interview contains items to assess demographics, mental status, and ages at onset for the bipolar disorder patients. To avoid the biases due to the low reliability of retrospective evaluation of prodromal symptoms, we defined age at onset as the first reliably diagnosed hypo/manic or depressive episode according to DSM-IV criteria.

Control subjects were enrolled from hospital staff and students of the School of Medicine in Shanghai that were interviewed by a specialized psychiatrist with SCID-P. Subjects with any psychiatric disorder and chronic physical disease were excluded from our analysis. All subjects were of Han Chinese origin and provided written informed consent before any study-related procedures were performed. This sample has been reported in a previous study.[18]

Replication-II sample information (see Table DS1)

UK sample

The cases consisted of 1218 individuals of which 29% were male. The mean age of recruitment was 46 (s.d.=12) years, with a mean age at first impairment because of bipolar disorder of 22 (s.d.=9) years. A lifetime diagnosis was made according to Research Diagnostic Criteria and the 1218 individuals were categorized as follows: bipolar I disorder/mania: 63% cases, bipolar II disorder/hypomania: 29% cases, schizoaffective disorder, bipolar type: 8% cases. Of those individuals for whom we were able to make a definite rating, 65% of the cases had a lifetime experience of psychotic symptoms (defined as a score over 9 on the Bipolar Affective Disorder Dimension Scale (BADDS)) and 25% had a lifetime experience of predominantly mood-incongruent psychotic symptoms (defined as a score over 29 on the BADDS mood incongruence scale). There were 2913 controls in the independent sample, of which 47% were male. This sample has been reported in a previous study.[19]

Analysis of hippocampal volume and cognitive performance

To analyse hippocampal volume, we used the data from a recent large-scale GWAS conducted by the Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) consortium.[20] The GWAS comprised 17 samples of European ancestry of which genome-wide SNP data and hippocampal volume data were collected, including a total of 5,775 young healthy individuals (mean age: 34.8 years). Evidence for potential association was assessed using the allelic dosage of the SNP and covariates controlling for population stratification (four MDS components), intracranial volume, age, age^2, sex and the interactions between age and sex, and age^2 and sex. Detailed information on the samples, imaging procedures, genotyping methods and statistical analysis can be found in the original GWAS report.[20]

For cognitive analysis, we utilized a Chinese sample that included 342 healthy Chinese college students from Beijing Normal University who had self-reported no known history of any neurological or psychiatric disorders (197 females and 145 males, aged 18-23). Cognitive and behavioral measures included working memory, executive functions (as assessed with the Attention Network Test, the Wisconsin Card Sorting Task, and a reversal learning test), and motivation traits etc. Detailed cognitive functions examined in this study are listed in Table DS2. This cognitive sample was previously used in several studies and shown to be effective in detecting authentic risk effects.[21-23] Genotyping was performed by Affymetrix 6.0 array using standard protocols. Since homozygotes for the rs6088662 minor allele (GG) are rare in this sample, we combined GG and GA genotypes as a single group denoted 'G carrier', and statistical analysis using two-tailed t-test was done with SPSS 16.0 (SPSS, Chicago, USA). This particular experiment was approved by the Institutional Review Board of the State Key Laboratory of Cognitive Neuroscience and Learning at Beijing Normal University, China. Written consent form was obtained from all participants following a full explanation of the study procedure.

Table DS1 Description of individual samples included in this study

Sample	Cases	Case diagnosis	Diagnosis	Interview	Controls	Genotyping	λ	Ref.
Discovery								
PGC1	7,481	BPD1,BPD2,SAB,BPD-NOS	DSMIIR,DSM-IV,RDC	multiple	9,250	multiple	1.15	24
Replication-I								
Germany II	181	BPD1,BPD2	DSM-IV	AMDP	527	Illumina	1.05	17,25
Germany III	490	BPD1,BPD2,SAB,BPD-NOS	DSM-IV	SCID-I,SADS-L	880	Illumina	1.00	17,25
Australia	330	BPD1,BPD2,SAB,BPD-NOS	DSM-IV	SCID,DIGS	1,811	Illumina	1.00	9,26
France	451	BPD1,BPD2,BPD-NOS	DSM-IV	DIGS	1,631	Illumina	1.03	27,28
Sweden I	836	BPD1,BPD2,BPD-NOS	DSM-IV	ADE,MINI	2,093	Affymetrix 6.0	1.07	27
Sweden II	1,415	BPD1,BPD2,SAB,BPD-NOS	DSM-IV	/	1,271	Affymetrix 6.0	1.03	14
Iceland	541	BPD1,BPD2,BPD-NOS	DSM-IV,ICD-10,	CID-I,SADS-L	34,426	Affymetrix 6.0	1.11	17
Romania	244	BPD1	DSM-IV	SCID-I-P/DIGS	174	Illumina	/	15-17
China	350	BPD1,BPD2	DSM-IV	SCID-P	888	SNaPShot	/	18
Total	**4,838**				**43,701**			
Replication-II								
UK	1,218	BPD1,BPD2,SAB	RDC	/	2,913	ImmunoChip	1.02	19
Grand Total	**13,537**				**55,864**			

BPD1, bipolar disorder type 1; BPD2, bipolar disorder type 2; BPD-NOS, bipolar disorder not otherwise specified; SCZ, schizophrenia; SAB, schizoaffective disorder (bipolar type); λ = genomic control lambda.

We primarily used the Illumina (San Diego, CA, USA), Affymetrix and SNaPShot platforms to genotype rs6088662. For the genotyping in UK and Romania samples we used proxy SNP rs13041792 in UK (r^2=1.00 with rs6088662 in Europeans using data from 1000-Human-Genome) and rs6088667 in Romania samples (r^2=0.90 with rs6088662) instead, as rs6088662 is not covered.

Table DS2 Cognitive performance assessment in Chinese sample

Domain	Task	Brief description	Index
Memory	Wechsler Memory Scale -3rd Edition (WMS-III)	Two subscales: Picture recall (Subjects were showed pictures of 20 simple objects for 30 seconds and then asked to recall as many as possible) and picture recognition (Subjects were showed pictures of 8 simple objects for 30 seconds and then asked to pick them out from 28 pictures).	Number of items correctly recalled or recognized
	Working memory	In the 2-back working memory task, subjects judged whether the current item was the same (or related) to the one presented two trials earlier. Three sessions involved morphological, phonological, and semantic judgment.	Overall accuracy
Executive function	Attention network test	Subjects saw several small arrows on the computer screen and had to judge the direction of the arrow in the middle (left or right). The 6 peripheral arrows can either in the same or inverse direction to the middle one. There were also cues to alert subjects or point to the position where arrows will be presented	Alert, orientation, conflict
	Wisconsin card sort task	Subjects had to select one from four cards that fits a rule. Rules included color, form, and amount of items on the cards, and rules changed during the experiment	Preserved error (Nelson)
Personality	Temperament and Character Inventory-Re	7 aspects of personality: Novelty Seeking, Harm Avoidance, Reward Dependence, Persistence, Self-Directedness, Cooperativeness, Self-Transcendence	7 subscales scores
Language abilities	Visual-auditory learning, from Woodcock Reading Mastery test Revised, Forms G.	This task consists of several sessions. In each session, subjects were asked to learn a few symbol-word pairs. Afterwards, they were asked to read out some sentences written in symbols using corresponding words they just learned.	Number of correct responses

Table DS3 Results of integrative analysis using brain eQTL and bipolar disorder GWAS data

Gene	Gene LBF	Gene p-val	SNP	Location	Proximity	eQTL p-val	BPD p-val	SNP LBF
GLT8D1	6.78	2.22e-06						
			rs2251219	3:52559827	cis	2.84e-17	5.45e-07	6.95
			rs17073273	6:144330243	trans	8.55e-06	0.73	-0.093
			rs2070968	10:73251566	trans	6.20e-06	0.67	-0.075
CXCL16	6.16	2.22e-06						
			rs12634640	3:187552259	trans	6.92e-07	1.63e-03	2.38
			rs810517	10:80612626	trans	1.14e-06	2.12e-04	3.78
TRPC4AP	5.57	8.89e-06						
			rs9883745	3:133715013	trans	2.86e-06	0.46	-0.13
			rs10501340	11:55439371	trans	6.73e-06	2.75e-02	0.28
			rs11049310	12:28100068	trans	8.31e-06	0.77	-0.056
			rs6088662	20:33011294	cis	5.44e-09	5.85e-05	5.48
TAF11	5.52	1.11e-05						
			rs4482754	4:87230328	trans	7.57e-06	3.62e-06	4.40
			rs7263316	20:19632036	trans	5.94e-07	2.37e-02	1.12

Table DS4 Association of rs2251219 with gene expression in 3p21.1 region

Author (Ref.)	**Myers *et al*[1]**	**Unpublished data**	**Colantuoni *et al*[29]**	**Webster *et al*[30]**		**Zou *et al*[31]**		**Heinzen *et al*[32]**
Region	Brain	DLPFC	DLPFC	Brain		Cerebellar	Temporal cortex	Frontal cortex
Dx (Number)	Control (N=193)	Control (N=320)	Control (N=261)	Control + AD (N=369)	AD (N=176)	AD (N=197)	AD (N=202)	Control (N=93)
STAB1	n.s.	/	n.s.	n.s.	n.s.	n.s.	n.s.	*0.095*
NT5DC2	/	/	n.s.	/	/	n.s.	n.s.	n.s.
PBRM1	/	n.s.	*0.085*	/	/	n.s.	n.s.	n.s.
GNL3	/	/	*0.017*	/	/	n.s.	n.s.	/
GLT8D1	**$<1.0\times10^{-16}$**	n.s.	*0.048*	**$<1.0\times10^{-30}$**	**$<1.0\times10^{-18}$**	n.s.	n.s.	n.s.
SPCS1	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
NEK4	/	*0.051*	n.s.	/	/	n.s.	n.s.	n.s.
ITIH1	/	/	n.s.	/	/	n.s.	n.s.	*0.055*
ITIH3	/	/	n.s.	/	/	n.s.	n.s.	n.s.
ITIH4	**$<1.0\times10^{-3}$**	/	**$<1.0\times10^{-2}$**	**$<1.0\times10^{-4}$**	**$<1.0\times10^{-2}$**	n.s.	n.s.	n.s.
TMEM110	/	*0.083*	/	/	/	n.s.	n.s.	n.s.

N.A., not available; Dx, diagnosis; AD, Alzheimer's disease; n.s., not significant; DLPFC, Dorsolateral prefrontal cortex

Table DS5 Replication of *trans* eQTL association in different samples

Author (Ref.)		**Myers *et al*[1]**	**Unpublished data**	**Colantuoni *et al*[29]**	**Webster *et al*[30]**		**Zou *et al*[31]**		**Heinzen *et al*[32]**
Region		Brain	DLPFC	DLPFC	Brain		Cerebellar	Temporal cortex	Frontal cortex
Dx (Number)		Control (N=193)	Control (N=320)	Control (N=261)	Control + AD (N=369)	AD (N=176)	AD (N=197)	AD (N=202)	Control (N=93)
CXCL16	rs12634640	$<1.0\times10^{-6}$	n.s.	n.s.	$<1.0\times10^{-2}$	n.s.	n.s.	n.s.	n.s.
	rs810517	$<1.0\times10^{-5}$	n.s.	n.s.	0.023	n.s.	n.s.	n.s.	n.s.
TAF11	rs4482754	$<1.0\times10^{-5}$	/	n.s.	$<1.0\times10^{-2}$	n.s.	n.s.	n.s.	n.s.

Dx, diagnosis; AD, Alzheimer's disease; n.s., not significant; DLPFC, Dorsolateral prefrontal cortex

Table DS6 Association of rs6088662 with gene expression in 20q11.22 region

Author (Ref.)	**Myers *et al*[1]**	**Unpublished data**	**Colantuoni *et al*[29]**	**Webster *et al*[30]**		**Zou *et al*[31]**		**Heinzen *et al*[32]**
Region	Brain	DLPFC	DLPFC	Brain		Cerebellar	Temporal cortex	Frontal cortex
Dx (Number)	Control (N=193)	Control (N=320)	Control (N=261)	Control + AD (N=369)	AD (N=176)	AD (N=197)	AD (N=202)	Control (N=93)
AHCY	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ITCH	n.s.	*0.067*	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
DYNLRB1	/	n.s.	n.s.	/	/	n.s.	n.s.	n.s.
PIGU	/	n.s.	n.s.	/	/	n.s.	n.s.	n.s.
NCOA6		n.s.	*0.036*	n.s.	n.s.	n.s.	n.s.	n.s.
GGT7	**$<1.0\times10^{-7}$**	**$<1.0\times10^{-8}$**	*0.054*	**$<1.0\times10^{-7}$**	**$<1.0\times10^{-2}$**	n.s.	**$<1.0\times10^{-2}$**	0.13
ACSS2	/	n.s.	*0.098*	/	/	**$<1.0\times10^{-2}$**	**$<1.0\times10^{-5}$**	n.s.
GSS	n.s.	/	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
MYH7B	n.s.	n.s.	**$<1.0\times10^{-3}$**	n.s.	n.s.	**$<1.0\times10^{-15}$**	n.s.	n.s.
TRPC4AP	**$<1.0\times10^{-8}$**	<0.005	/	**$<1.0\times10^{-8}$**	*0.023*	n.s.	n.s.	n.s.
EDEM2	*0.040*	*0.067*	**$<1.0\times10^{-2}$**	**$<1.0\times10^{-2}$**	*0.010*	n.s.	n.s.	n.s.
PROCR	/	/	n.s.	/	/	n.s.	n.s.	n.s.
MMP24	/	*0.098*	n.s.	/		n.s.	n.s.	0.11
UQCC1	/	n.s.	n.s.	/	/	n.s.	n.s.	n.s.

N.A., not available; Dx, diagnosis; AD, Alzheimer's disease; n.s., not significant; DLPFC, Dorsolateral prefrontal cortex

Table DS7 Association of rs6088662 with GGT7 exon expression in Heinzen *et al*[32]

Probe_Type	Gene_Symbol	Transcript	Transcript_Probe_ID	Exon_Probe_ID	Start	End	P-val
transcript	*GGT7*	NM_178026	3903598	-	32884010	32924318	0.128
exon	*GGT7*	NM_178026	3903598	3903603	32896517	32896683	0.2386
exon	*GGT7*	NM_178026	3903598	3903604	32896819	32896919	0.4164
exon	*GGT7*	NM_178026	3903598	3903606	32901439	32901524	**0.02122**
exon	*GGT7*	NM_178026	3903598	3903610	32902247	32902276	0.2765
exon	*GGT7*	NM_178026	3903598	3903611	32902349	32902375	0.2827
exon	*GGT7*	NM_178026	3903598	3903613	32902716	32902761	0.2265
exon	*GGT7*	NM_178026	3903598	3903614	32902789	32902817	0.2122
exon	*GGT7*	NM_178026	3903598	3903616	32903626	32903723	*0.07463*
exon	*GGT7*	NM_178026	3903598	3903618	32903901	32903942	*0.08682*
exon	*GGT7*	NM_178026	3903598	3903619	32903951	32903990	0.6926
exon	*GGT7*	NM_178026	3903598	3903620	32906001	32906080	0.2708
exon	*GGT7*	NM_178026	3903598	3903621	32906278	32906381	0.5625
exon	*GGT7*	NM_178026	3903598	3903623	32908286	32908357	0.6493
exon	*GGT7*	NM_178026	3903598	3903624	32910932	32911062	0.8358
exon	*GGT7*	NM_178026	3903598	3903626	32911433	32911460	*0.05013*
exon	*GGT7*	NM_178026	3903598	3903629	32911733	32911766	0.1856
exon	*GGT7*	NM_178026	3903598	3903633	32912864	32912890	0.1768
exon	*GGT7*	NM_178026	3903598	3903634	32912953	32913023	0.5577
exon	*GGT7*	NM_178026	3903598	3903636	32914307	32914408	0.2789
exon	*GGT7*	NM_178026	3903598	3903638	32914781	32914926	0.7815
exon	*GGT7*	NM_178026	3903598	3903643	32924120	32924243	0.938
exon	*GGT7*	NM_178026	3903598	3903644	32924280	32924317	0.2398

Table DS8 Association of rs6088662 with schizophrenia and major depression

Disorder	Sample	Cases	Controls	Allele	P-value	Odds ratio	95% CI
Schizophrenia	PGC2[33]	35,476	46,839	G	0.0037	1.04	1.00-1.08
Depression	PGC1[34]	9,240	9,519	G	0.27	1.03	0.98-1.08
	PsyCoLaus study[35]	1,301	1,689	G	0.90	0.99	0.88-1.12

Table DS9 SNPs in the LD area with potentially functional role on genes

SNP	Position	Distance (bp)	R^2	MAF	Function	Gene Name
rs3746444	33041912	30618	0.848	0.20	ncRNA	MIR499A
rs7268266	33045550	34256	0.898	0.20	cds-synon	MYH7B
rs3746436	33049854	38560	0.898	0.20	cds-synon	MYH7B
rs3746435	33050859	39565	0.898	0.20	missense	MYH7B
rs36003887	33052768	41474	0.898	0.20	cds-synon	MYH7B
rs8501	33054245	42951	0.898	0.20	3’ UTR	TRPC4AP

Table DS10 Association of rs6088662 with hippocampal volume in Europeans[20]

SNP	Position	Allele	Frequency	β (mm^3)	SE (mm^3)	P-value
rs6088662	20:33547633	G	0.1937	27.29	7.99	0.00063

SE, standard error; β represents the difference in hippocampal volumes per copy increase of effect allele.

The association analysis in 5,775 healthy European subjects was corrected for intracranial volume, sex, age, age^2, sex × age, sex × age^2 and four MDS components.

Table DS11 Association analysis between rs6088662 and cognitive performance in the Chinese sample

Cognitive function	Test or subscale	Mean (s.d.)		t	P-value
		G carrier	TT		
Executive function	Attention alert	0.013 (0.027)	0.0047 (0.025)	2.612	0.0094
Language abilities	Visual-auditory	124.81 (7.76)	121.73 (10.56)	2.539	0.012

Before performing two-tailed t-test, F-test was conducted to compare the variances between two genotype groups.

F-test in the analysis of visual-auditory was significant ($p<0.005$), i.e., assuming the two groups do not have equal standard deviations, thus we used unpaired t-test with Welch's correction.

F-test in the analysis of attention alert was not significant ($p>0.3$), i.e., assuming both groups have the same standard deviation, we used unpaired t-test with no correction.

Fig. DS1 Association of rs6088662 with *TRPC4AP* mRNA expression in Europeans in Dimas *et al* study (*n*=75).[4]

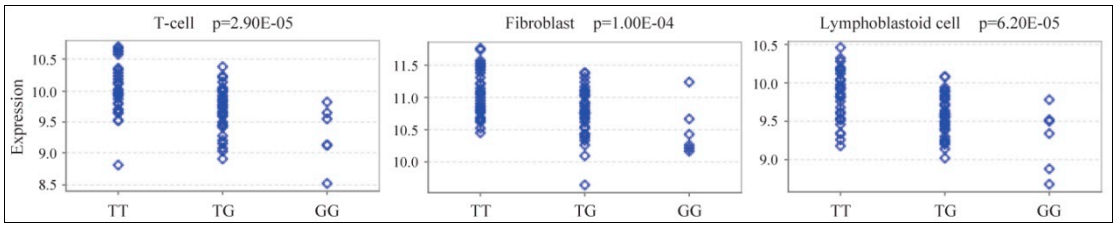


Fig. DS2 Association of rs6088662 with *TRPC4AP* mRNA expression in Europeans in Nica *et al* study (*n*=160).[3]

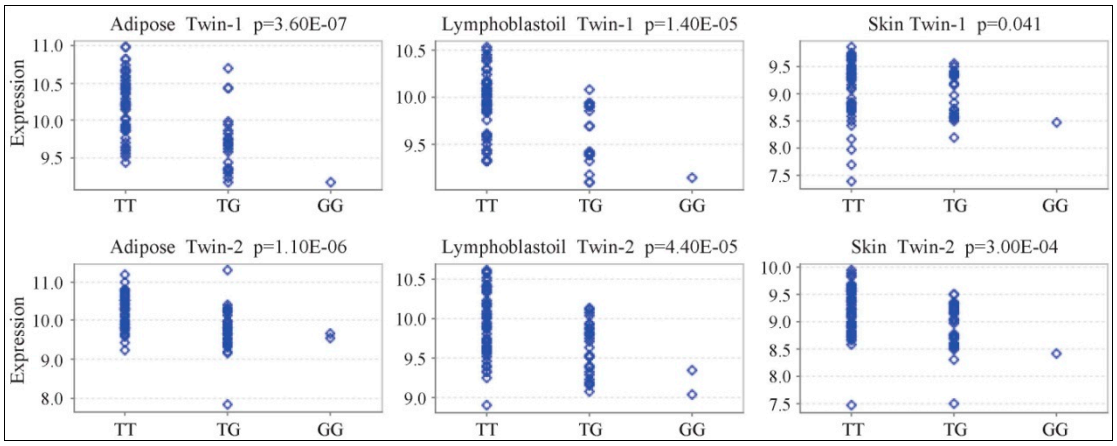


Fig. DS3 Association of rs6088662 with *TRPC4AP* mRNA expression in Europeans in Stranger *et al* study (*n*=109).[5]

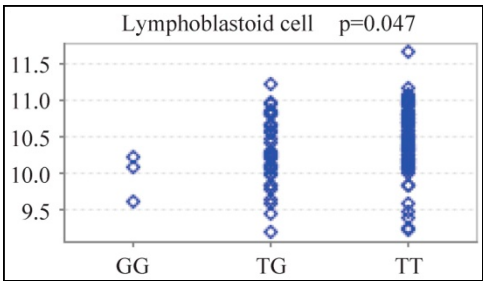
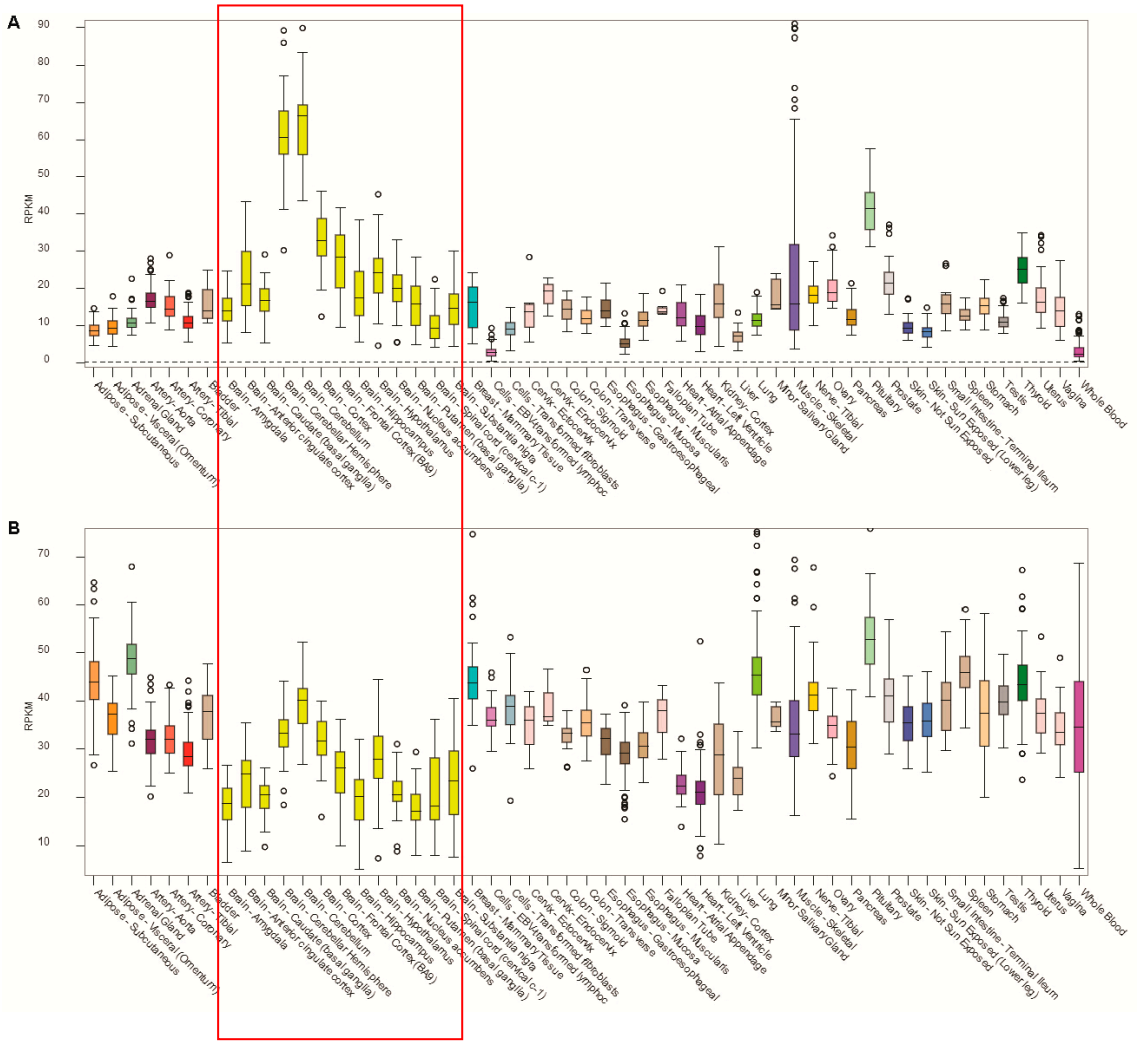


Fig. DS4 Spatial expression profiling of *GGT7* (A) and *TRPC4AP* (B) in human tissues. The results in brain tissues were marked in red rectangle.



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