Supplementary Information for

Transformer-Based Deep Learning Enhances Discovery in Migraine GWAS

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Supplementary Methods

Transformer-Based model

The Transformer model used in this study is based on an encoder architecture, designed to capture potential nonlinear relationships between different genetic features. The model extracts and represents complex feature relationships through stacked encoder layers, generating the final output to predict the association of target disease loci.

The encoder consists of multiple identical sublayers, each containing two key components: a multi-head self-attention layer and a feed-forward neural network. Each sublayer uses residual connections and layer normalization to improve model stability and training efficiency. The input features are first embedded and positionally encoded to ensure that the model understands positional relationships between features, including gene position information and relevant regulatory data. The input feature dimensions are mapped linearly to match the requirements of the multi-head self-attention mechanism. Each encoder layer has 4 attention heads, with 2 layers in total, and each feed-forward neural network has a hidden dimension of 64.

Unlike traditional encoder-decoder structures, the model in this study does not include a decoder but directly uses the output of the encoder for final prediction. Specifically, the first token representation from the encoder is passed through a fully connected layer and a sigmoid activation function for binary classification to determine the likelihood of disease association. The Transformer-Based model example is released on Github：https://github.com/ziangmeng/MA-MDD-Transformer-based-model-.

Self-Attention Mechanism

The core of the Transformer model lies in the self-attention mechanism, which dynamically assigns weights to each input feature, effectively capturing relationships between features. The calculation formula for self-attention is as follows:

$$Attention(Q, K, V) = softmax\left(\frac{QK^T}{\sqrt{d}}\right)V \quad (1)$$

where$Q$, K, $V$and represent the query, key, and value matrices, respectively, and is the dimension of the key vector. By calculating the dot product between the query and key,

scaling it, and applying the softmax function, the weights are obtained, which are used to compute a weighted sum of the values to generate the output. This mechanism allows the model to dynamically focus on important features based on the similarity between features, effectively handling feature dependencies.

In this study, the self-attention mechanism effectively models interactions between different genetic features, such as regulatory features (e.g., sQTL and eQTL). These complex feature relationships are crucial for understanding the genetic mechanisms of diseases. The self-attention mechanism allows the model to automatically capture potential complex relationships without explicitly defining feature interactions, thereby enhancing the prediction of disease-associated loci.

Multi-Head Attention Mechanism

The Transformer model uses a multi-head attention mechanism with multiple attention heads to capture the diversity of relationships between features. Each attention head independently computes self-attention, then concatenates all outputs and performs a linear transformation to obtain the final result, thus capturing relationships between features more comprehensively.

The calculation formula for multi-head attention is as follows:

$$MultiHead(Q,K,V) = Concat(head_1, head_2, \dots, head_h)W^O \quad (2)$$

$$head_i = Attention\left(QW_i^Q, VW_i^K, KW_i^V\right) \quad (3)$$

where QW_i^Q, VW_i^K and KW_i^V are the corresponding linear projection matrices, and W^O is the output linear transformation matrix.

By capturing feature relationships from different perspectives, the multi-head attention mechanism enhances the model's representation ability and flexibility. Each attention head focuses on different regulatory features, helping the model understand the relationship between genes and diseases. Through collaboration among multiple attention heads, the model gains richer information, reduces overfitting, increases feature interaction diversity, and is well-suited for complex biological data.

Input Features

Association Statistics and Population Genetics Features

Key predictors for this model include GWAS summary statistics and population genetics metrics relevant to migraine-associated loci. These features encompass effect sizes, p-values, sample sizes, and minor allele frequencies (MAF). To capture linkage disequilibrium (LD) patterns, LD scores were derived from European ancestry samples in the 1000 Genomes Project. For each variant, LD scores were computed by summing the r^2 values between the target variant and all neighboring variants within a 1 Mb window.

Functional Annotations

To enrich genetic interpretation, we incorporated multiple functional annotations:

Quantitative trait locus (QTL):

Brain sQTLs: Splicing QTL data were derived from BrainMeta v2 (1), incorporating RNA-seq data from 2,865 brain cortex samples across 2,443 unrelated individuals of European ancestry with genome-wide SNP data. These sQTLs were mapped using the THISTLE method (1) in combination with complementary sQTL mapping strategies.

Brain eQTLs: Brain eQTL data were derived from both BrainMeta v2 (1), containing RNA-seq analysis of 2,865 brain cortex samples from 2,443 unrelated individuals of European ancestry with genome-wide SNP data.

GTEx eQTLs: This feature set incorporates eQTL data from 49 human tissues based on GTEx V8 (2), focusing on variants located within 1 Mb of transcription start sites that demonstrate significant associations.

mQTLs: Methylation QTL data were derived from two primary sources. The first dataset includes mQTL summary statistics from a meta-analysis of 3,701 European ancestry samples conducted by Hatton et al (3). The second dataset provides mQTL summary statistics in SMR

BESD format, based on a meta-analysis of 1,980 European individuals, as reported in the studies by McRae et al. (4) and Wu et al. (5).

sc-eQTLs: Single-cell eQTL data specific to brain tissues, including astrocytes and neurons, were sourced from scQTLbase (https://bioinfo.szbl.ac.cn/scQTLbase/). Detailed information is provided in Supplementary Table 5.

Epigenomic and Chromatin Accessibility Features:

OCRs_brain (Infant): Infant-specific open chromatin regions were derived from the union of two datasets: GSE132403 (Chromatin accessibility dynamics in a model of human forebrain development) (5) and GSE95023 (Single-cell epigenomics reveals mechanisms of human cortical development) (6). Regions were marked as 1 if they overlapped with chromosomal annotations in either dataset.

OCRs_adult (Adult): Adult-specific open chromatin regions were obtained from GSE129017 (Allele-specific open chromatin in human iPSC neurons elucidates functional disease variants) (7, 8), with regions marked as 1 if they overlapped chromosomal annotations.

Digital Genomic Footprinting: Genomic DNase I footprinting data, which delineate transcription factor occupancy sites at nucleotide resolution within native chromatin, were sourced from Vierstra et al. (9). This dataset combines >67 billion DNase I cleavages across >240 human cell types and states, providing a comprehensive map of transcription factor recognition sites. Detailed information is available at https://www.vierstra.org/resources/dgf.

ENCODE Annotated Regions: Variants located within ENCODE-annotated genomic regions were identified and annotated using data from the ENCODE project (10). These annotations include transcribed regions, active promoter marks (H3K4Me3, H3K9Ac), active enhancer marks (H3K4Me1, H3K27Ac), active elongation marks (H3K36Me3, H3K79Me2), and repressive marks (H3K27Me3, H3K9Me3). These features were integrated into the InsightGWAS framework to refine variant prioritization and provide insights into regulatory activity and chromatin states across the genome.

Regulatory and Pathogenic Variant Annotations:

MicroRNA and snoRNA Disruption: Variants affecting microRNAs, snoRNAs, and predicted microRNA binding sites were annotated using ANNOVAR, an efficient software tool for functionally annotating genetic variants across various genomes. The wgRna table from UCSC Genome Browser (11), based on miRbase (12) and snoRNABase (13), was utilized to identify variants overlapping microRNA and snoRNA loci. Additionally, the TargetScan (14) database was employed to detect variants disrupting conserved mammalian microRNA regulatory target sites within 3' UTR regions of RefSeq genes. By leveraging ANNOVAR's capabilities, these annotations provide valuable insights into post-transcriptional regulation and the functional consequences of genetic variants.

Transcription Factor Binding Sites (TFBS): Annotation of transcription factor binding sites was performed using ANNOVAR (15), incorporating the tfbsConsSites database. This database provides the locations and scores of TFBS conserved across human, mouse, and rat alignments. Scores and thresholds are computed from the Transfac Database (15).

Segmental Duplications: Genetic variants mapped to segmental duplications are often alignment artifacts and should be interpreted with caution. These variants may appear as SNPs with high fold coverage and confidence scores but can represent non-polymorphic sites with identical flanking sequences in duplicated regions. Using ANNOVAR, we identified variants overlapping segmental duplications by leveraging relevant annotation databases (15). These annotations help flag potentially spurious variants, ensuring more accurate downstream analyses.

Previously Reported GWAS Variants: Variants associated with psychiatric and neurological diseases or related traits were annotated using data from gwasCatalog (16) and Open Targets (17). The gwasCatalog compiles findings from published GWAS, enabling the identification of variants linked to relevant traits or disorders. Open Targets enhances this by integrating evidence from GWAS, functional genomics, and curated literature, providing a comprehensive view of variant-disease and variant-trait relationships. These resources offer critical context for interpreting variant significance within psychiatric and neurological genetics.

Pathogenic Annotations: This feature integrates diverse predictive scores to evaluate the pathogenicity and functional impact of genetic variants. Conservation metrics, such as GERP++ (18), highlight variants in evolutionarily constrained regions under strong selective pressure. Functional impact predictions from tools like PolyPhen-2 (HDIV and HVAR), SIFT, LRT, MutationTaster, MutationAssessor, FATHMM, MetaSVM, and MetaLR assess missense variants for their potential to disrupt protein structure, biochemical properties, or function (19-25). The Combined Annotation Dependent Depletion (CADD) raw score (26) further quantifies variant deleteriousness by integrating multiple functional annotations. By synthesizing these predictive tools, this feature enables InsightGWAS to robustly prioritize variants with potential pathogenic effects, facilitating the identification of biologically relevant loci.

References

1. Qi T, Wu Y, Fang H, Zhang F, Liu S, Zeng J, Yang J. Genetic control of RNA splicing and its distinct role in complex trait variation. *Nat Genet* 2022; 54: 1355-1363.
2. Consortium GT. The GTEx Consortium atlas of genetic regulatory effects across human tissues. *Science* 2020; 369: 1318-1330.
3. Hatton AA, Cheng FF, Lin T, Shen RJ, Chen J, Zheng Z, Qu J, Lyu F, Harris SE, Cox SR, Jin ZB, Martin NG, Fan D, Montgomery GW, Yang J, Wray NR, Marioni RE, Visscher PM, McRae AF. Genetic control of DNA methylation is largely shared across European and East Asian populations. *Nat Commun* 2024; 15: 2713.
4. McRae AF, Marioni RE, Shah S, Yang J, Powell JE, Harris SE, Gibson J, Henders AK, Bowdler L, Painter JN, Murphy L, Martin NG, Starr JM, Wray NR, Deary IJ, Visscher PM, Montgomery GW. Identification of 55,000 Replicated DNA Methylation QTL. *Sci Rep* 2018; 8: 17605.
5. Wu Y, Zeng J, Zhang F, Zhu Z, Qi T, Zheng Z, Lloyd-Jones LR, Marioni RE, Martin NG, Montgomery GW, Deary IJ, Wray NR, Visscher PM, McRae AF, Yang J. Integrative analysis of omics summary data reveals putative mechanisms underlying complex traits. *Nat Commun* 2018; 9: 918.
6. de la Torre-Ubieta L, Stein JL, Won H, Opland CK, Liang D, Lu D, Geschwind DH. The Dynamic Landscape of Open Chromatin during Human Cortical Neurogenesis. *Cell* 2018; 172: 289-304 e218.
7. Zhang S, Zhang H, Zhou Y, Qiao M, Zhao S, Kozlova A, Shi J, Sanders AR, Wang G, Luo K, Sengupta S, West S, Qian S, Streit M, Avramopoulos D, Cowan CA, Chen M, Pang ZP, Gejman PV, He X, Duan J. Allele-specific open chromatin in human iPSC neurons elucidates functional disease variants. *Science* 2020; 369: 561-565.
8. Yao Y, Guo W, Zhang S, Yu H, Yan H, Zhang H, Sanders AR, Yue W, Duan J. Cell type-specific and

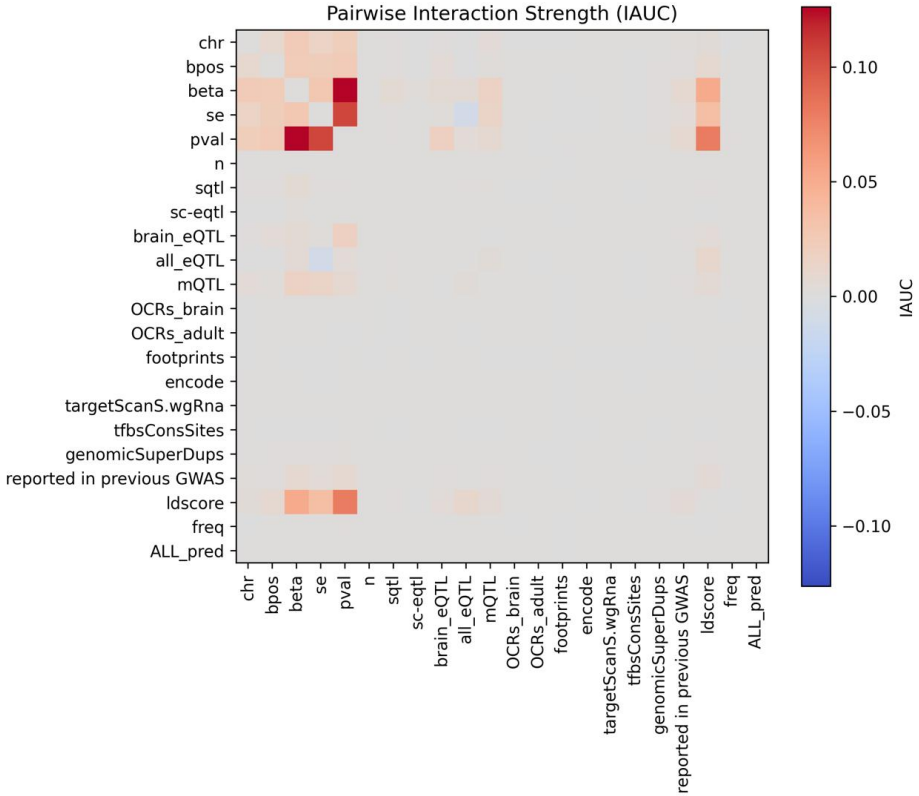
cross-population polygenic risk score analyses of MIR137 gene pathway in schizophrenia. *iScience* 2021; 24: 102785.

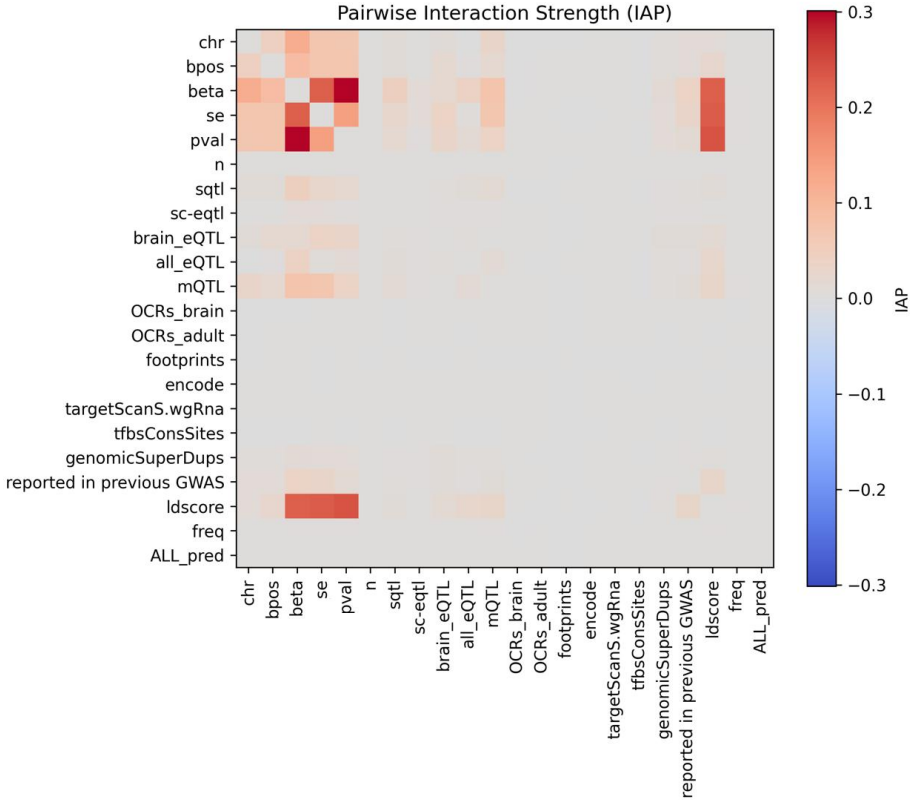
9. Vierstra J, Lazar J, Sandstrom R, Halow J, Lee K, Bates D, Diegel M, Dunn D, Neri F, Haugen E, Rynes E, Reynolds A, Nelson J, Johnson A, Frerker M, Buckley M, Kaul R, Meuleman W, Stamatoyannopoulos JA. Global reference mapping of human transcription factor footprints. *Nature* 2020; 583: 729-736.
10. Consortium EP, Moore JE, Purcaro MJ, Pratt HE, Epstein CB, Shoresh N, Adrian J, Kawli T, Davis CA, Dobin A, Kaul R, Halow J, Van Nostrand EL, Freese P, Gorkin DU, Shen Y, He Y, Mackiewicz M, Pauli-Behn F, Williams BA, Mortazavi A, Keller CA, Zhang XO, Elhajjajy SI, Huey J, Dickel DE, Snetkova V, Wei X, Wang X, Rivera-Mulia JC, Rozowsky J, Zhang J, Chhetri SB, Zhang J, Victorsen A, White KP, Visel A, Yeo GW, Burge CB, Lecuyer E, Gilbert DM, Dekker J, Rinn J, Mendenhall EM, Ecker JR, Kellis M, Klein RJ, Noble WS, Kundaje A, Guigo R, Farnham PJ, Cherry JM, Myers RM, Ren B, Graveley BR, Gerstein MB, Pennacchio LA, Snyder MP, Bernstein BE, Wold B, Hardison RC, Gingeras TR, Stamatoyannopoulos JA, Weng Z. Author Correction: Expanded encyclopaedias of DNA elements in the human and mouse genomes. *Nature* 2022; 605: E3.
11. Perez G, Barber GP, Benet-Pages A, Casper J, Clawson H, Diekhans M, Fischer C, Gonzalez JN, Hinrichs AS, Lee CM, Nassar LR, Raney BJ, Speir ML, van Baren MJ, Vaske CJ, Haussler D, Kent WJ, Haeussler M. The UCSC Genome Browser database: 2025 update. *Nucleic Acids Res* 2024.
12. Kozomara A, Birgaoanu M, Griffiths-Jones S. miRBase: from microRNA sequences to function. *Nucleic Acids Res* 2019; 47: D155-D162.
13. Xie J, Zhang M, Zhou T, Hua X, Tang L, Wu W. Sno/scaRNAbase: a curated database for small nucleolar RNAs and cajal body-specific RNAs. *Nucleic Acids Res* 2007; 35: D183-187.
14. McGeary SE, Lin KS, Shi CY, Pham TM, Bisaria N, Kelley GM, Bartel DP. The biochemical basis of microRNA targeting efficacy. *Science* 2019; 366.
15. Wang K, Li M, Hakonarson H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res* 2010; 38: e164.
16. Sollis E, Mosaku A, Abid A, Buniello A, Cerezo M, Gil L, Groza T, Gunes O, Hall P, Hayhurst J, Ibrahim A, Ji Y, John S, Lewis E, MacArthur JAL, McMahon A, Osumi-Sutherland D, Panoutsopoulou K, Pendlington Z, Ramachandran S, Stefancsik R, Stewart J, Whetzel P, Wilson R, Hindorff L, Cunningham F, Lambert SA, Inouye M, Parkinson H, Harris LW. The NHGRI-EBI GWAS Catalog: knowledgebase and deposition resource. *Nucleic Acids Res* 2023; 51: D977-D985.
17. Ghoussaini M, Mountjoy E, Carmona M, Peat G, Schmidt EM, Hercules A, Fumis L, Miranda A, Carvalho-Silva D, Buniello A, Burdett T, Hayhurst J, Baker J, Ferrer J, Gonzalez-Uriarte A, Jupp S, Karim MA, Koscielny G, Machlitt-Northen S, Malangone C, Pendlington ZM, Roncaglia P, Suveges D, Wright D, Vrousgou O, Papa E, Parkinson H, MacArthur JAL, Todd JA, Barrett JC, Schwartzentruber J, Hulcoop DG, Ochoa D, McDonagh EM, Dunham I. Open Targets Genetics: systematic identification of trait-associated genes using large-scale genetics and functional genomics. *Nucleic Acids Res* 2021; 49: D1311-D1320.
18. Davydov EV, Goode DL, Sirota M, Cooper GM, Sidow A, Batzoglou S. Identifying a high fraction of the human genome to be under selective constraint using GERP++. *PLoS Comput Biol* 2010; 6: e1001025.

19. Adzhubei I, Jordan DM, Sunyaev SR. Predicting functional effect of human missense mutations using PolyPhen-2. *Curr Protoc Hum Genet* 2013; Chapter 7: Unit7 20.
20. Kumar P, Henikoff S, Ng PC. Predicting the effects of coding non-synonymous variants on protein function using the SIFT algorithm. *Nat Protoc* 2009; 4: 1073-1081.
21. Chun S, Fay JC. Identification of deleterious mutations within three human genomes. *Genome Res* 2009; 19: 1553-1561.
22. Steinhaus R, Proft S, Schuelke M, Cooper DN, Schwarz JM, Seelow D. MutationTaster2021. *Nucleic Acids Res* 2021; 49: W446-W451.
23. Reva B, Antipin Y, Sander C. Predicting the functional impact of protein mutations: application to cancer genomics. *Nucleic Acids Res* 2011; 39: e118.
24. Shihab HA, Gough J, Cooper DN, Stenson PD, Barker GL, Edwards KJ, Day IN, Gaunt TR. Predicting the functional, molecular, and phenotypic consequences of amino acid substitutions using hidden Markov models. *Hum Mutat* 2013; 34: 57-65.
25. Kim S, Jhong JH, Lee J, Koo JY. Meta-analytic support vector machine for integrating multiple omics data. *BioData Min* 2017; 10: 2.
26. Kircher M, Witten DM, Jain P, O'Roak BJ, Cooper GM, Shendure J. A general framework for estimating the relative pathogenicity of human genetic variants. *Nat Genet* 2014; 46: 310-315.

Supplementary Figure 1. Pairwise interaction heatmaps of variant-level features in the Transformer model.

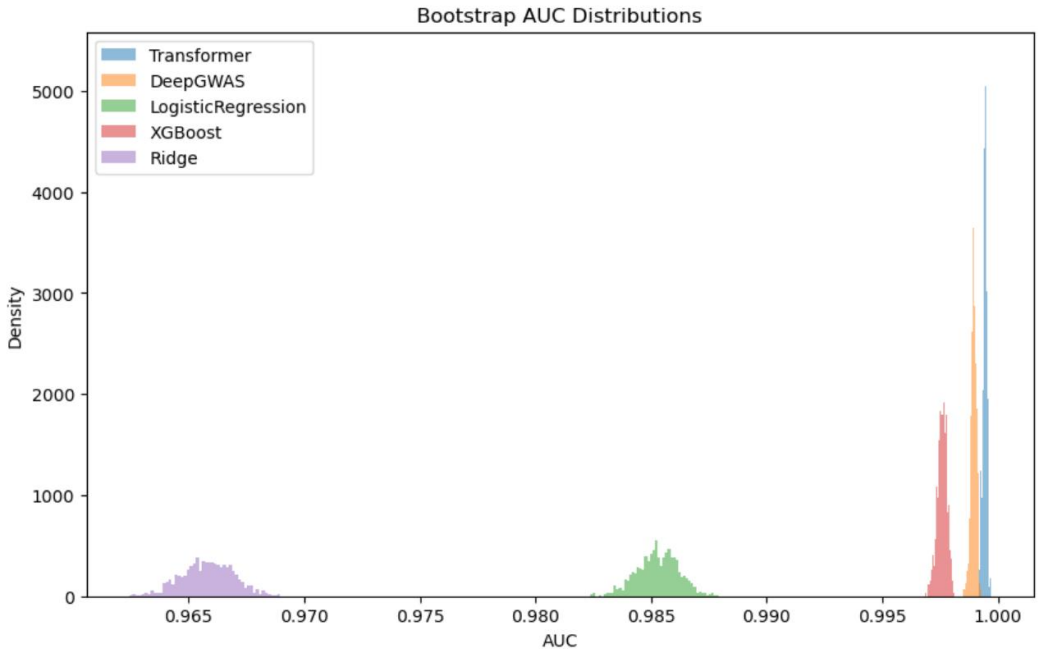
These heatmaps visualize pairwise feature interaction strengths based on permutation-derived decreases in predictive performance. The left panel shows interactions measured by area under the ROC curve (IAUC), and the right panel shows interactions measured by average precision (IAP). The x- and y-axes represent input feature dimensions, grouped into four functional categories: (1) position-related features (chromosome, base-pair position, LD score, and allele frequency); (2) GWAS statistical features (p-value, effect size, standard error, and sample size); (3) molecular QTL annotations (eQTL, sQTL, and other transcript-level QTLs); and (4) regulatory and OCR-based features (ENCODE signals, transcription factor footprints, and previously reported GWAS hits). For each feature pair, we compared the performance drop caused by shuffling both features simultaneously with the sum of the drops from shuffling each feature individually. Warmer colors indicate stronger evidence of non-additive interactions, where the joint perturbation exceeded the additive expectation. The results highlight that the strongest interactions cluster among GWAS statistical features (β, SE, p-value, and LD score), whereas QTL and regulatory annotations contribute primarily marginal effects.


Pairwise Interaction Strength (IAUC)
chr
bpos
beta
se
pval
n
sqtl
sc-eqtl
brain_eQTL
all_eQTL
mQTL
OCRs_brain
OCRs_adult
footprints
encode
targetScanS.wgRna
tfbsConsSites
genomicSuperDups
reported in previous GWAS
ldscore
freq
ALL_pred
0.10
0.05
0.00
−0.05
−0.10
IAUC


Pairwise Interaction Strength (IAP)
chr
bpos
beta
se
pval
n
sqtl
sc-eqtl
brain_eQTL
all_eQTL
mQTL
OCRs_brain
OCRs_adult
footprints
encode
targetScanS.wgRna
tfbsConsSites
genomicSuperDups
reported in previous GWAS
ldscore
freq
ALL_pred
0.3
0.2
0.1
0.0
−0.1
−0.2
−0.3
IAP

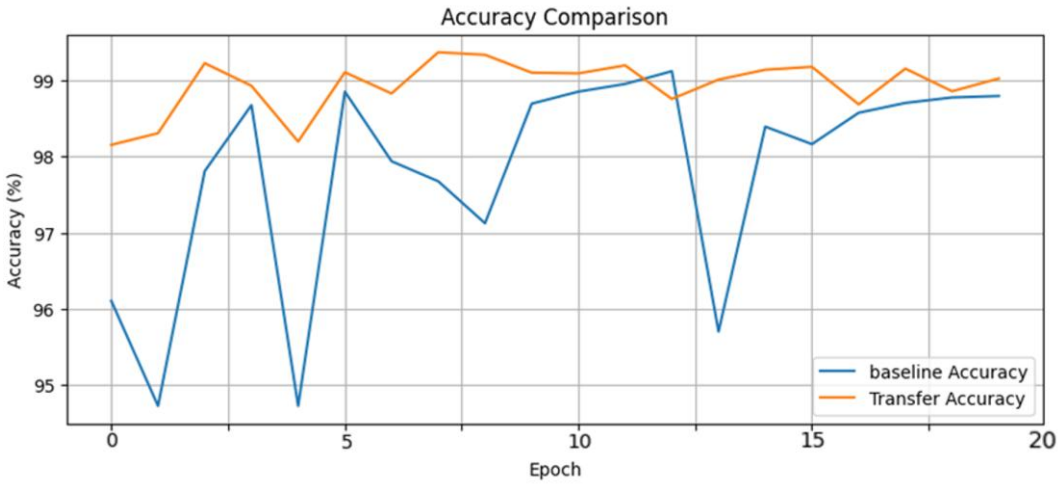
Supplementary Figure 2. Bootstrap AUC distributions across different models.

Distribution of AUC values computed from 10,000 bootstrap replicates for each model: Transformer-based InsightGWAS (blue, mean AUC = 0.9994, 95% CI = 0.9992–0.9996), DeepGWAS (orange, 0.9990, 0.9987–0.9992), Logistic Regression (green, 0.9853, 0.9834–0.9869), XGBoost (red, 0.9976, 0.9971–0.9980), and Ridge Regression (purple, 0.9658, 0.9635–0.9680).



Supplementary Figure 3. Comparison of classification accuracy between transfer learning and baseline models across training epochs.

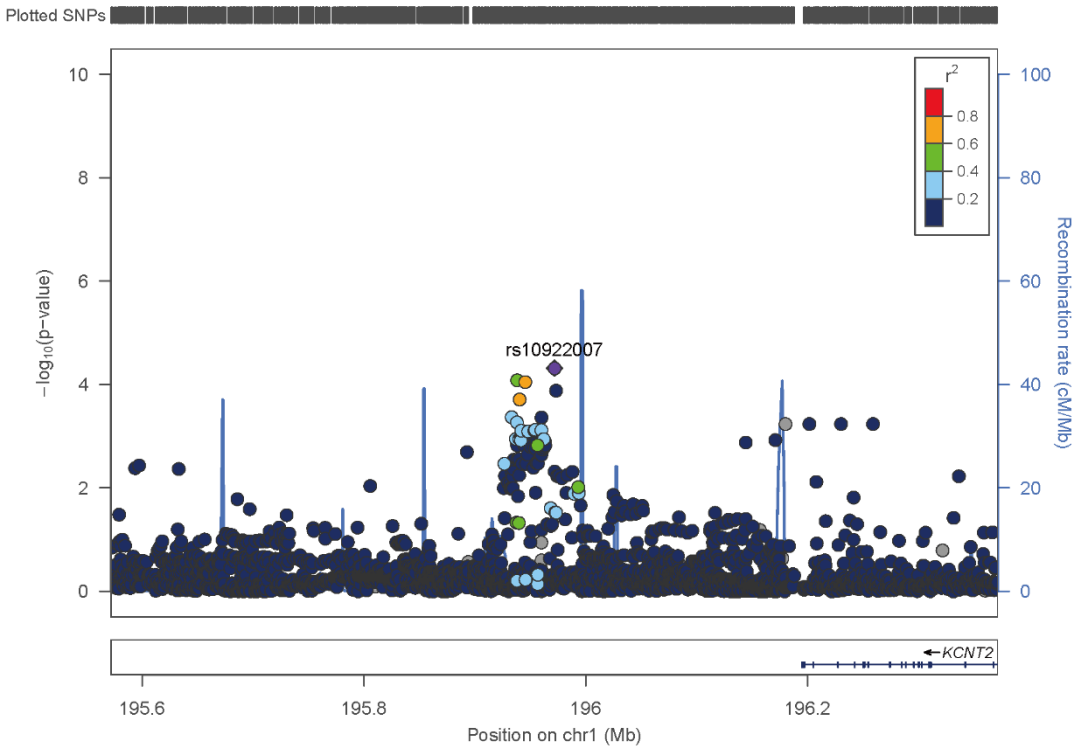
Training accuracy (%) over 20 epochs for the Transformer-based InsightGWAS model with (orange) and without (blue) transfer learning.



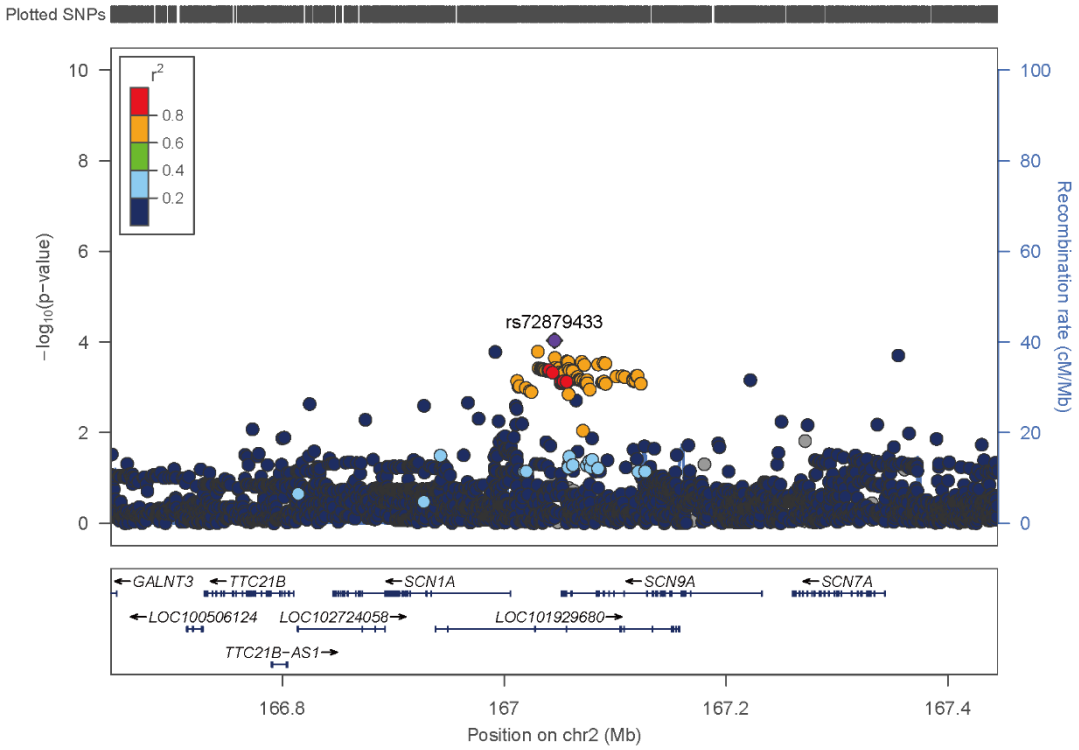
Supplementary Figure 4. Regional plots of selected novel loci predicted by InsightGWAS.

Purple diamond indicates the lead SNP, and circles represent the other SNPs in the region, with coloring from the linkage disequilibrium (r^2, based on the 1000 Genomes Project Europeans/Asians) between each SNP and the lead SNP.

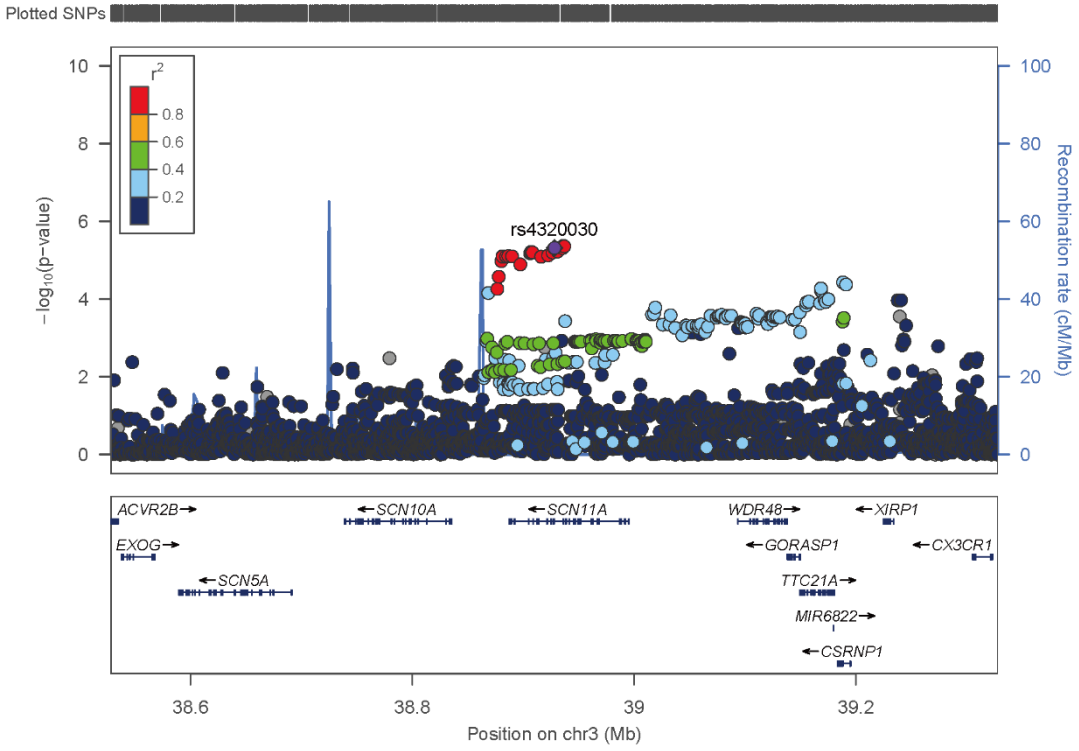
a. *KCNT2*



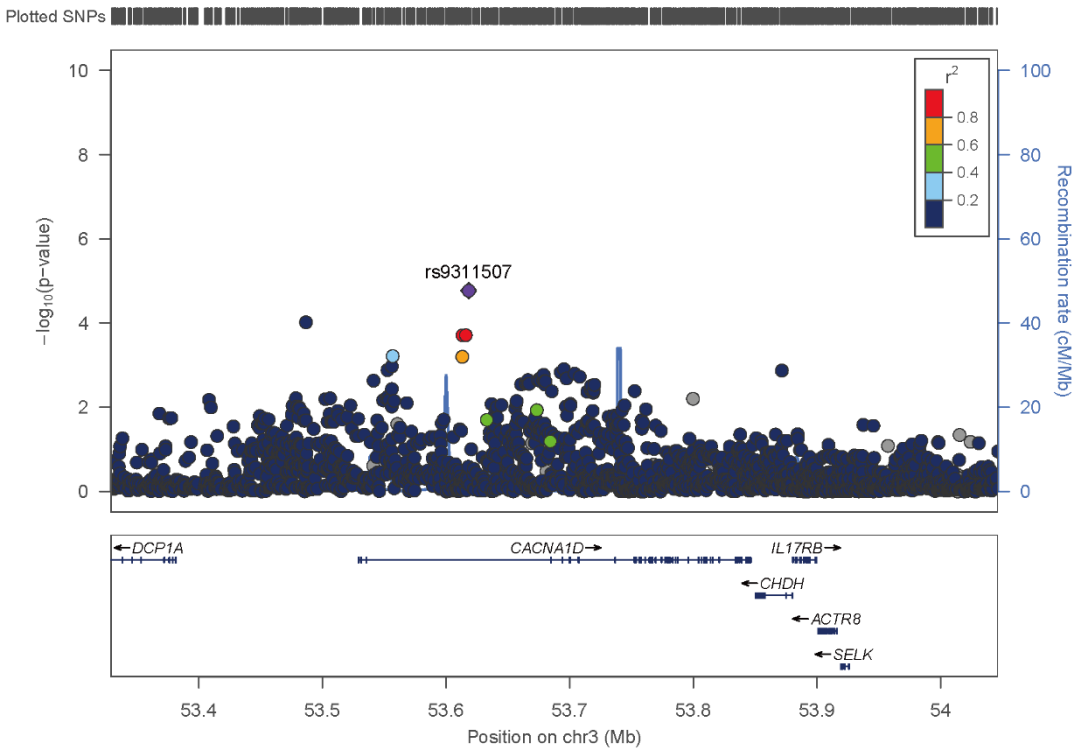
b. *SCN9A*



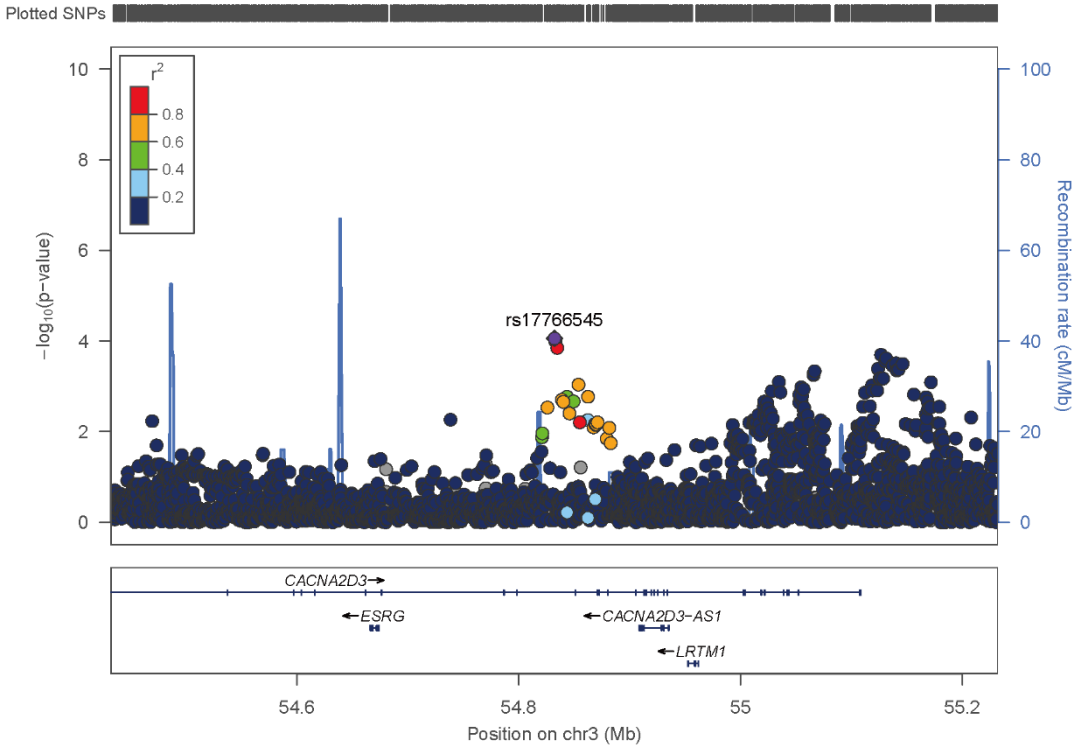
c. *SCN11A*



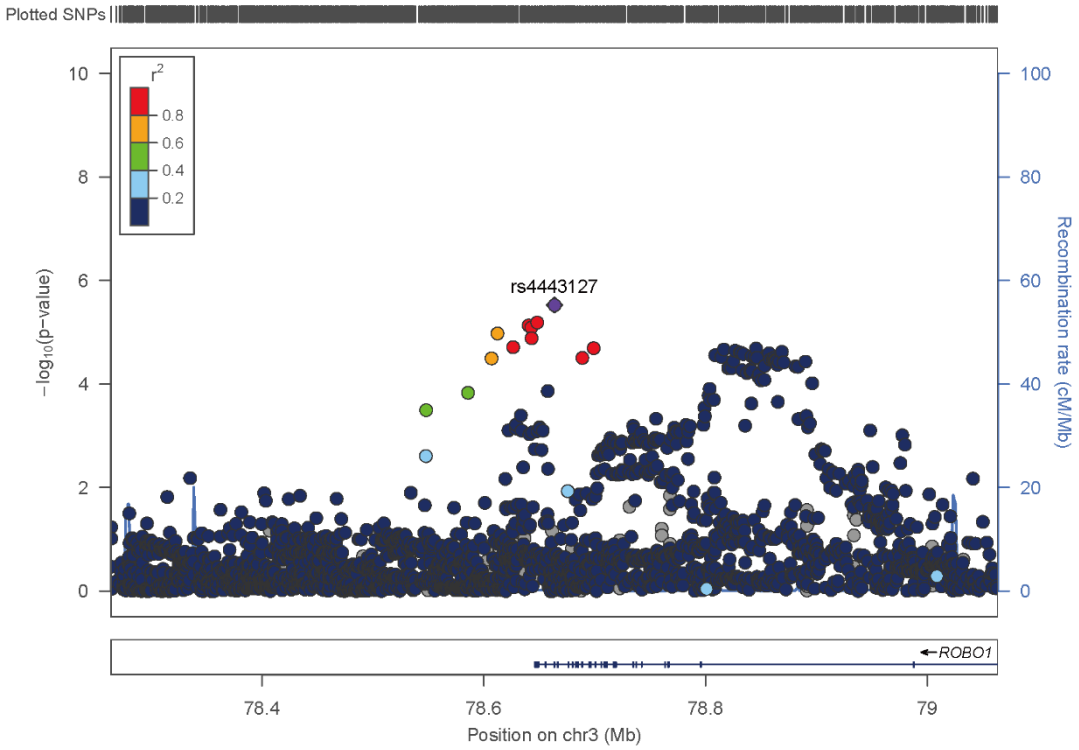
d. *CACNA1D*



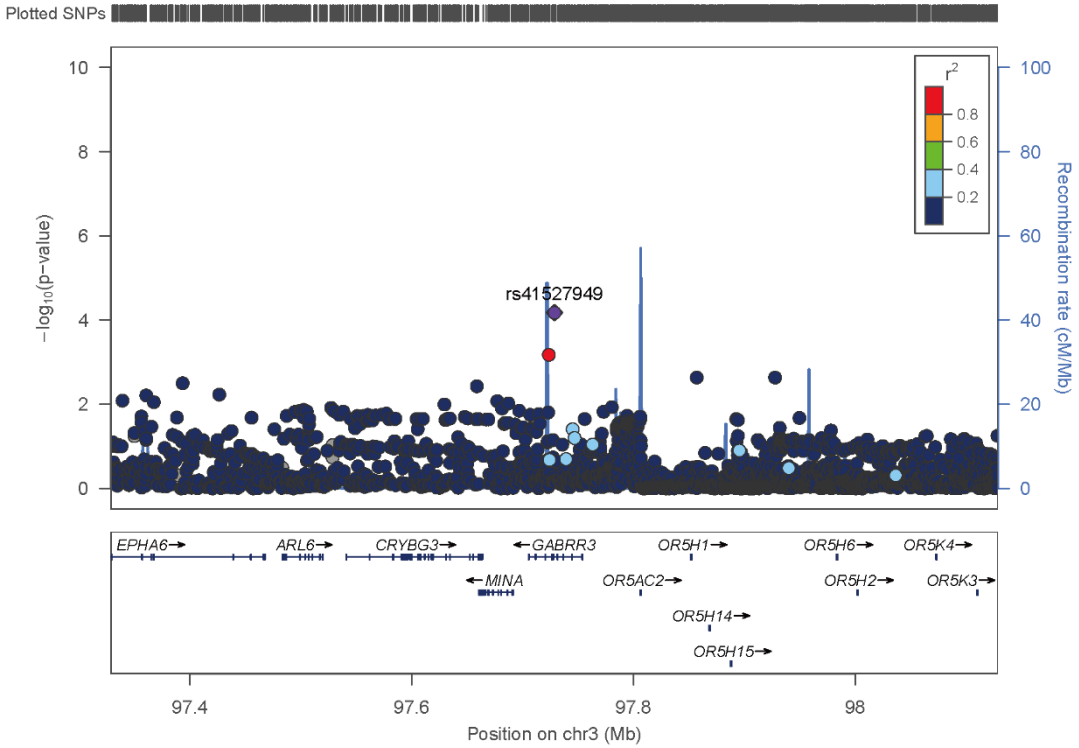
e. *CACNA2D3*



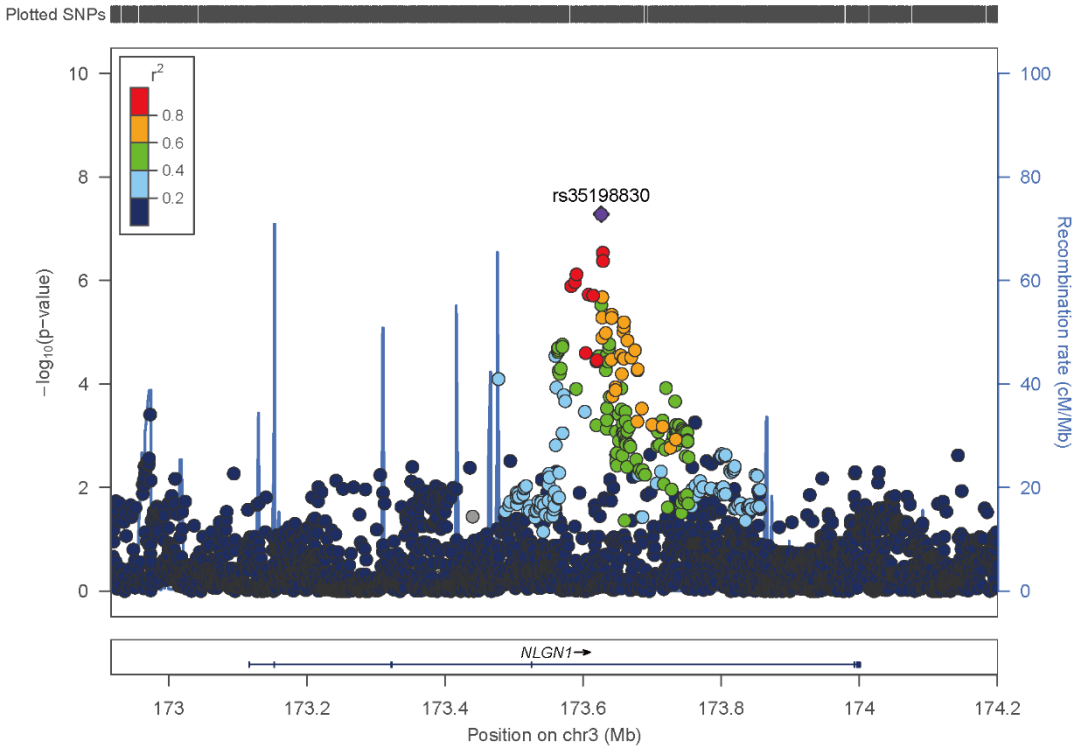
f. *ROBO1*



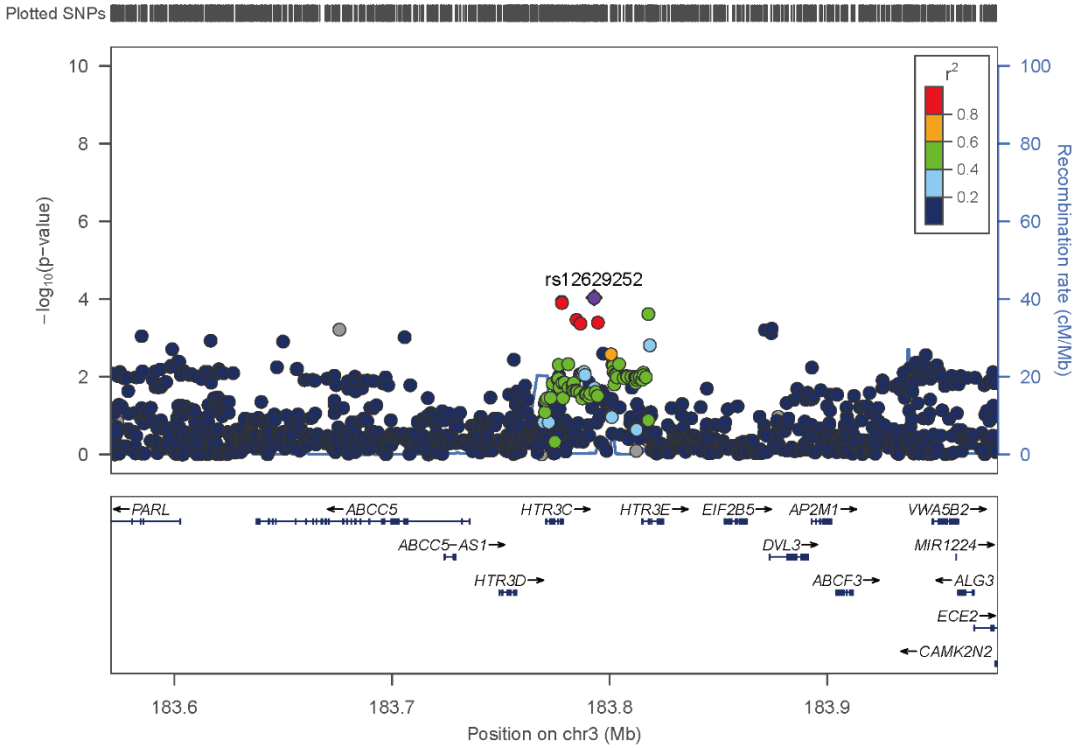
g. *GABRR3*



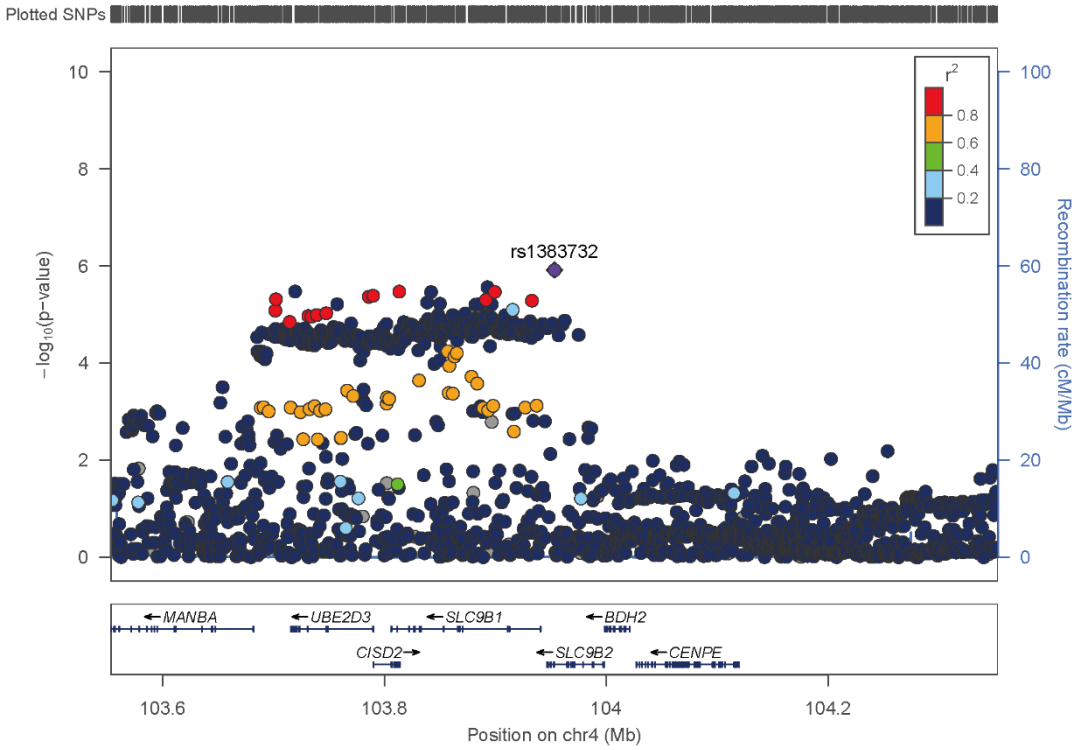
h. *NLGN1*



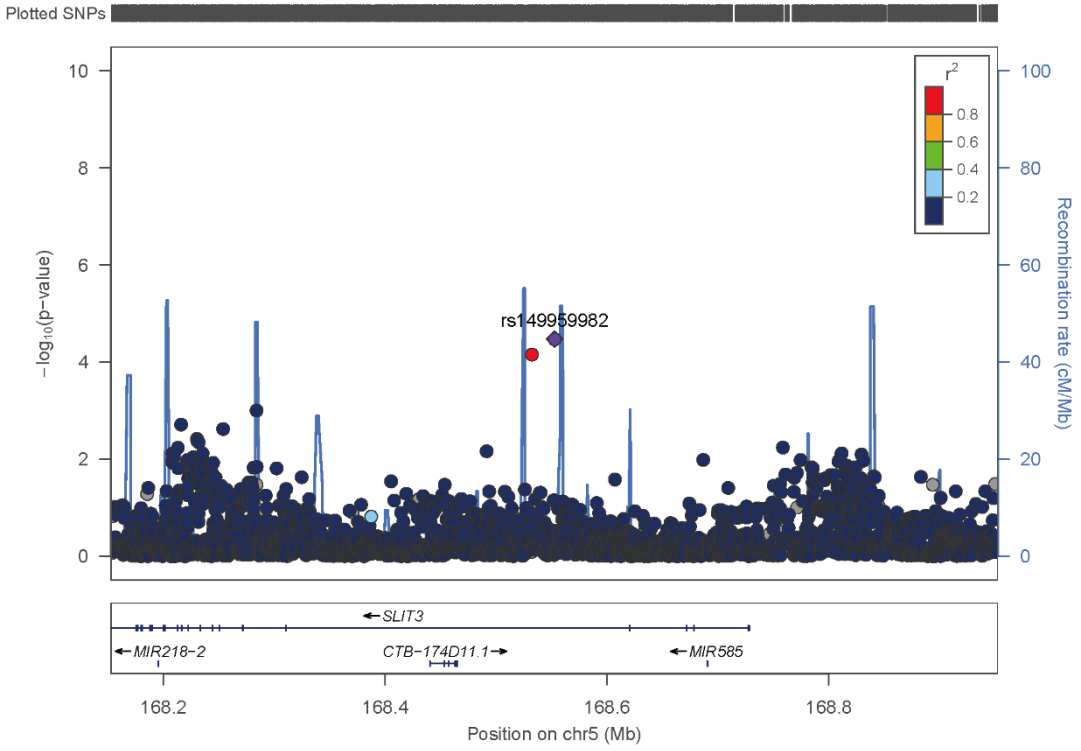
i. *HTR3C*



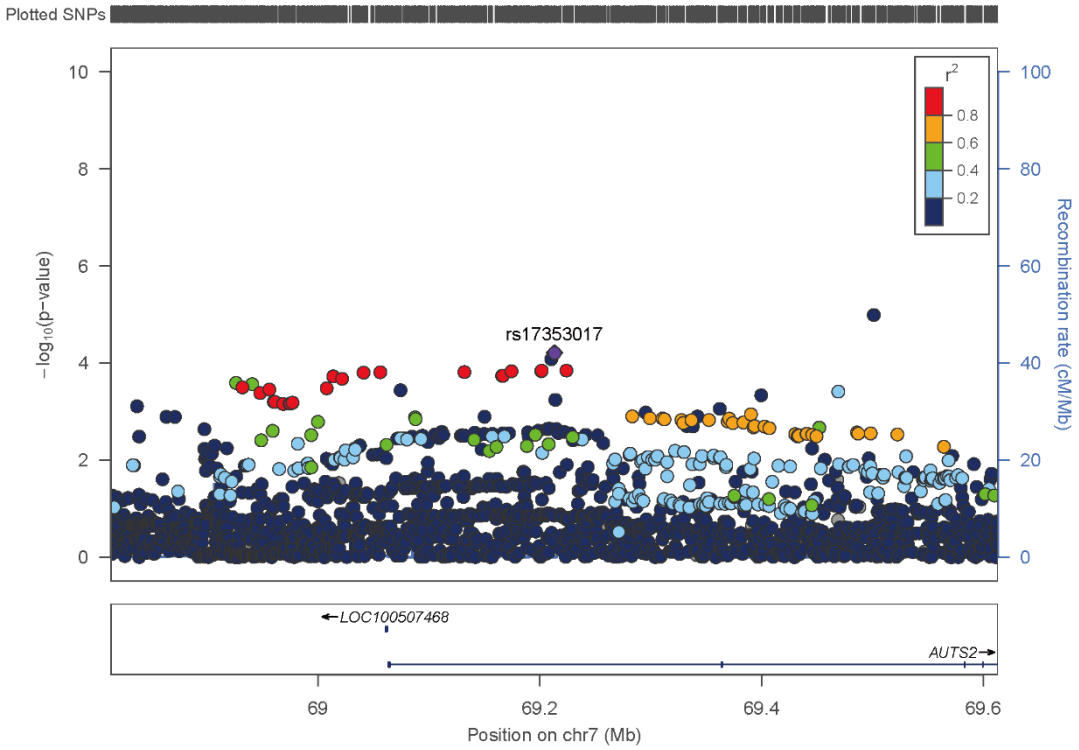
j. *SLC9B1*



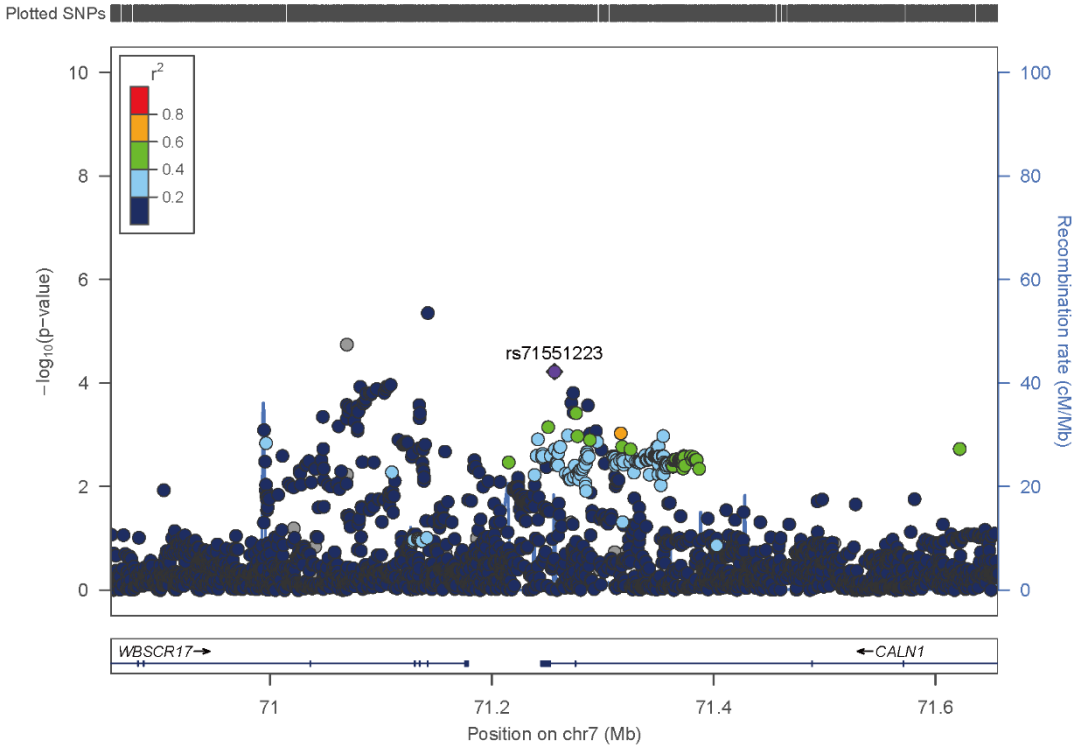
k. *SLIT3*



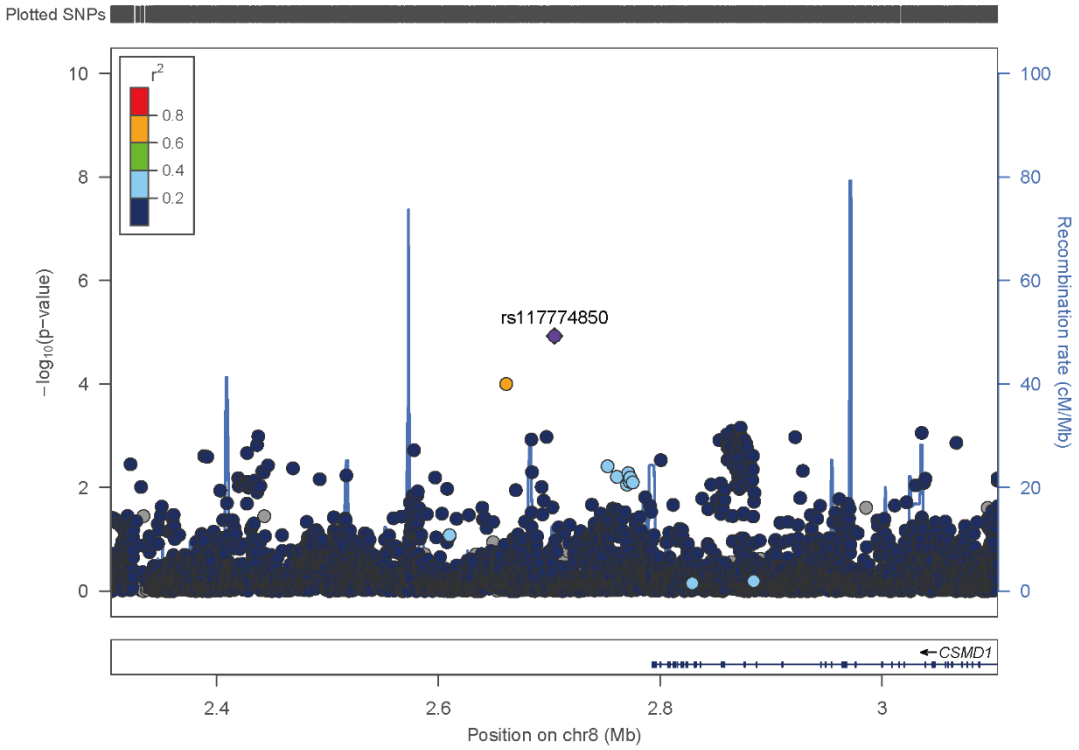
l. *AUTS2*



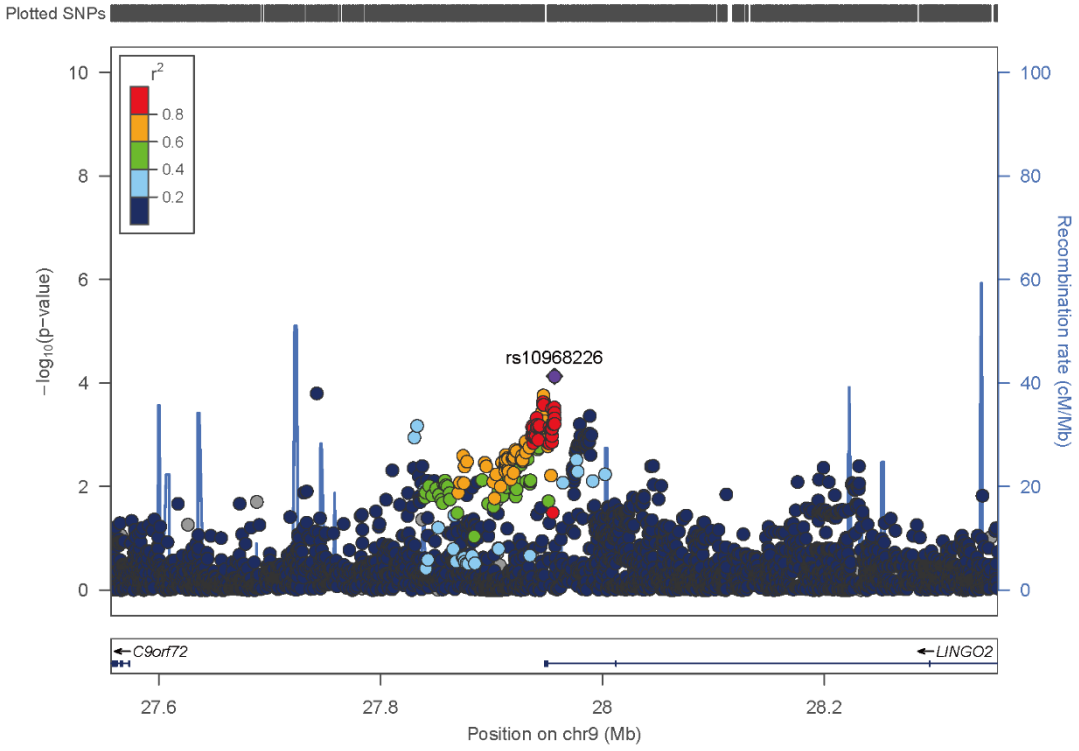
m. *CALN1*



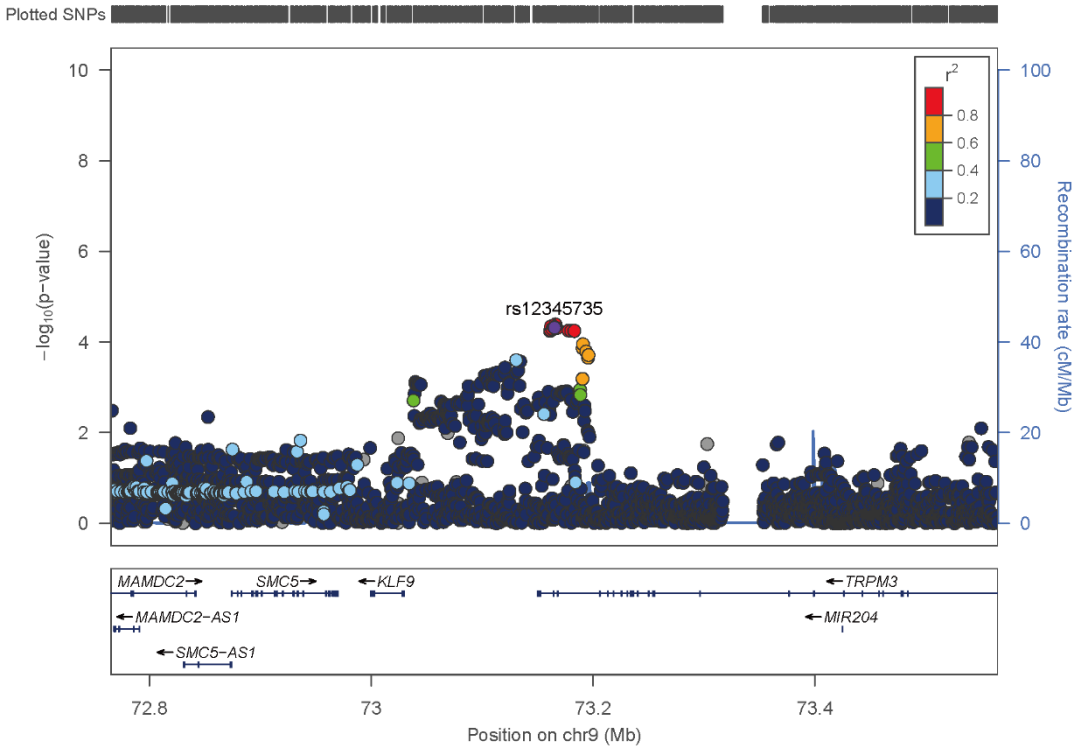
n. *CSMD1*



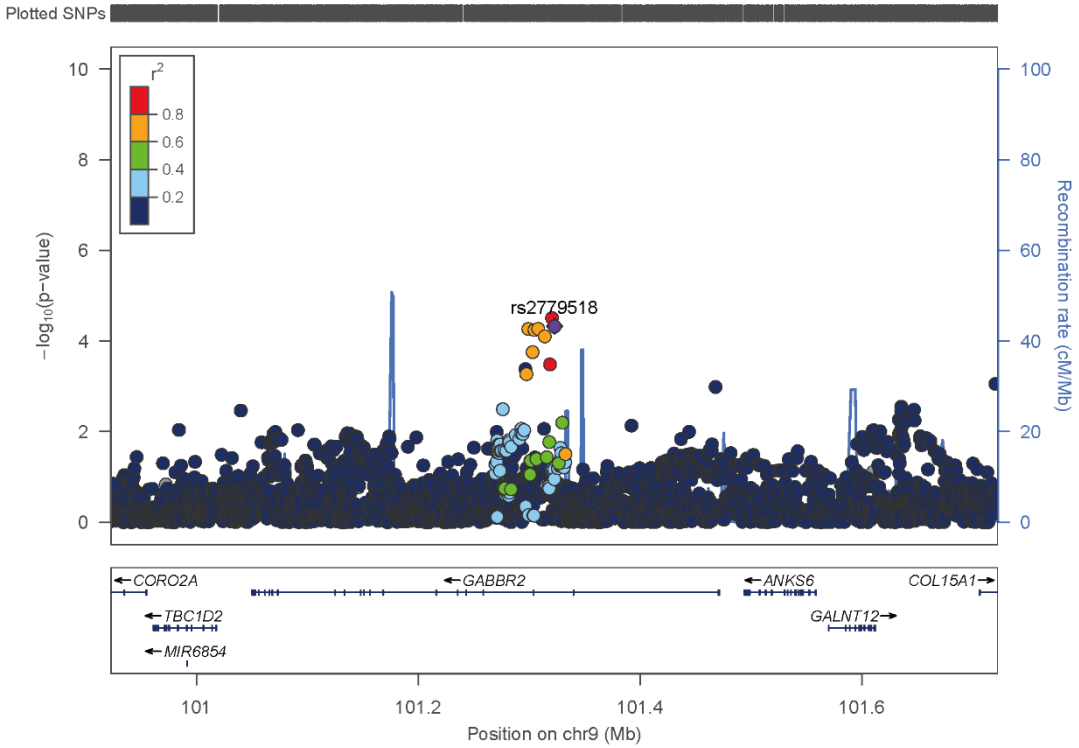
o. *LINGO2*



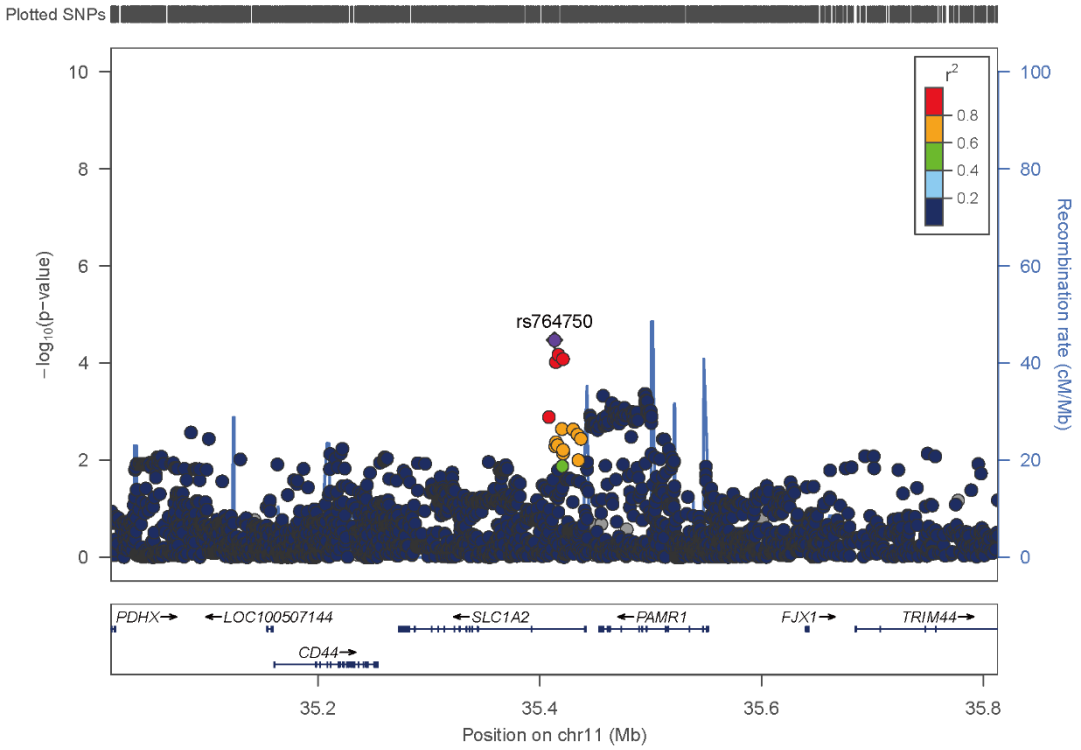
p. *TRPM3*



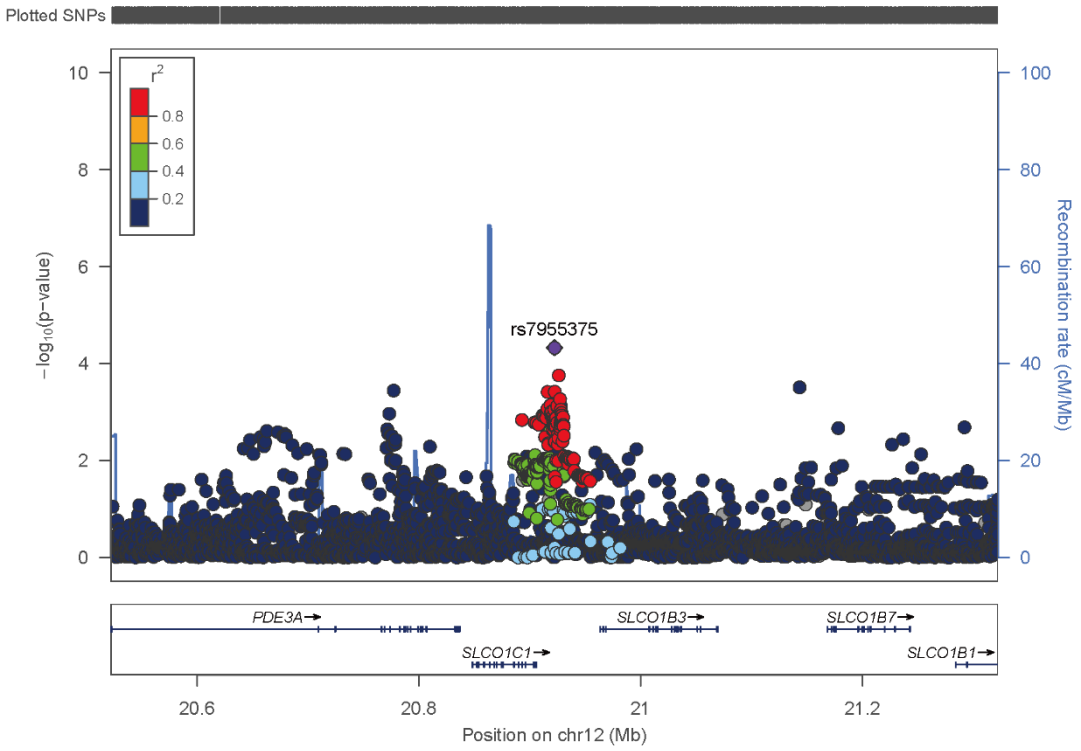
q. *GABBR2*



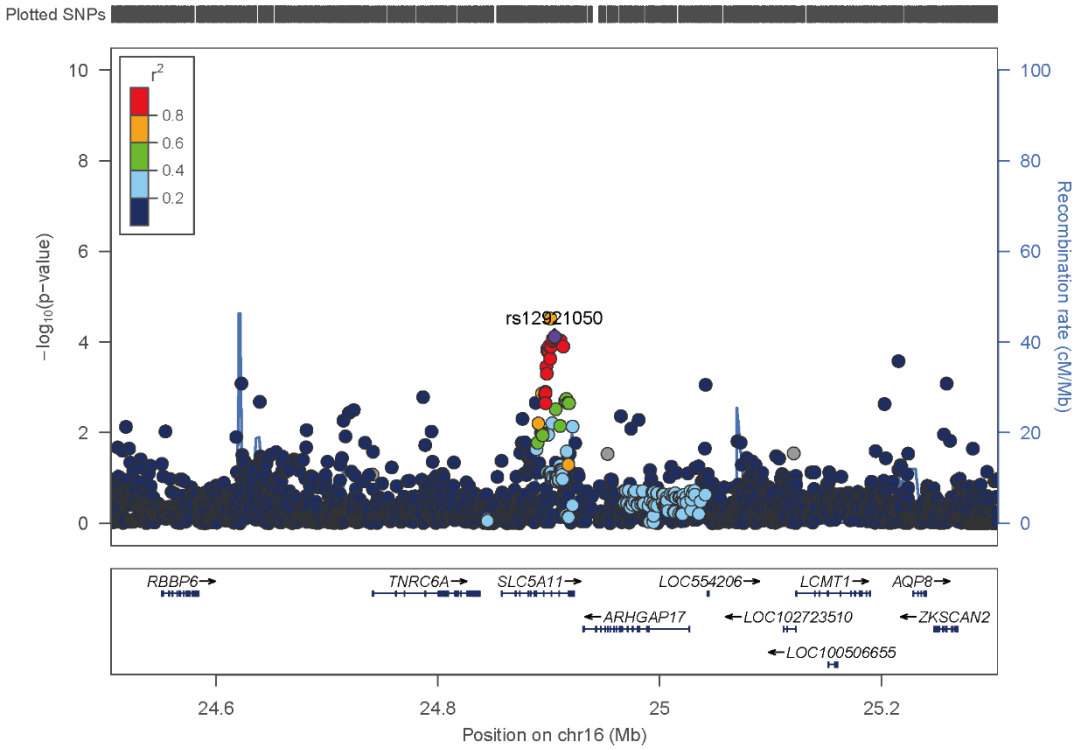
r. *SLC1A2*



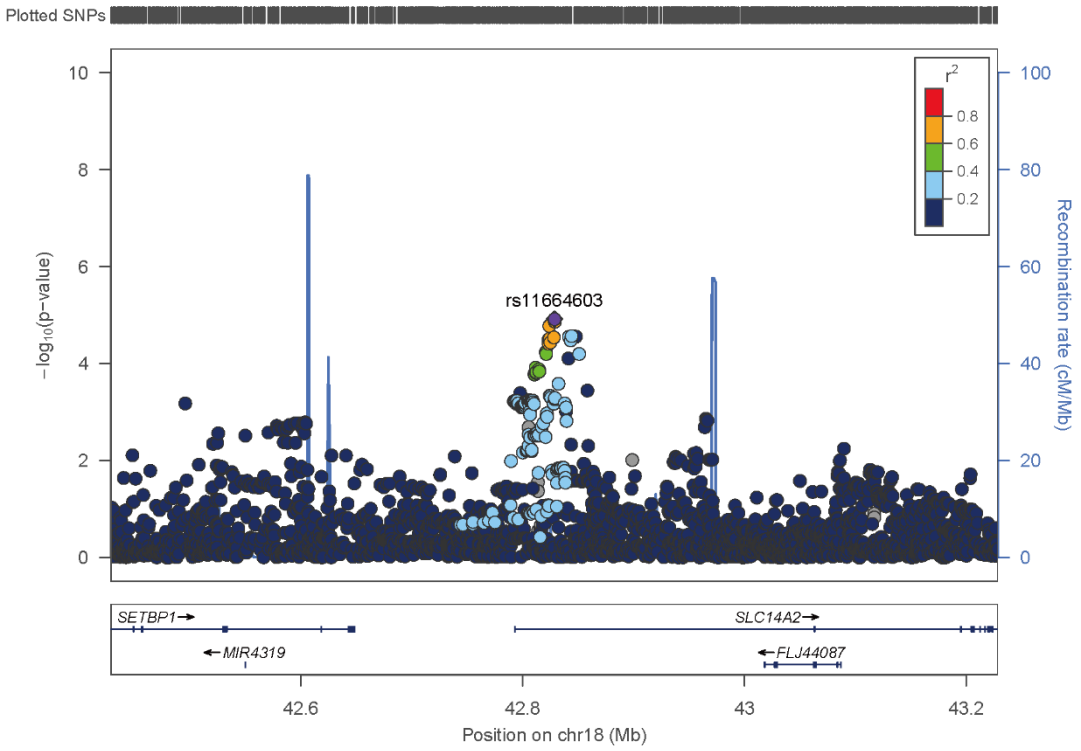
s. *SLCO1C1*



t. *SLC5A11*



u. *SLC14A2*



Supplementary Table 1. Summary statistics for migraine and psychiatric disorders used in this Study.

Traits	Title	PMID	N_{Cases}	$N_{Controls}$
Migraine	Genome-wide analysis of 102,084 migraine cases identifies 123 risk loci and subtype-specific risk alleles.	35115687 (no23andMe)	53,109	316,078
	Meta-analysis of 375,000 individuals identifies 38 susceptibility loci for migraine	27322543 (no23andMe)	29,209	172,931
Major Depression Disorder (MDD)	Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions	30718901 (no23andMe)	170,756	329,443
	Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression	29700475 (no23andMe)	59,851	113,154
Bipolar Disorder (BIP)	Genome-wide association study of more than 40,000 bipolar disorder cases provides new insights into the underlying biology	34002096	41,917	371,549
Attention-Deficit/Hyperactivity Disorder (ADHD)	Genome-wide analyses of ADHD identify 27 risk loci, refine the genetic architecture and implicate several cognitive domains	36702997	38,691	186,843
Autism Spectrum Disorder (ASD)	Identification of common genetic risk variants for autism spectrum disorder	30804558	18,381	27,969
Anxiety Disorders (ANX)	Meta-analysis of genome-wide association studies of anxiety disorders	26754954	7,016	14,745
Schizophrenia (SCZ)	Mapping genomic loci implicates genes and synaptic biology in schizophrenia	35396580	76,755	243,649

Supplementary Table 2. Significant loci identified by MTAG between migraine and MDD.

SNP	CHR	BP	A1	A2	MTAG		MDD		Migraine		Annotation
					Beta	*P*-value	Beta	P-value	Beta	*P*-value	
rs11800270	1	115158978	A	C	0.02831819	1.68E-08	-0.0028	0.7517	-0.114788	1.36E-10	known
rs11800270	1	115158978	A	C	0.02831819	1.68E-08	-0.0028	0.7517	-0.114788	1.36E-10	known
rs12025158	1	15212763	A	G	0.01466599	7.59E-09	0.0016	0.7279	0.050878	1.69E-10	known
rs1553287	1	3184713	A	G	0.01583758	4.89E-08	0.0019	0.7167	0.054028	1.71E-09	known
rs2078371	1	115134562	T	C	-0.0366425	1.69E-22	0.0102	0.1258	0.130542	5.34E-30	known
rs2274319	1	156481081	T	C	0.02180249	8.29E-18	0.0011	0.8084	0.07603	9.25E-22	known
rs7518255	1	3169900	A	G	0.03416781	2.55E-31	-0.0081	0.125	0.121654	1.66E-41	known
rs7544256	1	115281777	A	G	0.0151863	2.22E-09	0.0053	0.2391	-0.050908	1.67E-10	known
rs10166942	2	233916448	T	C	0.03309552	1.95E-27	0.0082	0.1299	-0.114712	5.89E-32	known
rs16872768	5	75686382	T	C	-0.016966	1.61E-11	0.0032	0.4773	0.060829	8.13E-15	known
rs77960	5	104628884	A	G	0.01484326	1.14E-08	0.0363	2.36E-15	0.034496	2.37E-05	new
rs10456100	6	39215694	T	C	0.01693901	3.06E-10	-0.0017	0.7207	0.060734	7.75E-13	known
rs11153082	6	96611790	A	G	-0.0282287	1.19E-27	-0.0015	0.737	0.097701	6.02E-34	known
rs1983551	6	96348174	A	G	0.02183378	7.68E-10	0.0099	0.1135	0.071719	9.72E-11	known
rs2179071	6	22114096	T	C	-0.0138122	1.94E-08	-0.0064	0.1438	-0.046323	3.54E-09	known
rs28581202	6	121501348	A	G	0.02655686	2.06E-15	0.0064	0.2849	0.089936	6.88E-18	known
rs9349379	6	12903725	A	G	0.02343211	1.85E-21	0.0025	0.5619	-0.083752	6.69E-26	known
rs17303101	9	116419515	A	G	0.02160173	5.23E-16	0.0156	0.001067	0.069093	2.37E-16	known
rs953588	9	69089911	T	C	0.01603236	1.47E-10	0.0056	0.2091	0.053487	7.38E-12	known
rs11187838	10	94278929	A	G	-0.0179632	2.09E-13	0.0042	0.3319	-0.06569	1.68E-17	known

rs112255710	10	98841189	T	C	-0.0272558	1.72E-09	8.00E-04	0.921	-0.099362	1.13E-11	known
rs10833535	11	3238248	A	G	0.01451574	2.21E-09	-0.0023	0.5989	0.05296	6.89E-12	known
rs7940646	11	10647681	T	C	-0.0184228	1.23E-12	0.0024	0.5987	-0.066302	4.78E-16	known
rs11172113	12	57133500	T	C	0.03404141	8.93E-44	0.0073	0.09551	-0.117366	1.15E-51	known
rs2160875	12	4418156	T	C	-0.0178167	2.02E-13	8.00E-04	0.8609	0.063007	1.03E-16	known
rs324017	12	57094031	A	C	0.01495255	2.03E-08	0.0049	0.3029	0.050079	1.86E-09	known
rs7140660	14	74878942	T	C	-0.0133513	4.17E-08	-0.0223	2.49E-07	-0.036192	2.33E-06	new
rs11657101	17	62559465	A	G	0.01459418	5.96E-09	-9.00E-04	0.8515	0.061037	4.54E-11	known
rs8075138	17	49436009	T	C	0.01381501	2.42E-08	0.0022	0.6187	0.047889	9.07E-10	known
rs1019990	18	47340365	T	C	-0.0152984	7.61E-09	0.0021	0.6587	-0.055414	3.87E-11	known
rs6046147	20	19499152	T	C	0.01835253	5.84E-11	0.0025	0.6093	0.062723	5.61E-13	known

Note: The effect sizes (Beta, MTAG) and two-sided P-values from the MTAG analysis are shown for each SNP. The P-values are derived from a z-test based on the MTAG beta and its standard error. The genome-wide significance threshold was set at $P<5\times10^{-8}$. No additional multiple testing correction beyond the standard genome-wide threshold was applied. SNPs are annotated as "known" if they were significant in the original migraine GWAS or "new" if identified through the MTAG analysis. A1, effect allele; A2, alternative allele.

Supplementary Table 3. Significant loci identified by condFDR between migraine and MDD.

SNP	CHR	BP	A1	A2	cfdr12	conjFDR	Migraine		MDD		Annotation
							Beta	*P*-value	Beta	*P*-value	
rs12138127	1	3070634	G	C	1.13E-06	0.984813	0.061941	2.59E-14	-0.0011	0.8158	known
rs7544256	1	15539259	A	G	2.40E-05	0.786891	-0.05091	1.67E-10	0.0053	0.2391	known
rs12131921	1	115657613	G	A	6.77E-06	0.788043	0.115262	3.21E-11	-0.0111	0.2412	known
rs207195	1	115682353	G	C	1.13E-06	0.995026	0.089127	3.56E-28	0.0004	0.9361	known
rs77226757	1	115824398	C	T	1.13E-06	0.986111	0.113598	1.92E-12	0.0021	0.8303	known
rs12025158	1	156403681	G	A	2.42E-05	0.973335	0.050878	1.69E-10	0.0016	0.7279	known
rs72926788	2	203820923	T	C	0.000911	0.782753	-0.13026	2.02E-08	0.0135	0.2317	known
rs213543	2	234774025	C	T	1.13E-06	0.999339	-0.10101	3.02E-12	0.0001	0.9913	known
rs2108809	2	234848231	C	T	1.13E-06	0.578235	-0.07493	2.09E-12	-0.014	0.01909	known
rs7640543	3	30462403	G	A	0.000688	0.800559	0.046099	1.34E-08	0.0051	0.2652	known
rs13078967	3	80302512	A	C	1.78E-05	0.769631	-0.16296	1.11E-10	-0.018	0.2005	known
rs950570	3	154289946	C	T	0.00067	0.764726	0.084732	1.29E-08	0.0106	0.1894	known
rs7684253	4	57727311	C	T	0.000554	0.79245	-0.04389	1.00E-08	-0.005	0.2494	known
rs34351	5	74952861	A	C	1.13E-06	0.803906	0.056367	2.16E-12	0.005	0.272	known
rs148466297	6	12873775	C	T	5.14E-05	0.980001	0.12963	4.70E-10	-0.0038	0.764	known
rs9381462	6	22128962	G	A	1.13E-06	0.959298	0.062876	3.86E-16	0.0019	0.667	known
rs77153179	6	39165859	G	A	0.000618	0.9793	0.125676	1.16E-08	0.0042	0.7567	known
rs34466473	6	96703520	G	A	1.13E-06	0.943195	0.068981	3.14E-12	0.0029	0.6029	known
rs6904682	6	96841762	T	C	0.000253	0.76006	-0.04514	3.52E-09	-0.0058	0.1794	known
rs9394578	6	97050396	C	A	1.13E-06	0.99828	0.061379	1.77E-12	-0.0001	0.9775	known

rs2499787	6	121781659	C	G	1.13E-06	0.86475	0.095526	1.85E-20	-0.0048	0.4044	known
rs73320559	7	40360982	G	T	1.13E-06	0.80293	0.085618	1.15E-12	-0.0076	0.27	known
rs17303101	9	71704827	G	A	1.35E-07	0.214261	0.069093	2.37E-16	0.0156	0.001067	known
rs953588	9	119181794	C	T	1.99E-06	0.773254	0.053487	7.38E-12	0.0056	0.2091	known
rs112255710	10	96012950	C	T	2.86E-06	0.993809	-0.09936	1.13E-11	0.0008	0.921	known
rs12260436	10	100600946	A	C	6.76E-05	0.741663	0.053511	6.55E-10	0.0071	0.149	known
rs7080472	10	104741114	G	T	1.13E-06	0.82723	-0.06387	1.80E-16	0.0043	0.3216	known
rs2672592	10	124230750	G	T	0.000896	0.860922	0.044135	1.97E-08	0.0038	0.3951	known
rs6484437	11	3259478	G	A	1.13E-06	0.919418	-0.06268	1.34E-14	0.0029	0.5296	known
rs10833535	11	10667275	A	G	1.87E-06	0.942138	0.05296	6.89E-12	-0.0023	0.5989	known
rs703816	12	4515374	T	C	1.86E-07	0.244004	-0.07475	1.16E-21	0.0136	0.001896	known
rs10774231	12	57497005	T	C	1.13E-06	0.965242	0.055076	1.04E-12	0.0017	0.6922	known
rs35616842	12	57524108	T	C	0.000866	0.929946	0.068561	1.87E-08	0.0039	0.5568	known
rs715948	12	57532982	C	T	1.13E-06	0.996707	0.060406	2.18E-13	0.0003	0.9573	known
rs28540738	14	93591673	A	G	5.07E-05	0.365503	-0.05123	9.70E-10	-0.013	0.005326	known
rs11657101	17	47513371	A	G	8.95E-06	0.987974	0.061037	4.54E-11	-0.0009	0.8515	known
rs8075138	17	60636826	C	T	8.76E-05	0.947305	0.047889	9.07E-10	0.0022	0.6187	known
rs1019990	18	44866736	C	T	7.94E-06	0.957295	-0.05541	3.87E-11	0.0021	0.6587	known
rs1025497	19	41871254	G	A	3.57E-05	0.794653	-0.04993	2.89E-10	0.0051	0.2536	known
rs6081612	20	19460951	G	C	1.13E-06	0.942773	0.060529	3.50E-12	0.0026	0.6013	known
rs16980673	20	19473155	A	G	0.000813	0.825498	-0.06885	1.70E-08	0.0067	0.3182	known

Note: Variants were considered significant for the primary trait (migraine) if they passed a condFDR threshold (cfdr12) of < 0.01; this threshold inherently controls for multiple comparisons.

Supplementary Table 4. Significant loci identified by MTAG between migraine and ADHD.

SNP	CHR	BP	A1	A2	MTAG		Migraine		ADHD		Annotation
					Beta	P-value	Beta	P-value	Beta	P-value	
rs7518255	1	3086464	G	A	-0.036270	6.56E-36	-0.121654	1.66E-41	0.0366983	0.007062	known
rs1171557	1	156451264	C	T	-0.021344	5.81E-14	-0.065884	1.59E-13	-0.0346018	0.009349	known
rs727241	2	145694454	A	G	-0.015708	9.57E-09	-0.044646	1.94E-07	-0.0460021	0.00001667	known
rs4662236	2	146034665	A	G	-0.014874	9.75E-09	-0.0444	5.76E-08	-0.0307995	0.002952	known
rs72926788	2	203820923	T	C	0.037347	3.29E-09	0.130256	2.02E-08	0.0669014	0.006426	known
rs72940158	2	204263036	A	G	0.030682	3.16E-08	0.095452	7.23E-07	0.0884961	0.00008265	known
rs12202891	6	12768218	C	T	0.019953	1.29E-10	0.069856	5.58E-10	0.0336959	0.01166	known
rs6911827	6	22130601	C	T	0.014258	2.55E-09	0.044565	5.81E-09	0.0200967	0.04843	known
rs716192	6	96511689	G	A	0.013971	6.20E-09	0.042306	3.04E-08	0.0248975	0.008153	known
rs4839683	6	96851933	A	G	0.028899	3.67E-23	0.090067	3.94E-23	0.025502	0.04775	known
rs75510803	6	97062220	T	C	-0.040165	4.65E-08	-0.127361	3.06E-09	0.0745043	0.02251	known
rs17303101	9	119181794	G	A	-0.021718	1.25E-16	-0.069093	2.37E-16	-0.0235962	0.02403	known
rs17102884	14	75374899	C	T	0.014063	4.34E-08	0.042464	1.86E-07	0.0255995	0.01089	known
rs28929474	14	94844947	C	T	-0.047276	3.16E-08	-0.144046	8.61E-08	-0.0906033	0.007059	known
rs6119269	20	31167877	G	A	-0.014647	6.01E-09	-0.044548	3.69E-08	-0.0307995	0.002565	known

Note: The effect sizes (Beta, MTAG) and two-sided P-values from the MTAG analysis are shown for each SNP. The P-values are derived from a z-test based on the MTAG beta and its standard error. The genome-wide significance threshold was set at $P<5\times10^{-8}$. No additional multiple testing correction beyond the standard genome-wide threshold was applied. SNPs are annotated as "known" if they were significant in the original migraine GWAS or "new" if identified through the MTAG analysis. A1, effect allele; A2, alternative allele.

Supplementary Table 5. Significant loci identified by condFDR between migraine and ADHD.

SNP	CHR	BP	A1	A2	cfdr21	conjFDR	Migraine		ADHD		Annotation
							Beta	*P*-value	Beta	*P*-value	
rs1736522	1	3080940	C	G	0.000000	0.102060	-0.07744	3.12E-24	0.0397975	0.0006976	known
rs2354888	2	7991865	G	A	0.002485	0.330832	0.040463	4.48E-07	0.0280042	0.01428	known
rs12711738	2	113030784	C	T	0.004081	0.508068	0.03845	4.25E-07	0.0192044	0.04034	known
rs727241	2	145694454	A	G	0.001142	0.013129	-0.044646	1.94E-07	-0.0460021	1.667E-05	known
rs4662236	2	146034665	A	G	0.000544	0.203442	-0.0444	5.76E-08	-0.0307995	0.002952	known
rs72926788	2	203820923	T	C	0.000321	0.263976	0.130256	2.02E-08	0.0669014	0.006426	known
rs116219813	2	204081675	C	T	0.004629	0.012830	0.049487	2.57E-05	0.0621012	1.59E-05	known
rs146902012	2	204352252	C	T	0.001753	0.254759	0.109448	3.22E-07	0.0680978	0.005728	known
rs7640543	3	30462403	G	A	0.000564	0.531841	-0.046099	1.34E-08	0.0199007	0.04593	known
rs11919589	3	38935192	A	G	0.009843	0.388473	-0.039986	4.85E-06	0.0247024	0.02044	known
rs62261725	3	85898626	A	G	0.002361	0.009216	-0.036112	7.1E-06	0.045002	5.884E-06	known
rs73138150	3	86149109	A	T	0.002000	0.007345	-0.040622	1.29E-06	0.0489044	2.852E-06	known
rs9850281	3	86848765	C	G	0.001232	0.155697	0.040782	2.17E-07	-0.0341981	0.001795	known
rs10516474	4	101989816	C	T	0.009326	0.106628	0.049378	2.88E-05	0.0515008	0.0007644	known
rs3974602	4	103849997	T	C	0.002136	0.017896	0.0349	5.98E-06	0.0394995	3.199E-05	known
rs1496332	5	92439320	A	G	0.002232	0.050713	0.036635	1.52E-06	0.0350003	0.0001786	known
rs2431108	5	103947968	T	C	0.004307	0.004307	-0.034592	2.21E-05	-0.0730009	2.879E-13	known
rs716192	6	96511689	G	A	0.000443	0.280998	0.042306	3.04E-08	0.0248975	0.008153	known
rs77153179	6	96703520	G	A	0.000176	0.140734	-0.125676	1.16E-08	0.0919044	0.001367	known
rs2983898	6	97041635	C	T	0.000010	0.095411	-0.119475	1.3E-09	0.0880017	0.0005999	known

rs118203	6	111658220	T	G	0.007308	0.261946	0.042873	7.13E-06	0.0323994	0.006246	known
rs6923836	6	113393530	G	A	0.007844	0.151262	-0.033381	1.26E-05	0.0294035	0.001705	known
rs2944772	8	141548419	C	G	0.005302	0.227855	0.044827	5.39E-06	0.0329995	0.004219	known
rs17303101	9	119181794	G	A	0.000001	0.417220	-0.069093	2.37E-16	-0.0235962	0.02403	known
rs61886179	10	96348694	G	A	0.004460	0.516495	0.09004	4.66E-07	0.0425996	0.04224	known
rs7930346	11	15119961	T	A	0.007172	0.215045	0.035528	8.79E-06	0.0285	0.003412	known
rs11031126	11	30553514	C	T	0.004227	0.299837	-0.042751	9.63E-07	-0.0278955	0.01002	known
rs7932866	11	46548094	A	G	0.006910	0.416776	0.051923	1.19E-06	-0.0316042	0.02397	known
rs705702	12	56390636	A	G	0.002783	0.012612	0.036288	9.01E-06	0.0437968	1.534E-05	known
rs17619763	12	110645829	G	A	0.008981	0.306985	0.062565	7.25E-06	0.0454035	0.01083	known
rs4765150	12	124970087	G	A	0.006427	0.216495	0.055685	7.53E-06	0.0425996	0.003495	known
rs57044214	14	58833909	G	A	0.000670	0.149380	0.045227	8.2E-08	-0.0322959	0.001639	known
rs12437105	14	69161331	G	A	0.003507	0.353921	-0.041569	6.26E-07	-0.0243029	0.01682	known
rs17102884	14	75374899	C	T	0.001260	0.307493	0.042464	1.86E-07	0.0255995	0.01089	known
rs61980636	14	94784618	C	T	0.004597	0.124771	-0.042814	6.28E-06	-0.0386992	0.001052	known
rs28929474	14	94844947	C	T	0.000761	0.270692	-0.144046	8.61E-08	-0.0906033	0.007059	known
rs7145262	14	100125721	C	T	0.002396	0.220839	0.039206	5.49E-07	-0.0266007	0.003756	known
rs2759310	15	81015065	T	C	0.002000	0.031337	-0.036929	5.04E-06	-0.0385953	0.00007804	known
rs7183740	15	91558457	G	A	0.008000	0.329443	-0.053485	4.21E-06	-0.0352024	0.01405	known
rs2236374	17	1989637	C	T	0.006104	0.184625	0.03438	7.86E-06	-0.0286979	0.002411	known
rs6057599	20	31168439	C	T	0.000351	0.227927	-0.044739	3.2E-08	-0.0281012	0.004224	known

Note: Variants were considered significant for the primary trait (migraine) if they passed a condFDR threshold (cfdr12) of < 0.01; this threshold inherently controls for multiple comparisons.

Supplementary Table 6. Significant loci identified by MTAG between migraine and ASD.

SNP	CHR	BP	A1	A2	MTAG		Migraine		ASD		Annotation
					Beta	P-value	Beta	P-value	Beta	P-value	
rs10166942	2	234825093	T	C	0.034473	1.37E-29	0.114712	5.89E-32	-0.0383979	0.02754	known
rs7684253	4	57727311	T	C	0.014280	5.44E-09	0.043886	1.00E-08	0.034498	0.01398	known
rs716192	6	96511689	A	G	-0.014042	1.10E-08	-0.042306	3.04E-08	-0.0442968	0.001463	known
rs4839828	6	96863326	A	G	-0.029581	1.10E-30	-0.092097	4.87E-31	-0.0292023	0.04375	known
rs151048610	6	97081199	T	C	0.040533	4.01E-08	0.126351	6.32E-09	-0.0868987	0.04335	known
rs12523888	6	121781385	T	C	-0.018746	7.80E-11	-0.059019	1.07E-10	-0.0347985	0.0402	known
rs953588	9	71704827	T	C	0.017364	4.78E-12	0.053487	7.38E-12	0.0326995	0.02214	known
rs17303101	9	119181794	A	G	0.022113	1.40E-16	0.069093	2.37E-16	0.0400953	0.009001	known
rs61888680	10	96198782	A	C	0.029822	1.95E-08	0.095243	6.46E-08	0.111801	0.0004058	known
rs112255710	10	100600946	T	C	-0.029012	1.43E-10	-0.099362	1.13E-11	0.0639977	0.0161	known
rs112635299	14	94838142	T	G	0.048715	1.31E-08	0.145021	1.01E-07	0.220997	3.044E-07	known

Note: The effect sizes (Beta, MTAG) and two-sided P-values from the MTAG analysis are shown for each SNP. The P-values are derived from a z-test based on the MTAG beta and its standard error. The genome-wide significance threshold was set at $P<5\times10^{-8}$. No additional multiple testing correction beyond the standard genome-wide threshold was applied. SNPs are annotated as "known" if they were significant in the original migraine GWAS or "new" if identified through the MTAG analysis. A1, effect allele; A2, alternative allele.

Supplementary Table 7. Significant loci identified by condFDR between migraine and ASD.

SNP	CHR	BP	A1	A2	cfdr21	conjFDR	Migraine		ASD		Annotation
							Beta	*P*-value	Beta	*P*-value	
rs2478819	1	208274114	T	C	0.009461	0.339343	0.036569	2.81E-06	0.0347975	0.01398	known
rs34623958	2	113031217	A	G	0.003423	0.527026	0.038644	3.72E-07	0.0278	0.04527	known
rs114287800	3	49450137	A	C	0.009492	0.341546	0.142285	2.1E-06	0.114899	0.01427	known
rs7433888	3	49838053	T	C	0.008915	0.322695	-0.127461	2.83E-06	-0.113796	0.01265	known
rs1437055	3	86831077	A	C	0.000575	0.233277	0.041726	8.1E-08	-0.0430015	0.002367	known
rs7684253	4	57727311	T	C	0.000276	0.339343	0.043886	1.00E-08	0.034498	0.01398	known
rs4699042	4	103892823	T	C	0.005997	0.233277	0.03623	2.72E-06	0.0404027	0.003485	known
rs6883741	5	92491481	A	T	0.003091	0.132039	-0.037083	1.12E-06	-0.0492007	4.07E-04	known
rs513886	5	127646426	T	C	0.004225	0.141586	0.036411	1.69E-06	-0.0484972	4.58E-04	known
rs1322537	6	19023726	T	C	0.002421	0.160717	0.049507	8.25E-07	-0.0628972	6.35E-04	known
rs716192	6	96511689	A	G	0.000184	0.233277	-0.042306	3.04E-08	-0.0442968	0.001463	known
rs77153179	6	96703520	A	G	0.000309	0.505539	0.125676	1.16E-08	-0.0857976	0.04111	known
rs13246993	7	73022746	A	G	0.006960	0.266277	-0.055551	3.31E-06	-0.0551956	0.008566	known
rs953588	9	71704827	T	C	0.000001	0.404761	0.053487	7.38E-12	0.0326995	0.02214	known
rs17303101	9	119181794	A	G	0.000001	0.272535	0.069093	2.37E-16	0.0400953	0.009001	known
rs61886179	10	96348694	A	G	0.001537	0.173955	-0.09004	4.66E-07	-0.102997	8.06E-04	known
rs112255710	10	100600946	T	C	0.000001	0.354497	-0.099362	1.13E-11	0.0639977	0.0161	known
rs12266070	10	100871223	A	G	0.006204	0.485560	-0.071101	8.16E-07	0.0535976	0.0374	known
rs1902910	12	41778982	A	G	0.006870	0.256245	0.04486	4.22E-06	-0.048004	0.00553	known
rs28929474	14	94844947	T	C	0.000388	0.003482	0.144046	8.61E-08	0.209799	1.58E-06	known

Note: Variants were considered significant for the primary trait (migraine) if they passed a condFDR threshold (cfdr12) of < 0.01; this threshold inherently controls for multiple comparisons.

Supplementary Table 8. Significant loci identified by MTAG between migraine and ANX.

SNP	CHR	BP	A1	A2	MTAG		Migraine		ANX		Annotation
					Beta	P-value	Beta	P-value	Beta	P-value	
rs7544256	1	115824398	A	G	0.016244	2.31E-10	0.050908	1.67E-10	0.0539	0.04873	known
rs17863842	2	234842119	T	C	-0.041537	3.32E-24	-0.135556	1.06E-24	-0.1081	0.02006	known
rs9399923	6	96850379	A	G	-0.029235	3.69E-23	-0.090982	1.32E-23	-0.0731	0.02082	known
rs79692456	7	40380529	T	G	0.038199	4.49E-10	0.118789	2.56E-10	0.5184	0.004455	known
rs11026091	11	3259809	A	G	0.016375	2.54E-11	0.051251	1.75E-11	0.054	0.04581	known

Note: The effect sizes (Beta, MTAG) and two-sided P-values from the MTAG analysis are shown for each SNP. The P-values are derived from a z-test based on the MTAG beta and its standard error. The genome-wide significance threshold was set at $P<5\times10^{-8}$. No additional multiple testing correction beyond the standard genome-wide threshold was applied. SNPs are annotated as "known" if they were significant in the original migraine GWAS or "new" if identified through the MTAG analysis. A1, effect allele; A2, alternative allele.

Supplementary Table 9. Significant loci identified by condFDR between migraine and ANX.

SNP	CHR	BP	A1	A2	cfdr21	conjFDR	Migraine		ANX		Annotation
							Beta	*P*-value	Beta	*P*-value	
rs7544256	1	115824398	A	G	1.21951E-05	0.944175	0.050908	1.67E-10	0.0539	0.04873	known
rs12472063	2	7990214	T	C	0.005486503	0.916322	-0.040378	4E-07	0.0656	0.0282	known
rs7558436	2	234835679	C	G	2.36141E-07	0.916322	0.130558	2.14E-23	0.0961	0.0268	known
rs9296512	6	12894904	C	G	2.53808E-07	0.943677	-0.075108	1.84E-21	-0.0585	0.04789	known
rs2499787	6	96841762	C	G	2.36141E-07	0.916322	-0.095526	1.85E-20	-0.0773	0.02836	known
rs11601864	11	3258522	C	G	8.33096E-07	0.908411	-0.054478	7.34E-12	-0.0853	0.006664	known

Note: Variants were considered significant for the primary trait (migraine) if they passed a condFDR threshold (cfdr12) of < 0.01; this threshold inherently controls for multiple comparisons.

Supplementary Table 10. Significant loci identified by MTAG between migraine and BIP.

SNP	CHR	BP	A1	A2	MTAG		Migraine		BIP		Annotation
					Beta	P-value	Beta	P-value	Beta	P-value	
rs746527	1	156460511	C	T	-0.020320	3.97E-13	-0.064184	2.1E-13	-0.021704	0.04947	known
rs71308498	3	154436444	C	T	0.043917	1.37E-09	0.163336	8.88E-10	0.078099	0.01452	known
rs9381401	6	12801967	A	C	0.015676	1.81E-10	0.050876	1.04E-10	-0.021101	0.02711	known
rs6939383	6	96847181	A	G	0.019310	2.77E-15	0.060997	1.2E-15	-0.020999	0.02498	known
rs12260436	10	104741114	A	C	-0.017195	1.00E-09	-0.053511	6.55E-10	0.027498	0.01236	known
rs4559	12	57489648	C	T	0.014556	1.57E-08	0.045469	1.01E-08	-0.019499	0.04955	known
rs11172113	12	57527283	T	C	0.036793	2.19E-50	0.117366	1.15E-51	-0.019101	0.04545	known
rs6504612	17	47498134	G	T	-0.014011	1.18E-08	-0.044495	7.5E-09	-0.022000	0.02643	known

Note: The effect sizes (Beta, MTAG) and two-sided P-values from the MTAG analysis are shown for each SNP. The P-values are derived from a z-test based on the MTAG beta and its standard error. The genome-wide significance threshold was set at $P<5\times10^{-8}$. No additional multiple testing correction beyond the standard genome-wide threshold was applied. SNPs are annotated as "known" if they were significant in the original migraine GWAS or "new" if identified through the MTAG analysis. A1, effect allele; A2, alternative allele.

Supplementary Table 11. Significant loci identified by condFDR between migraine and BIP.

SNP	CHR	BP	A1	A2	cfdr21	conjFDR	Migraine		BIP		Annotation
							Beta	*P*-value	Beta	*P*-value	
rs2272785	1	175161599	G	T	0.004277	0.211356	0.044264	2.86E-07	0.0341985	0.001208	known
rs2287431	2	211320288	A	C	0.009709	0.563349	0.042534	7.98E-07	-0.0232993	0.026	known
rs1047891	2	211540507	C	A	0.009869	0.195246	-0.041306	8.22E-07	0.034498	0.001021	known
rs6939383	6	96847181	A	G	8.51E-07	0.557328	0.060997	1.2E-15	-0.0209989	0.02498	known
rs12260436	10	104741114	A	C	0.000055	0.483781	-0.053511	6.55E-10	0.0274984	0.01236	known
rs12807220	11	102077200	G	A	0.006918	0.421554	-0.040396	4.68E-07	-0.0263953	0.007678	known
rs324015	12	57490100	T	C	2.98E-07	0.150320	0.06207	1.88E-12	-0.0383043	0.0005991	known
rs35616842	12	57524108	T	C	0.000772	0.494822	-0.068561	1.87E-08	-0.0367988	0.01367	known
rs6581124	12	57545756	G	A	0.003932	0.285827	0.047071	1.91E-07	-0.0328952	0.00248	known
rs1190824	14	58671059	G	A	0.000726	0.075387	0.042682	1.19E-07	-0.0383043	0.0001549	known

Note: Variants were considered significant for the primary trait (migraine) if they passed a condFDR threshold (cfdr12) of < 0.01; this threshold inherently controls for multiple comparisons.

Supplementary Table 12. Significant loci identified by MTAG between migraine and SCZ.

SNP	CHR	BP	A1	A2	MTAG		Migraine		SCZ		Annotation
					Beta	P-value	Beta	P-value	Beta	P-value	
rs2078371	1	115677183	T	C	-0.041462	2.22E-28	-0.130542	5.34E-30	-0.055301	3.07E-05	known
rs2112347	5	75015242	T	G	-0.019251	2.80E-14	-0.061529	6.55E-15	-0.017604	0.04902	known
rs7454157	6	12909874	G	A	-0.022729	2.94E-19	-0.072502	4.40E-20	-0.018001	0.04434	known
rs7030607	9	119245183	G	A	0.013778	4.02E-08	0.044775	1.60E-08	0.017899	0.04781	known
rs74154360	10	100750382	T	C	0.028166	7.69E-10	0.091886	2.61E-10	0.031499	0.04433	known
rs12260436	10	104741114	A	C	-0.017794	2.37E-10	-0.053511	6.55E-10	0.052801	5.93E-08	known
rs10766806	11	3258448	C	A	-0.014644	1.69E-09	-0.048055	5.49E-10	-0.019601	0.02353	known
rs7961602	12	57273481	C	T	0.014949	1.44E-09	0.046343	2.51E-09	-0.033505	1.49E-04	known
rs4559	12	57489648	C	T	0.015003	5.15E-09	0.045469	1.01E-08	-0.038897	1.79E-05	known
rs11172113	12	57527283	T	C	0.036965	3.75E-51	0.117366	1.15E-51	-0.024200	5.94E-03	known

Note: The effect sizes (Beta, MTAG) and two-sided P-values from the MTAG analysis are shown for each SNP. The P-values are derived from a z-test based on the MTAG beta and its standard error. The genome-wide significance threshold was set at $P<5\times10^{-8}$. No additional multiple testing correction beyond the standard genome-wide threshold was applied. SNPs are annotated as "known" if they were significant in the original migraine GWAS or "new" if identified through the MTAG analysis. A1, effect allele; A2, alternative allele.

Supplementary Table 13. Significant loci identified by condFDR between migraine and SCZ.

SNP	CHR	BP	A1	A2	cfdr21	conjFDR	Migraine		SCZ		Annotation
							Beta	*P*-value	Beta	*P*-value	
rs1472662	1	39590409	G	T	0.007695	0.179950	-0.045482	8.53E-07	0.031402	3.09E-03	known
rs598202	1	60498083	A	G	0.006925	0.484149	-0.038972	5.41E-07	0.018203	0.04	known
rs7511672	1	66178918	A	G	0.005511	0.184958	-0.038885	3.60E-07	-0.025605	3.29E-03	known
rs2078371	1	115677183	T	C	0.000001	0.019701	-0.130542	5.34E-30	-0.055301	3.07E-05	known
rs2272784	1	175161849	G	T	0.003481	0.020099	-0.038019	7.28E-07	-0.035897	3.88E-05	known
rs2287431	2	211320288	A	C	0.008813	0.303269	0.042534	7.98E-07	-0.024703	0.01	known
rs3974602	4	103849997	T	C	0.008529	0.017649	0.0349	5.98E-06	-0.037795	1.58E-05	known
rs1496332	5	92439320	A	G	0.007669	0.058661	0.036635	1.52E-06	0.030898	3.69E-04	known
rs1322537	6	19023726	T	C	0.007594	0.133177	0.049507	8.25E-07	0.036100	1.70E-03	known
rs7805733	7	120450658	G	A	0.003841	0.497130	-0.045906	1.86E-07	-0.020897	0.04	known
rs7835270	8	103668320	A	G	0.008286	0.008286	-0.036941	5.60E-06	0.044199	8.96E-07	known
rs12260436	10	104741114	A	C	0.000055	0.000845	-0.053511	6.55E-10	0.052801	5.93E-08	known
rs12574668	11	46422686	C	A	0.004033	0.004033	0.050332	1.05E-06	-0.083903	1.90E-13	known
rs61884307	11	46755388	G	C	0.004849	0.004849	0.065315	1.46E-06	-0.094300	2.37E-10	known
rs1352307	11	47168254	A	G	0.006500	0.006500	0.064616	2.49E-06	-0.096698	1.64E-10	known
rs1843314	12	57362422	G	A	0.000001	0.035639	0.061346	1.57E-14	-0.034695	1.35E-04	known
rs7398375	12	57540848	C	G	0.000405	0.176961	-0.054416	7.57E-09	0.030898	2.98E-03	known
rs17619763	12	110645829	G	A	0.008982	0.023839	0.062565	7.25E-06	0.062299	6.21E-05	known
rs55707505	14	75362552	T	C	0.003516	0.027239	0.041577	2.82E-07	0.036197	8.18E-05	known
rs8046785	16	4570350	C	T	0.009769	0.043747	0.037647	4.28E-06	0.034401	2.06E-04	known
rs34523388	18	20204573	G	A	0.005266	0.369942	0.039284	3.23E-07	0.020596	0.02	known

Note: Variants were considered significant for the primary trait (migraine) if they passed a condFDR threshold (cfdr12) of < 0.01; this threshold inherently

controls for multiple comparisons.

Supplementary Table 14. Detailed information for single-cell eQTL data used in this Study.

Cell Type	Cell State	Study	DOI
conventional Dendritic Cell	SARS-CoV-2-stimulated	Aquino, Y., et al, Nature (2023)	https://doi.org/10.1038/s41586-023-06422-9
Conventional dendritic Cell	Influenza A virus-stimulated		
Conventional Dendritic Cell	Influenza A virus-stimulated		
Conventional Dendritic Cell	Non-stimulated		
Excitatory neurons	NA	Bryois, J., et al, Nat Neurosci (2022)	https://doi.org/10.1038/s41593-022-01128-z
Inhibitory neurons	NA		
dopaminergic neurons	Cell proliferation on day 52	Jerber, J., et al, Nat Genet (2021)	https://doi.org/10.1038/s41588-021-00801-6
serotonergic-like neurons	Cell proliferation on day 52; treated with rotenone		
serotonergic-like neurons	Cell proliferation on day 52		
dopaminergic neurons	Cell proliferation on day 30		
serotonergic-like neurons	Cell proliferation on day 30		
dopaminergic neurons	Cell proliferation on day 52; treated with rotenone		
Conventional Dendritic Cell	cDC1	Natri HM., et al, bioRxiv [Preprint] (2023)	https://doi.org/10.1101/2023.03.17.533161
Conventional Dendritic Cell	cDC2		
Conventional Dendritic Cell	cDC1 / cDC2	Perez RK., et al, Science (2022)	https://doi.org/10.1126/science.abf1970
Conventional Dendritic Cell	cDC1 / cDC2; type 1 interferon activation		