ANCO-GeneDB

1. Home Page:

ANCO-Gene DB | Alcohol Nicotine Cocaine Opioid

About ANCO-GeneDB

Addiction is a brain disorder characterized by compulsive engagement in rewarding stimuli despite adverse consequences. Addiction may involve the use of substances such as alcohol, nicotine, cocaine, opioids, and others, or behaviors such as gambling; there is scientific evidence that the addictive substances and behaviors share a key neurobiological feature—they intensely activate brain pathways of reward and reinforcement, many of which involve the neurotransmitter dopamine.

The ANCO-GeneDB (Alcohol Nicotine Cocaine Opiate addiction-associated Gene Database) is a comprehensive online resource for addiction researches. Built in 2018, ANCO-GeneDB curates data from genetics studies, transcriptome studies, and epigenetics studies. ANCO-GeneDB is a one-stop shop for addictions. Our long-term goal is to provide resources and tools for researchers to have a better understanding of addictions and to find cure approaches. Our ultimate goal is to reduce the pain and troubles that addiction brings to life, improve the life quality, and to contribute to successful therapies for patients.

Currently, the ANCO-Gene Database contains 6 types of datasets by retrieving literature and online resources collection.

Recent News

Jun 22, 2018 - Results of Tissue-Specific Enrichment Analysis (TSEA) are available.

Jun 10, 2018 - MetaXcan analysis has been done.

May 26, 2018 - Sherlock and Pascal Analysis have been done.

May 18, 2018 - DNA methylation data are added to ANCO-GeneDB.

Apr 20, 2018 - CNV calls are now available in the ANCO-GeneDB.

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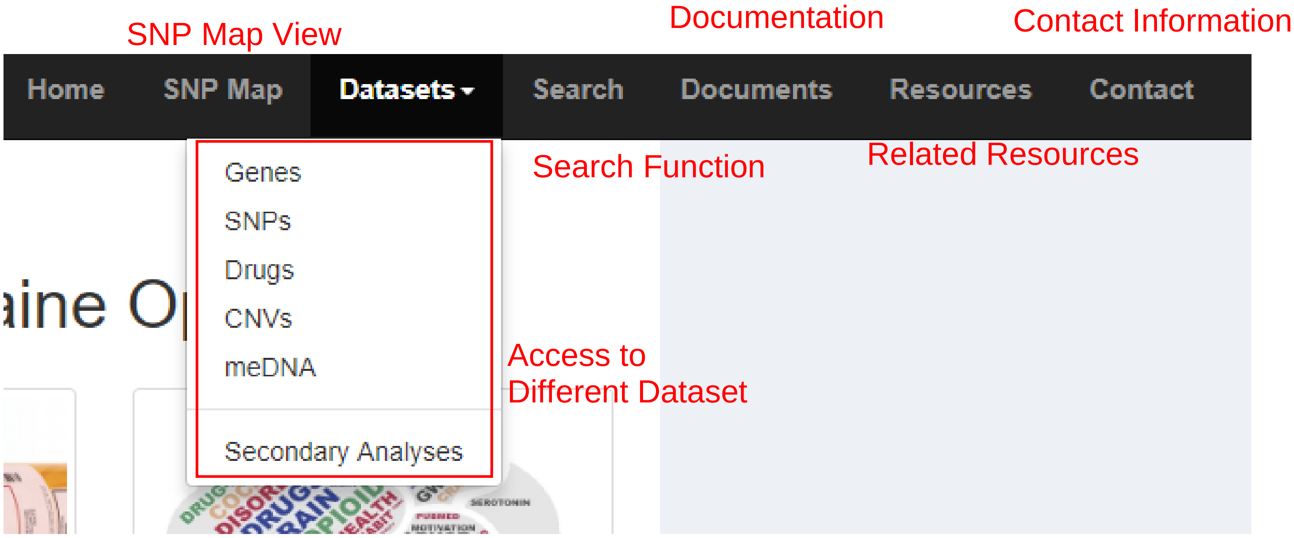
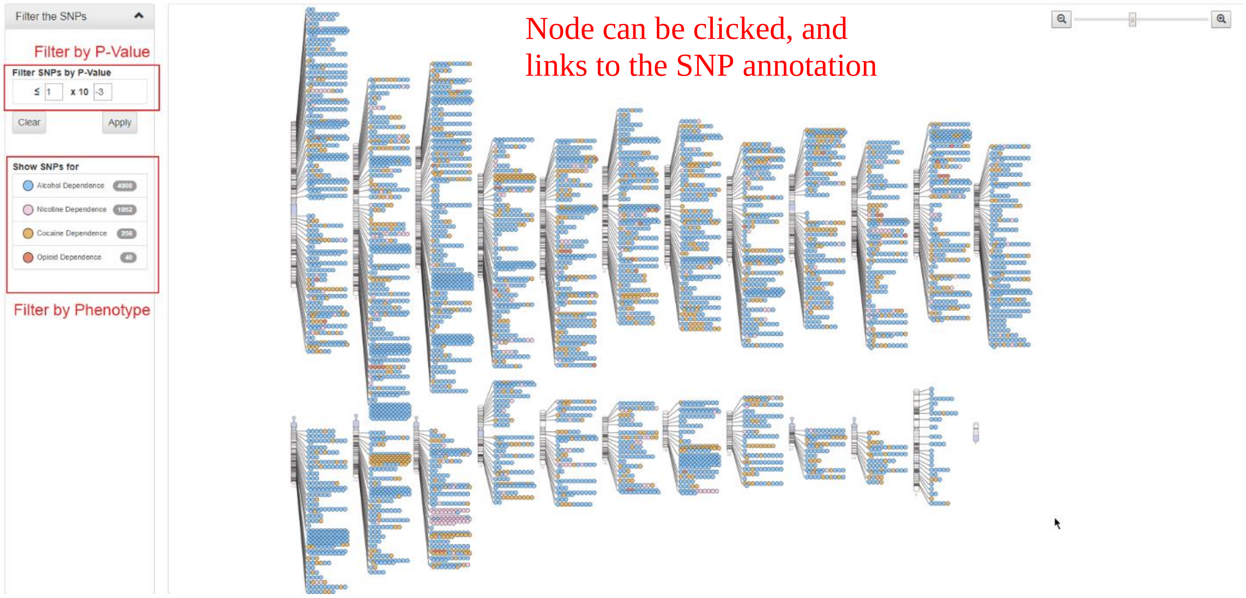
2. Main menu



3. SNP Map View

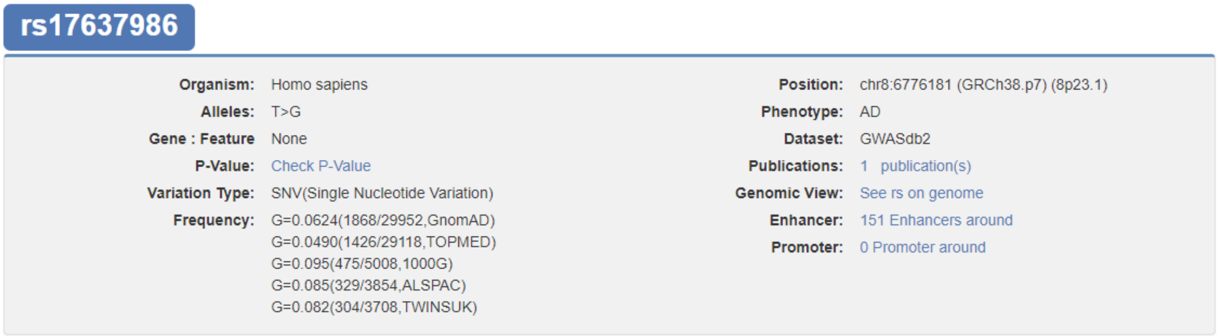


Node can be clicked, and links to the SNP annotation

4. SNP Annotation Page

This is a page for the annotations of each SNP. The SNP page starts with a summary table of the SNP basic information. Following the summary table, a group of tables show the related annotations, including Variant Details(Genomic Placements, Gene Variants), Frequencies in different populations, supportive publications, P-Values in different studies, eQTL (if the SNP is an eSNP in brain), meQTL (if the SNP is a meSNP in brain). A genomic view is available to look the around of the SNP. Enhancers (if there are any within 50kb of the SNP), and promoters (if any) are presented at last.

4.1 The basic information of the SNP



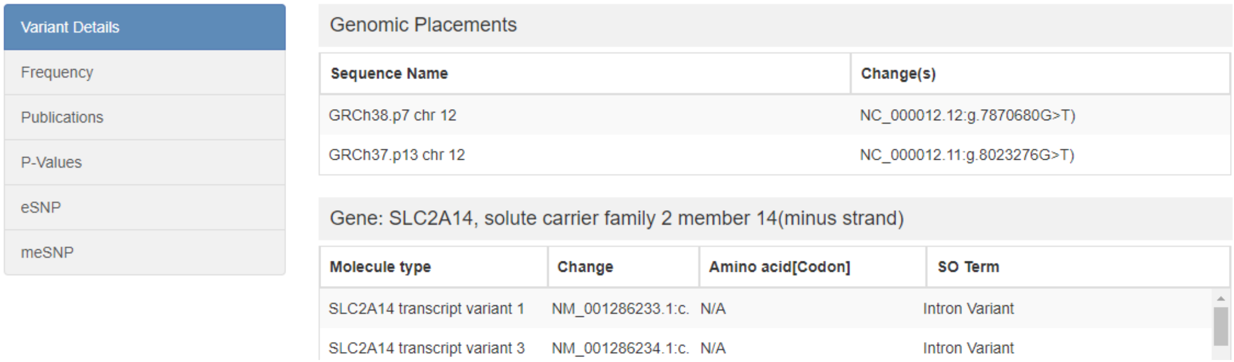
rs17637986

Organism: Homo sapiens
Alleles: T>G
Gene : Feature None
P-Value: Check P-Value
Variation Type: SNV(Single Nucleotide Variation)
Frequency: G=0.0624(1868/29952,GnomAD)
G=0.0490(1426/29118,TOPMED)
G=0.095(475/5008,1000G)
G=0.085(329/3854,ALSPAC)
G=0.082(304/3708,TWINSUK)

Position: chr8:6776181 (GRCh38.p7) (8p23.1)
Phenotype: AD
Dataset: GWASdb2
Publications: 1 publication(s)
Genomic View: See rs on genome
Enhancer: 151 Enhancers around
Promoter: 0 Promoter around

It shows the basic information of the SNP.

4.2 The basic information of the SNP



Genomic Placements

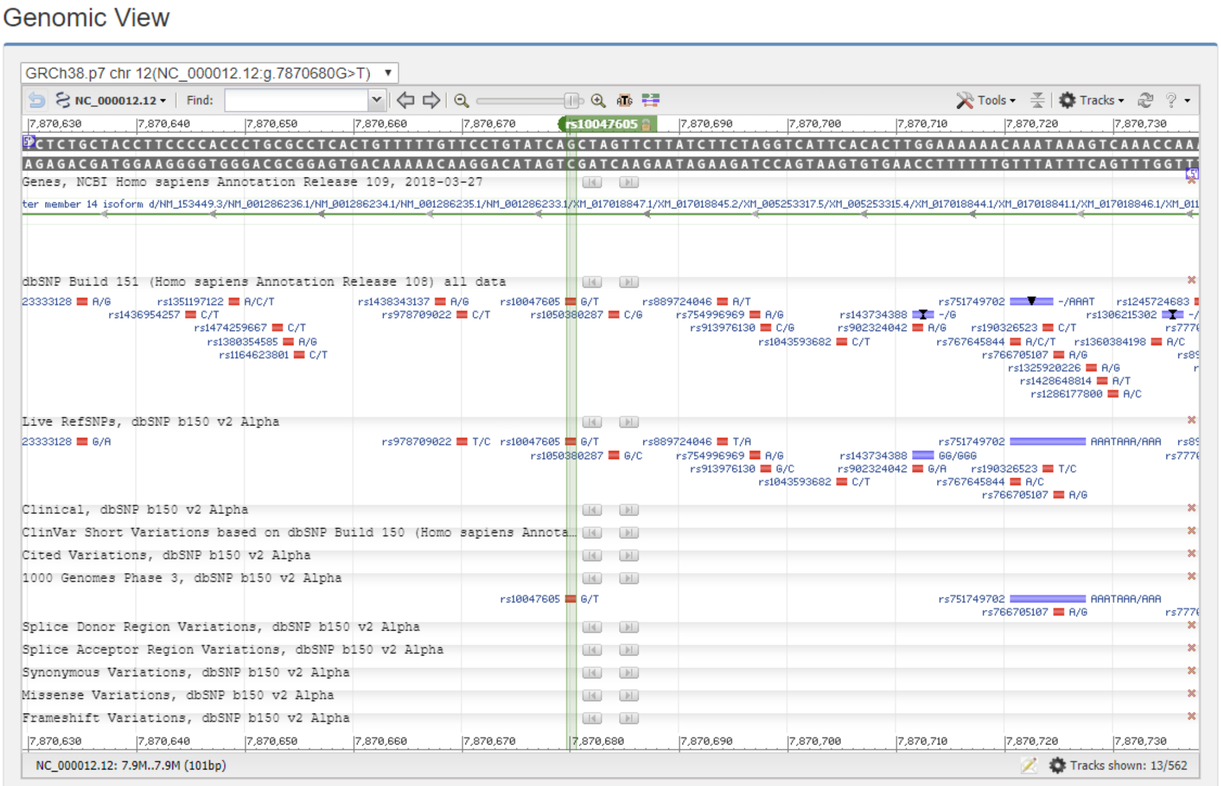
Sequence Name	Change(s)
GRCh38.p7 chr 12	NC_000012.12:g.7870680G>T)
GRCh37.p13 chr 12	NC_000012.11:g.8023276G>T)

Gene: SLC2A14, solute carrier family 2 member 14(minus strand)

Molecule type	Change	Amino acid[Codon]	SO Term
SLC2A14 transcript variant 1	NM_001286233.1:c.	N/A	Intron Variant
SLC2A14 transcript variant 3	NM_001286234.1:c.	N/A	Intron Variant

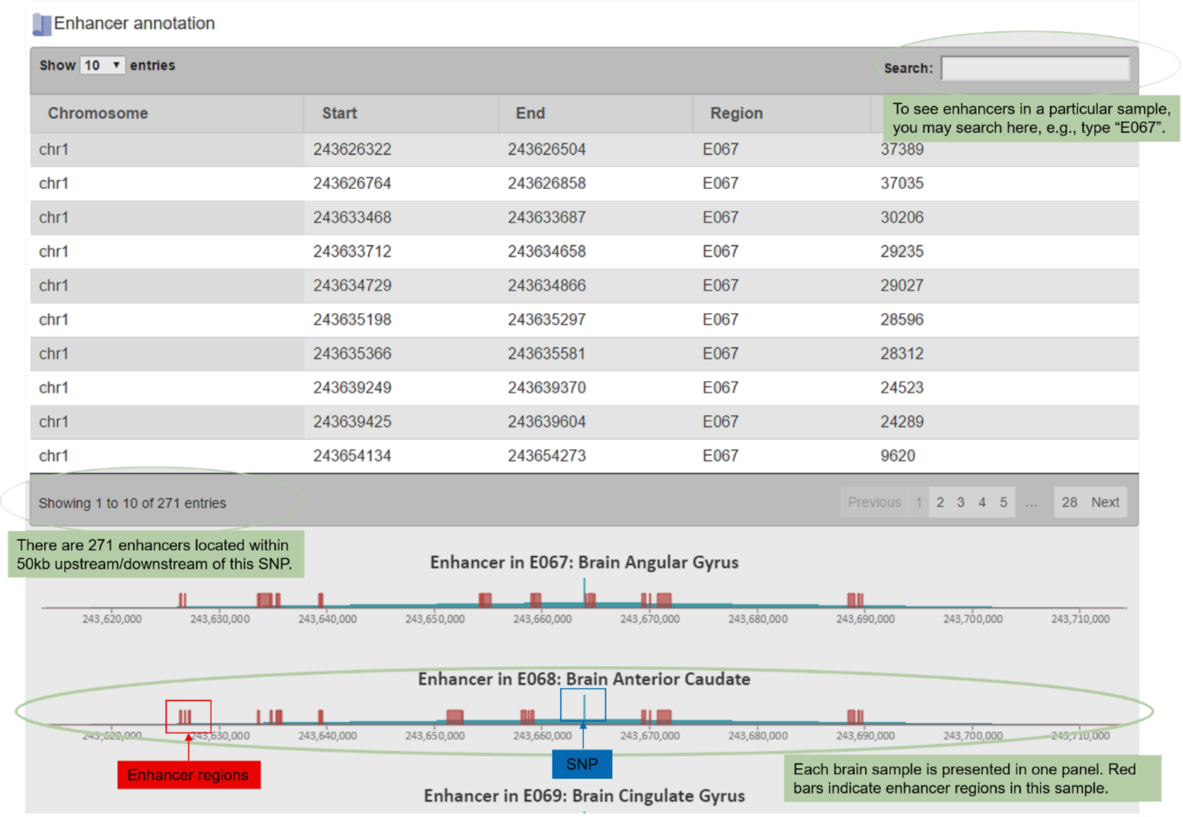
A group of tables was used to show more annotation information. The tabs on the left side can be clicked, and the table on the right side will be changed correspondingly.

4.3 Genomic View



The Genomic View shows the position of the SNP and the nearby genomic information.

4.4 Enhancers and Promoters



Enhancer annotation

Show 10 entries

Search:

To see enhancers in a particular sample, you may search here, e.g., type "E067".

Chromosome	Start	End	Region	
chr1	243626322	243626504	E067	37389
chr1	243626764	243626858	E067	37035
chr1	243633468	243633687	E067	30206
chr1	243633712	243634658	E067	29235
chr1	243634729	243634866	E067	29027
chr1	243635198	243635297	E067	28596
chr1	243635366	243635581	E067	28312
chr1	243639249	243639370	E067	24523
chr1	243639425	243639604	E067	24289
chr1	243654134	243654273	E067	9620

Showing 1 to 10 of 271 entries

There are 271 enhancers located within 50kb upstream/downstream of this SNP.

Enhancer in E067: Brain Angular Gyrus

Enhancer in E068: Brain Anterior Caudate

Enhancer in E069: Brain Cingulate Gyrus

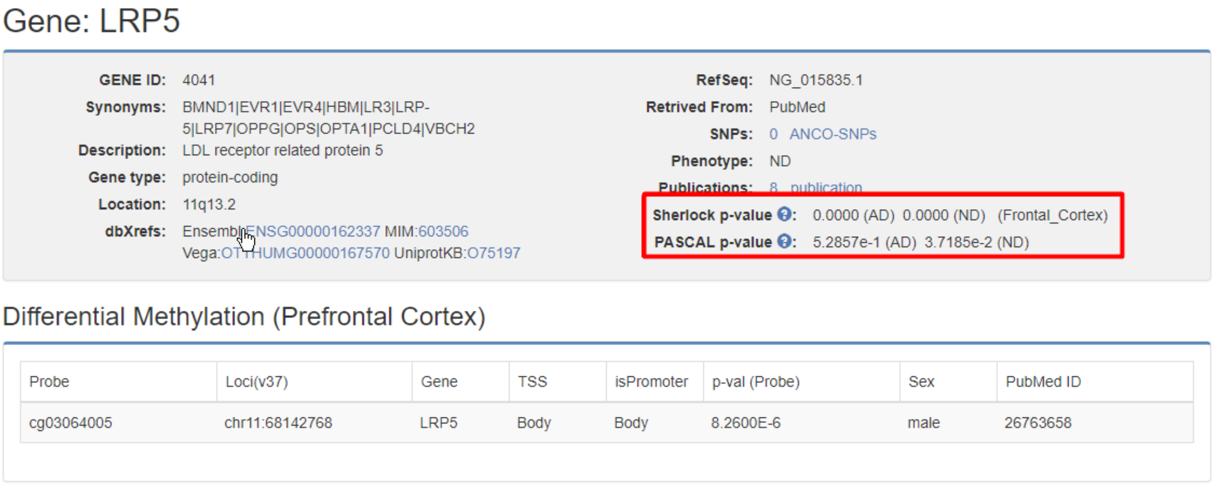
Each brain sample is presented in one panel. Red bars indicate enhancer regions in this sample.

The enhancer and promoter information is listed as both tables and figures.

5. Gene Page

This page shows the annotation information for a gene. The GENE page is heavily loaded with many types of information. It typically takes a few seconds to load.

5.1 The basic information of a Gene



Gene: LRP5

GENE ID: 4041

Synonyms: BMND1|EVR1|EVR4|HBM|LR3|LRP-5|LRP7|OPPG|OPS|OPTA1|PCLD4|VBCH2

Description: LDL receptor related protein 5

Gene type: protein-coding

Location: 11q13.2

dbXrefs: Ensembl:ENSG00000162337 MIM:603506 Vega:OTTHUMG00000167570 UniprotKB:O75197

RefSeq: NG_015835.1

Retrived From: PubMed

SNPs: 0 ANCO-SNPs

Phenotype: ND

Publications: 8 publication

Sherlock p-value: 0.0000 (AD) 0.0000 (ND) (Frontal_Cortex)

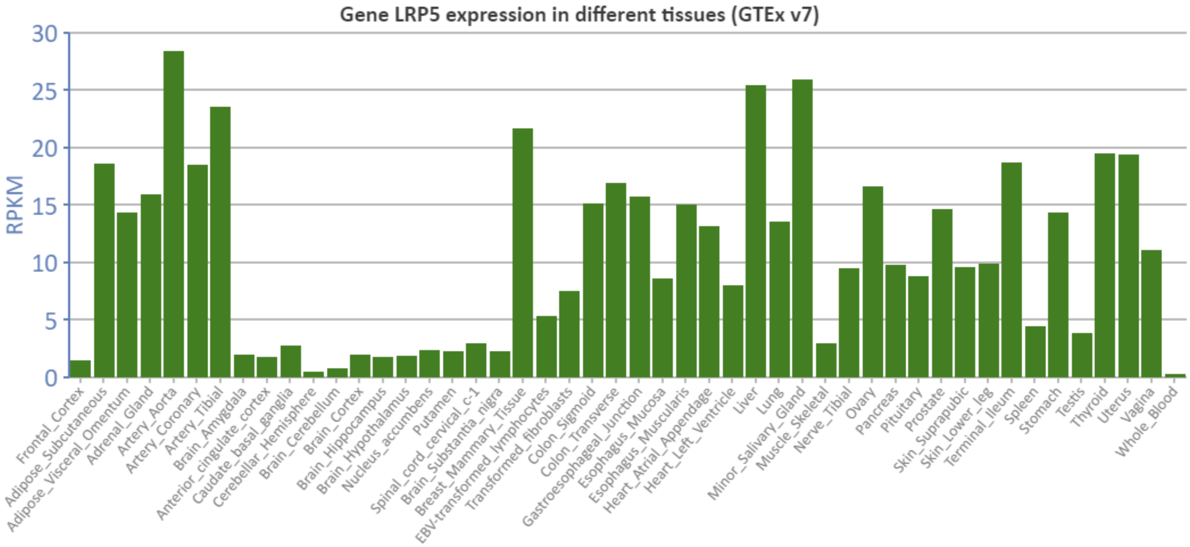
PASCAL p-value: 5.2857e-1 (AD) 3.7185e-2 (ND)

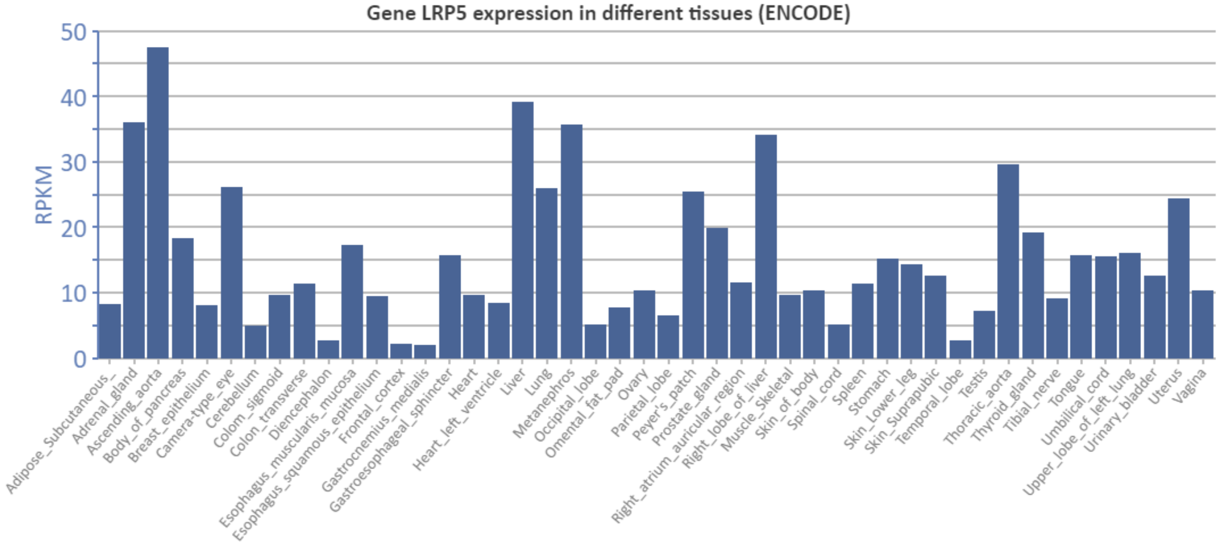
Differential Methylation (Prefrontal Cortex)

Probe	Loci(v37)	Gene	TSS	isPromoter	p-val (Probe)	Sex	PubMed ID
cg03064005	chr11:68142768	LRP5	Body	Body	8.2600E-6	male	26763658

It shows the basic information of the Gene. Sherlock p-value and Logarithm Bayes Factor (LBF), and Pascal p-value are calculated for each gene. If this gene is associated with DNA Methylation in Brain-Prefrontal Cortex, a Differential Methylation table will be shown.

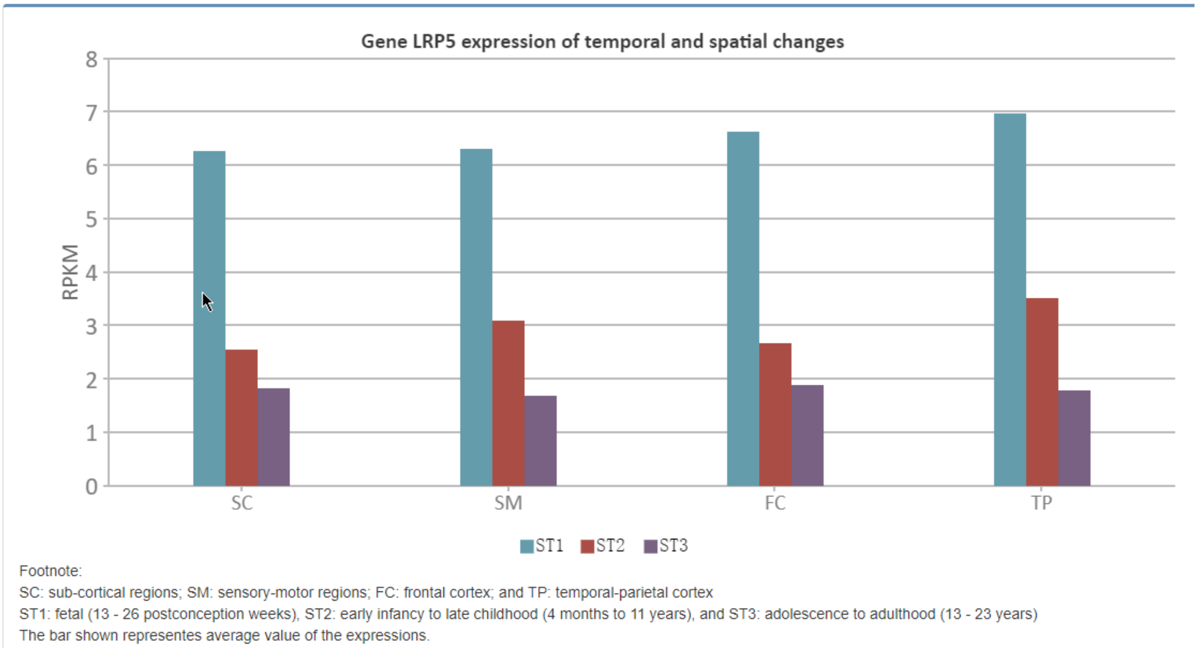
5.2 Gene expression in different tissues





Gene expression data from GTEx v7 and ENCODE are shown as a Column Chart.

5.3 Temporal and Spatial Expressions

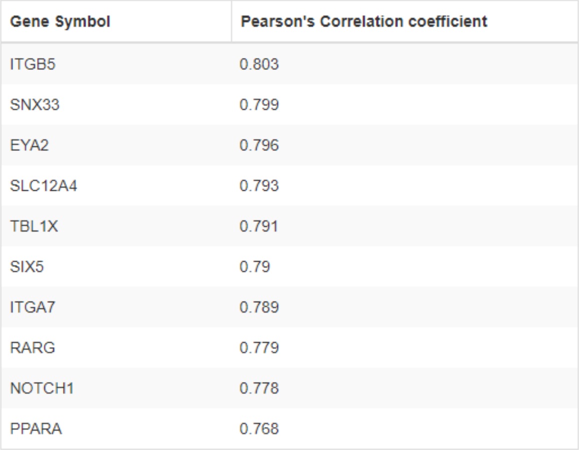


Footnote:
SC: sub-cortical regions; SM: sensory-motor regions; FC: frontal cortex; and TP: temporal-parietal cortex
ST1: fetal (13 - 26 postconception weeks), ST2: early infancy to late childhood (4 months to 11 years), and ST3: adolescence to adulthood (13 - 23 years)
The bar shown representes average value of the expressions.

Temporal and Spatial Expression data from BrainSpan were shown.

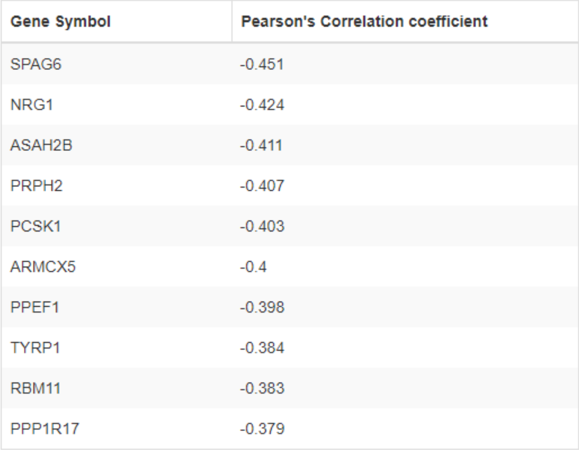
5.4 Top co-expressed genes

Top 10 positively co-expressed genes



Gene Symbol	Pearson's Correlation coefficient
ITGB5	0.803
SNX33	0.799
EYA2	0.796
SLC12A4	0.793
TBL1X	0.791
SIX5	0.79
ITGA7	0.789
RARG	0.779
NOTCH1	0.778
PPARA	0.768

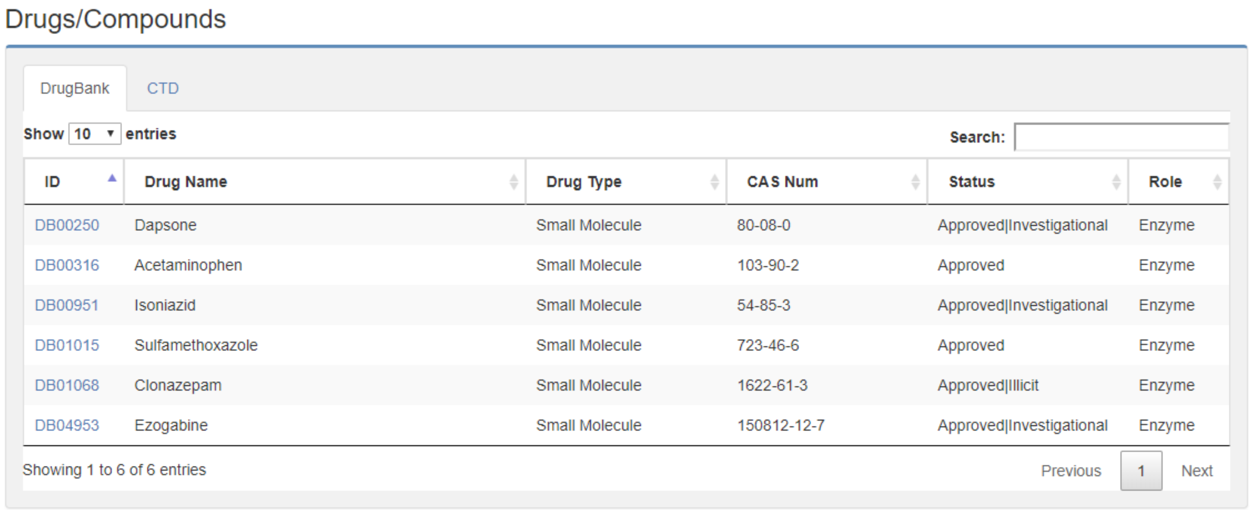
Top 10 negatively co-expressed genes



Gene Symbol	Pearson's Correlation coefficient
SPAG6	-0.451
NRG1	-0.424
ASAH2B	-0.411
PRPH2	-0.407
PCSK1	-0.403
ARMCX5	-0.4
PPEF1	-0.398
TYRP1	-0.384
RBM11	-0.383
PPP1R17	-0.379

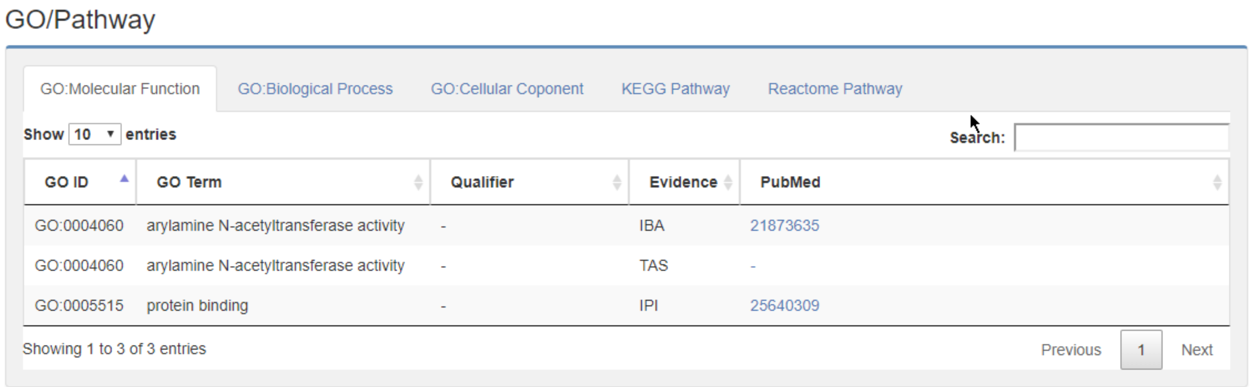
Top 10 positively and negatively co-expressed genes in Brain-Frontal Cortex (BA9) were calculated by using GTEx v7 dataset.

5.5 Drug, GO/Pathway, PPI, and Publication



ID	Drug Name	Drug Type	CAS Num	Status	Role
DB00250	Dapsone	Small Molecule	80-08-0	Approved|Investigational	Enzyme
DB00316	Acetaminophen	Small Molecule	103-90-2	Approved	Enzyme
DB00951	Isoniazid	Small Molecule	54-85-3	Approved|Investigational	Enzyme
DB01015	Sulfamethoxazole	Small Molecule	723-46-6	Approved	Enzyme
DB01068	Clonazepam	Small Molecule	1622-61-3	Approved|Illicit	Enzyme
DB04953	Ezogabine	Small Molecule	150812-12-7	Approved|Investigational	Enzyme

Showing 1 to 6 of 6 entries



GO ID	GO Term	Qualifier	Evidence	PubMed
GO:0004060	arylamine N-acetyltransferase activity	-	IBA	21873635
GO:0004060	arylamine N-acetyltransferase activity	-	TAS	-
GO:0005515	protein binding	-	IPI	25640309

Showing 1 to 3 of 3 entries

At last, Gene related drugs/Compounds from DrugBank and CTD were listed, also, GO term, pathway data from KEGG and Reactome are provided, and the supportive publications are listed at the bottom.

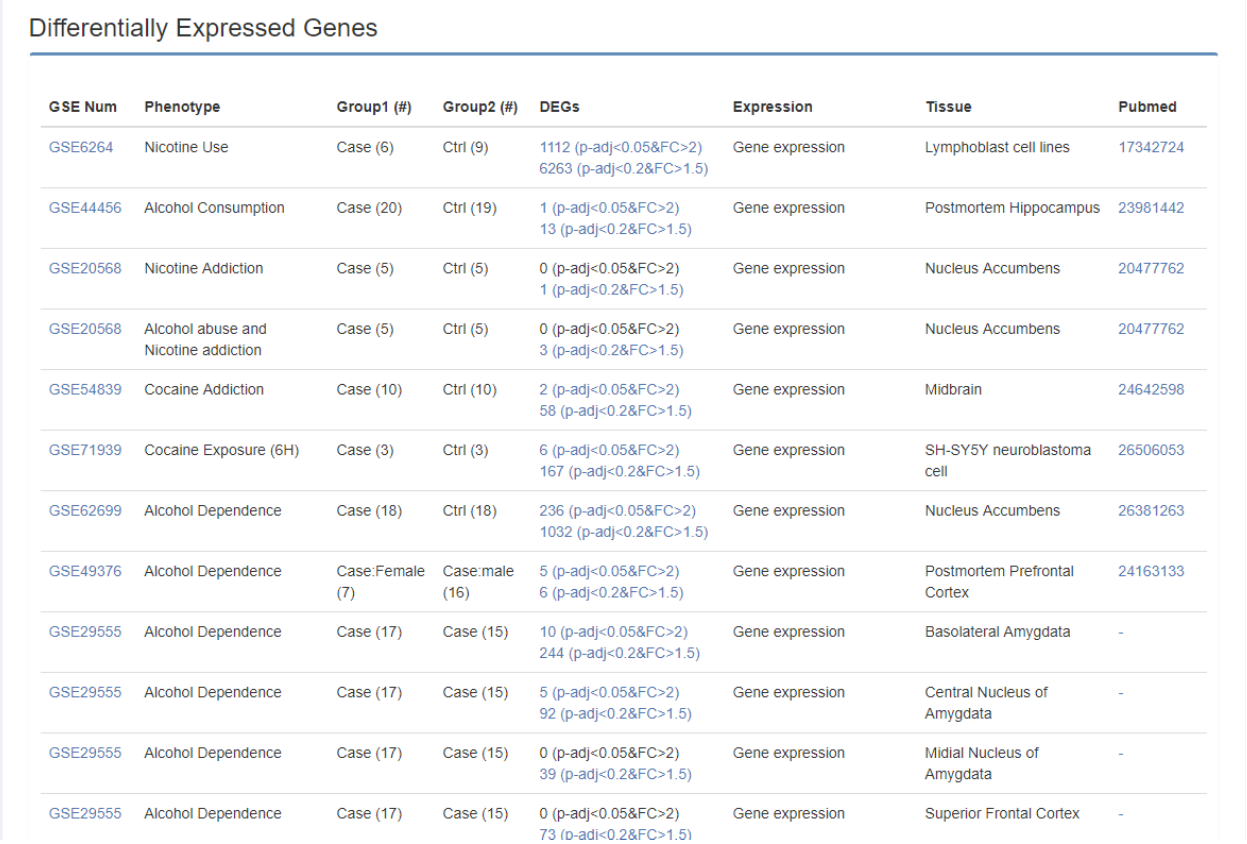
6. Secondary Analyses

- We searched the GEO database and collected related datasets to get Differentially Expressed Genes (DEGs). GEO2R was used to define the differentially expressed genes.
- Two Genome Wide Association Study (GWAS) datasets about AD and ND were collected. Sherlock, Psacal and MetaXcan Analyses had been done on these two datasets.
    - Summary statistics data of a Genome-Wide Association Study of Alcohol Dependence in an European-American Population is from Study of Addiction: Genetics and Environment (SAGE) (phs000092)[1] (https://www.ncbi.nlm.nih.gov/projects/SNP/gViewer/gView.cgi?aid=2906)
    - Summary statistics data of a Genome-Wide Association Study meta-analysis of Nicotine Dependence (cigs per day) in an European Ancestry population is from Tobacco and Genetics Consortium (TAG)[2] (https://www.med.unc.edu/pgc/results-and-downloads)

Reference:
[1]. Bierut, Laura J., et al. "A genome-wide association study of alcohol dependence." Proceedings of the National Academy of Sciences 107.11 (2010): 5082-5087.
[2]. Furberg, Helena, et al. "Genome-wide meta-analyses identify multiple loci associated with smoking behavior." Nature genetics 42.5 (2010): 441.

- Tissue-Specific Enrichment Analysis (TSEA):
  To check the ANCO genes distribution enriched in different tissues based on GTEx data, we have done the Tissue-Specific Enrichment Analysis (TSEA) using Fisher's Exact Test. ANCO dependence-associated genes were found to be specifically enriched in brain regions.

6.1 Differentially Expressed Genes

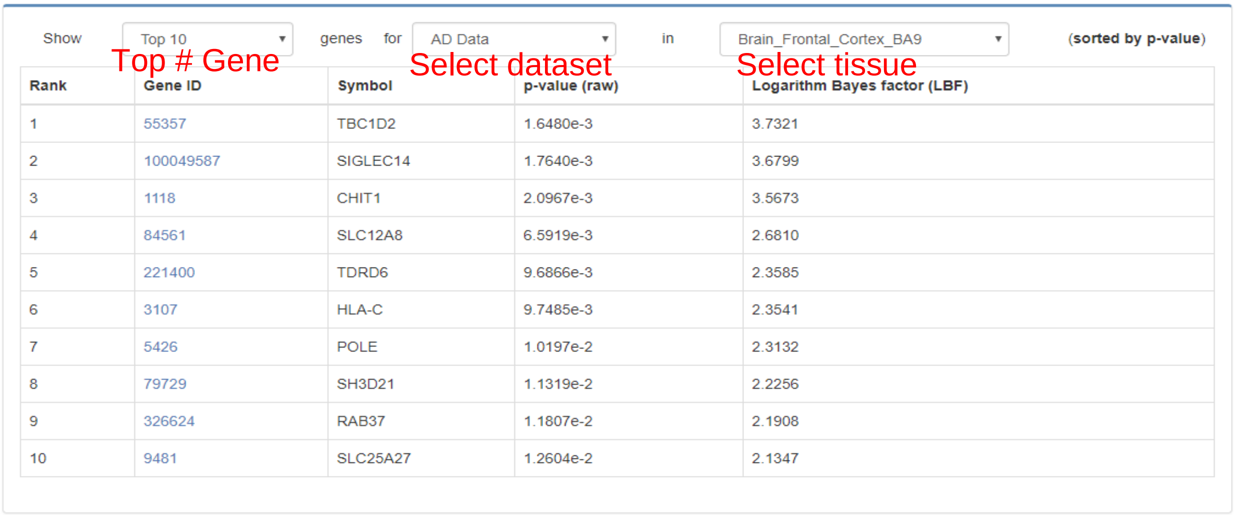


Differentially Expressed Genes

GSE Num	Phenotype	Group1 (#)	Group2 (#)	DEGs	Expression	Tissue	Pubmed
GSE6264	Nicotine Use	Case (6)	Ctrl (9)	1112 (p-adj<0.05&FC>2) 6263 (p-adj<0.2&FC>1.5)	Gene expression	Lymphoblast cell lines	17342724
GSE44456	Alcohol Consumption	Case (20)	Ctrl (19)	1 (p-adj<0.05&FC>2) 13 (p-adj<0.2&FC>1.5)	Gene expression	Postmortem Hippocampus	23981442
GSE20568	Nicotine Addiction	Case (5)	Ctrl (5)	0 (p-adj<0.05&FC>2) 1 (p-adj<0.2&FC>1.5)	Gene expression	Nucleus Accumbens	20477762
GSE20568	Alcohol abuse and Nicotine addiction	Case (5)	Ctrl (5)	0 (p-adj<0.05&FC>2) 3 (p-adj<0.2&FC>1.5)	Gene expression	Nucleus Accumbens	20477762
GSE54839	Cocaine Addiction	Case (10)	Ctrl (10)	2 (p-adj<0.05&FC>2) 58 (p-adj<0.2&FC>1.5)	Gene expression	Midbrain	24642598
GSE71939	Cocaine Exposure (6H)	Case (3)	Ctrl (3)	6 (p-adj<0.05&FC>2) 167 (p-adj<0.2&FC>1.5)	Gene expression	SH-SY5Y neuroblastoma cell	26506053
GSE62699	Alcohol Dependence	Case (18)	Ctrl (18)	236 (p-adj<0.05&FC>2) 1032 (p-adj<0.2&FC>1.5)	Gene expression	Nucleus Accumbens	26381263
GSE49376	Alcohol Dependence	Case:Female (7)	Case:male (16)	5 (p-adj<0.05&FC>2) 6 (p-adj<0.2&FC>1.5)	Gene expression	Postmortem Prefrontal Cortex	24163133
GSE29555	Alcohol Dependence	Case (17)	Case (15)	10 (p-adj<0.05&FC>2) 244 (p-adj<0.2&FC>1.5)	Gene expression	Basolateral Amygdata	-
GSE29555	Alcohol Dependence	Case (17)	Case (15)	5 (p-adj<0.05&FC>2) 92 (p-adj<0.2&FC>1.5)	Gene expression	Central Nucleus of Amygdata	-
GSE29555	Alcohol Dependence	Case (17)	Case (15)	0 (p-adj<0.05&FC>2) 39 (p-adj<0.2&FC>1.5)	Gene expression	Midial Nucleus of Amygdata	-
GSE29555	Alcohol Dependence	Case (17)	Case (15)	0 (p-adj<0.05&FC>2) 73 (p-adj<0.2&FC>1.5)	Gene expression	Superior Frontal Cortex	-

The first part of the page shows the Differentially Expressed Genes (DEGs) retrieved from GEO Database.

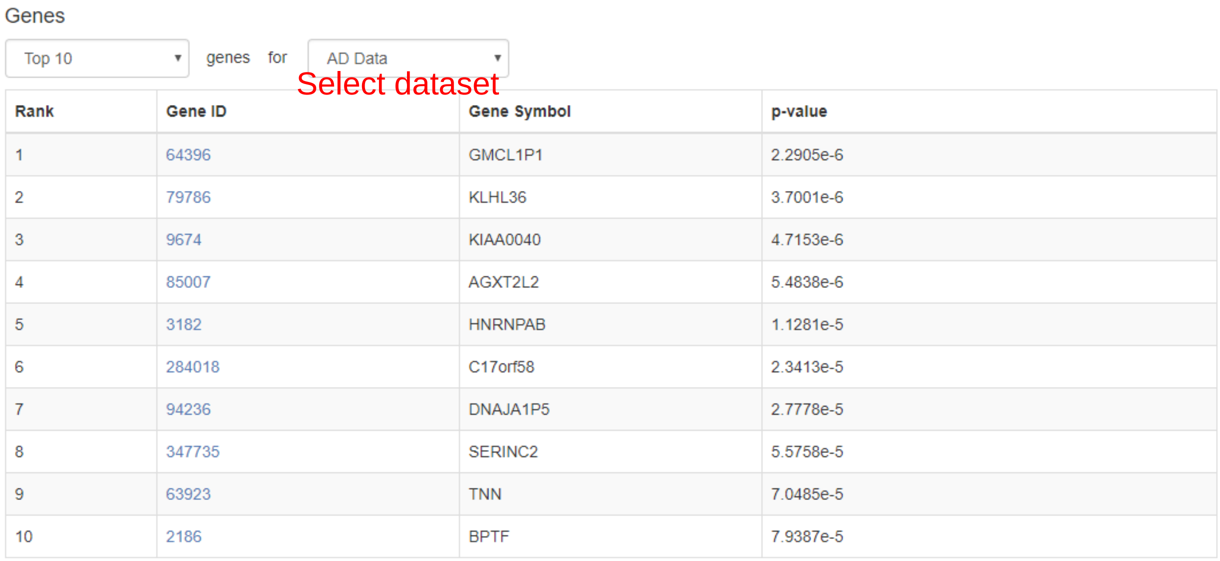
6.2 Top Ranked Genes in Different Tissues Based on Sherlock Analysis



Show Top 10 genes for AD Data in Brain_Frontal_Cortex_BA9 (sorted by p-value)

Rank	Gene ID	Symbol	p-value (raw)	Logarithm Bayes factor (LBF)
1	55357	TBC1D2	1.6480e-3	3.7321
2	100049587	SIGLEC14	1.7640e-3	3.6799
3	1118	CHIT1	2.0967e-3	3.5673
4	84561	SLC12A8	6.5919e-3	2.6810
5	221400	TDRD6	9.6866e-3	2.3585
6	3107	HLA-C	9.7485e-3	2.3541
7	5426	POLE	1.0197e-2	2.3132
8	79729	SH3D21	1.1319e-2	2.2256
9	326624	RAB37	1.1807e-2	2.1908
10	9481	SLC25A27	1.2604e-2	2.1347

6.3 Top Ranked Genes/Pathways Based on Pascal Analysis

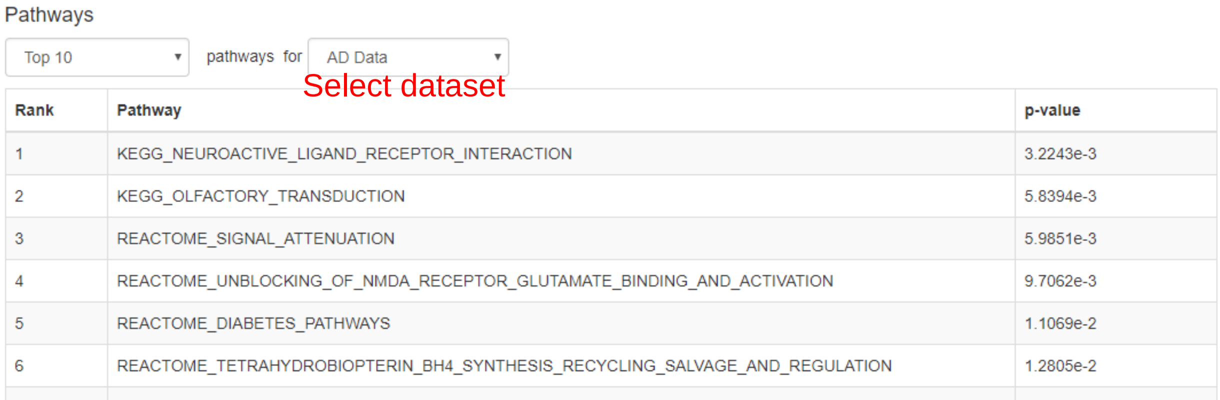


Genes

Top 10 genes for AD Data

Select dataset

Rank	Gene ID	Gene Symbol	p-value
1	64396	GMCL1P1	2.2905e-6
2	79786	KLHL36	3.7001e-6
3	9674	KIAA0040	4.7153e-6
4	85007	AGXT2L2	5.4838e-6
5	3182	HNRNPAB	1.1281e-5
6	284018	C17orf58	2.3413e-5
7	94236	DNAJA1P5	2.7778e-5
8	347735	SERINC2	5.5758e-5
9	63923	TNN	7.0485e-5
10	2186	BPTF	7.9387e-5



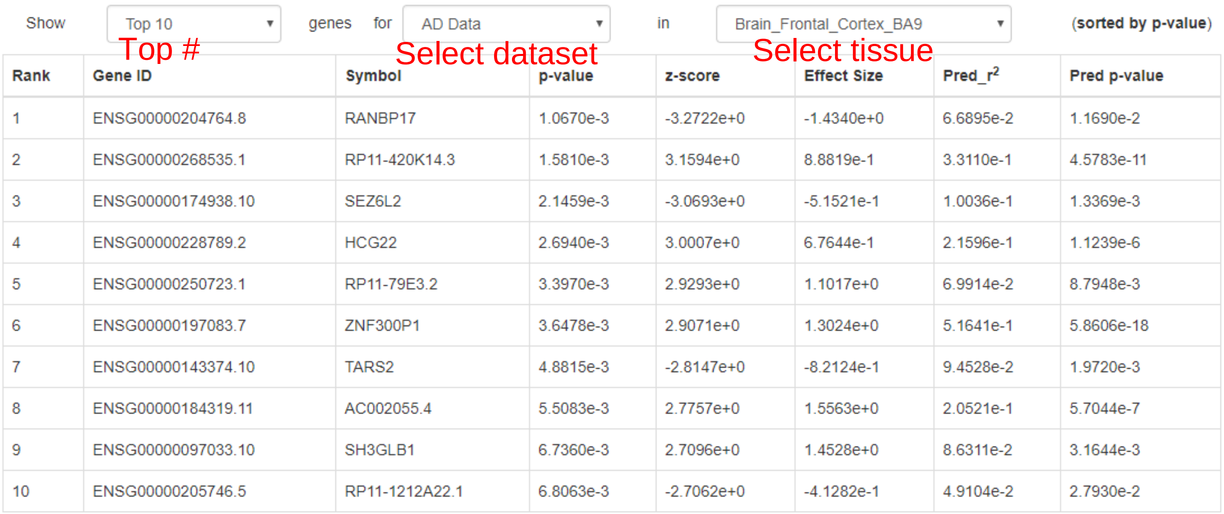
Pathways

Top 10 pathways for AD Data

Select dataset

Rank	Pathway	p-value
1	KEGG_NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION	3.2243e-3
2	KEGG_OLFACTORY_TRANSDUCTION	5.8394e-3
3	REACTOME_SIGNAL_ATTENUATION	5.9851e-3
4	REACTOME_UNBLOCKING_OF_NMDA_RECEPTOR_GLUTAMATE_BINDING_AND_ACTIVATION	9.7062e-3
5	REACTOME_DIABETES_PATHWAYS	1.1069e-2
6	REACTOME_TETRAHYDROBIOPTERIN_BH4_SYNTHESIS_RECYCLING_SALVAGE_AND_REGULATION	1.2805e-2

6.4 Top Ranked Genes in Different Tissues Based on MetaXcan Analysis



Show Top 10 genes for AD Data in Brain_Frontal_Cortex_BA9 **(sorted by p-value)**

Top # Select dataset Select tissue

Rank	Gene ID	Symbol	p-value	z-score	Effect Size	Pred_r^2	Pred p-value
1	ENSG00000204764.8	RANBP17	1.0670e-3	-3.2722e+0	-1.4340e+0	6.6895e-2	1.1690e-2
2	ENSG00000268535.1	RP11-420K14.3	1.5810e-3	3.1594e+0	8.8819e-1	3.3110e-1	4.5783e-11
3	ENSG00000174938.10	SEZ6L2	2.1459e-3	-3.0693e+0	-5.1521e-1	1.0036e-1	1.3369e-3
4	ENSG00000228789.2	HCG22	2.6940e-3	3.0007e+0	6.7644e-1	2.1596e-1	1.1239e-6
5	ENSG00000250723.1	RP11-79E3.2	3.3970e-3	2.9293e+0	1.1017e+0	6.9914e-2	8.7948e-3
6	ENSG00000197083.7	ZNF300P1	3.6478e-3	2.9071e+0	1.3024e+0	5.1641e-1	5.8606e-18
7	ENSG00000143374.10	TARS2	4.8815e-3	-2.8147e+0	-8.2124e-1	9.4528e-2	1.9720e-3
8	ENSG00000184319.11	AC002055.4	5.5083e-3	2.7757e+0	1.5563e+0	2.0521e-1	5.7044e-7
9	ENSG00000097033.10	SH3GLB1	6.7360e-3	2.7096e+0	1.4528e+0	8.6311e-2	3.1644e-3
10	ENSG00000205746.5	RP11-1212A22.1	6.8063e-3	-2.7062e+0	-4.1282e-1	4.9104e-2	2.7930e-2

6.5 Tissue-Specific Enrichment Analysis (TSEA)

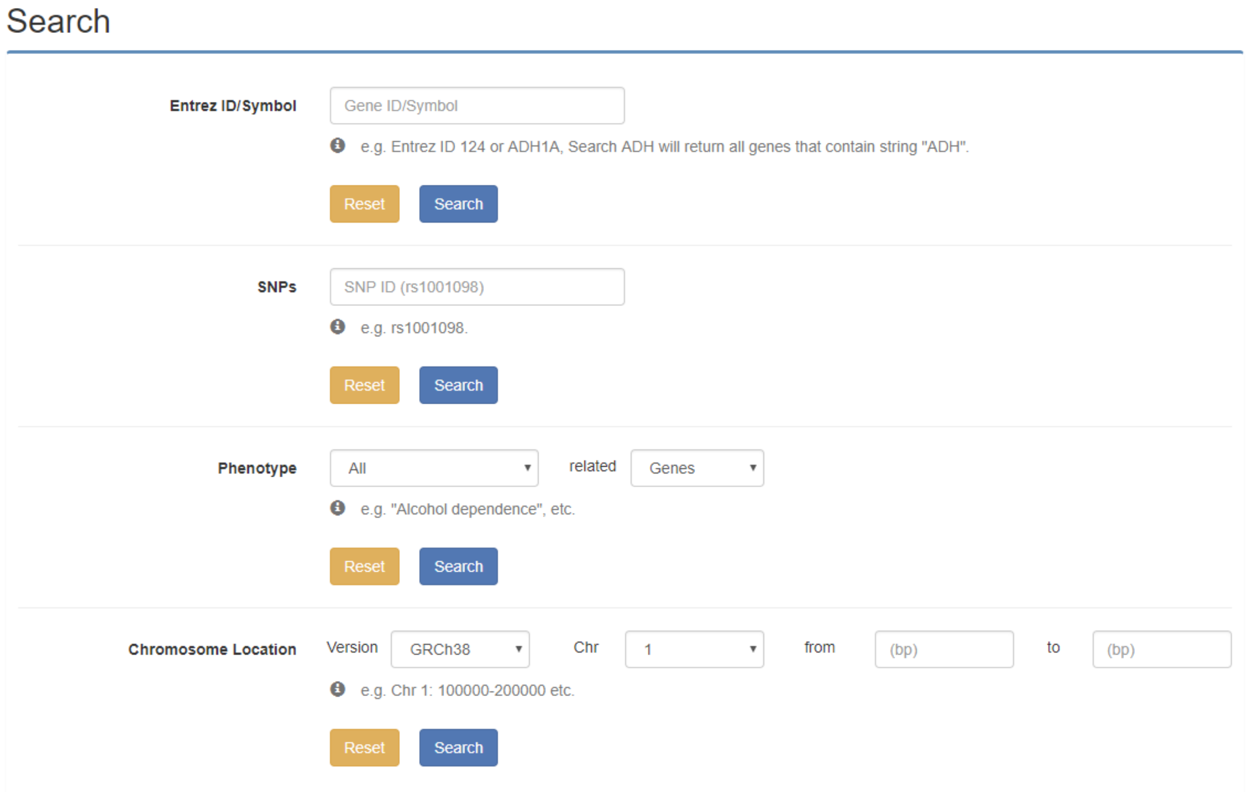
The Tissue-Specific Enrichment Analysis (TSEA) was done by using SNP-Mapped Genes.

*: The Most (1st) Enriched Tissue.

+: The Second (2nd) Enriched Tissue.

-: The Third (3rd) Enriched Tissue

7. Search Functions



Search

Entrez ID/Symbol Gene ID/Symbol

e.g. Entrez ID 124 or ADH1A, Search ADH will return all genes that contain string "ADH".

SNPs SNP ID (rs1001098)

e.g. rs1001098.

Phenotype All related Genes

e.g. "Alcohol dependence", etc.

Chromosome Location Version GRCh38 Chr 1 from (bp) to (bp)

e.g. Chr 1: 100000-200000 etc.

To search for a gene, please use the gene symbol or gene ID. A list of genes whose symbols contain the query string will be listed. For example, searching using "AKT" will lead to AKT1, AKT2, and AKT3. A brief illustration of the resultant page is shown below.

To search for SNPs, you may use the function to search directly using the rs ID (if you know the ID). This will lead to the SNP page (see section "4. Illustration of the SNP page" below for illustration).

Alternatively, if the user only knows the genomic region where the SNP is listed, the function "search by region" can be applied.

Additionally, we provide a combinatorial query function, phenotype related Genes/Drugs/SNPs can be retrieved.

8. Contact

ANCO-Gene DB appreciates your feedback. Please send an Email if you wish to make a request, a comment, or report a bug.

Zhongming Zhao, PhD, MS
Dr. Doris L. Ross Professor
School of Biomedical Informatics and School of Public Health
University of Texas Health Science Center at Houston
Web site: https://www.uth.edu/bioinfo/index.htm
Phone: 713-500-3631
Email: Zhongming.Zhao-at-uth.tmc.edu

Peilin Jia, PhD,
Assistant Professor

School of Biomedical Informatics
University of Texas Health Science Center at Houston
Phone: 713-500-3633
Email: Peilin.Jia-at-uth.tmc.edu

Ruifeng Hu, PhD,
Postdoctoral Research Fellow
School of Biomedical Informatics
University of Texas Health Science Center at Houston
Email: Ruifeng.Hu-at-uth.tmc.edu