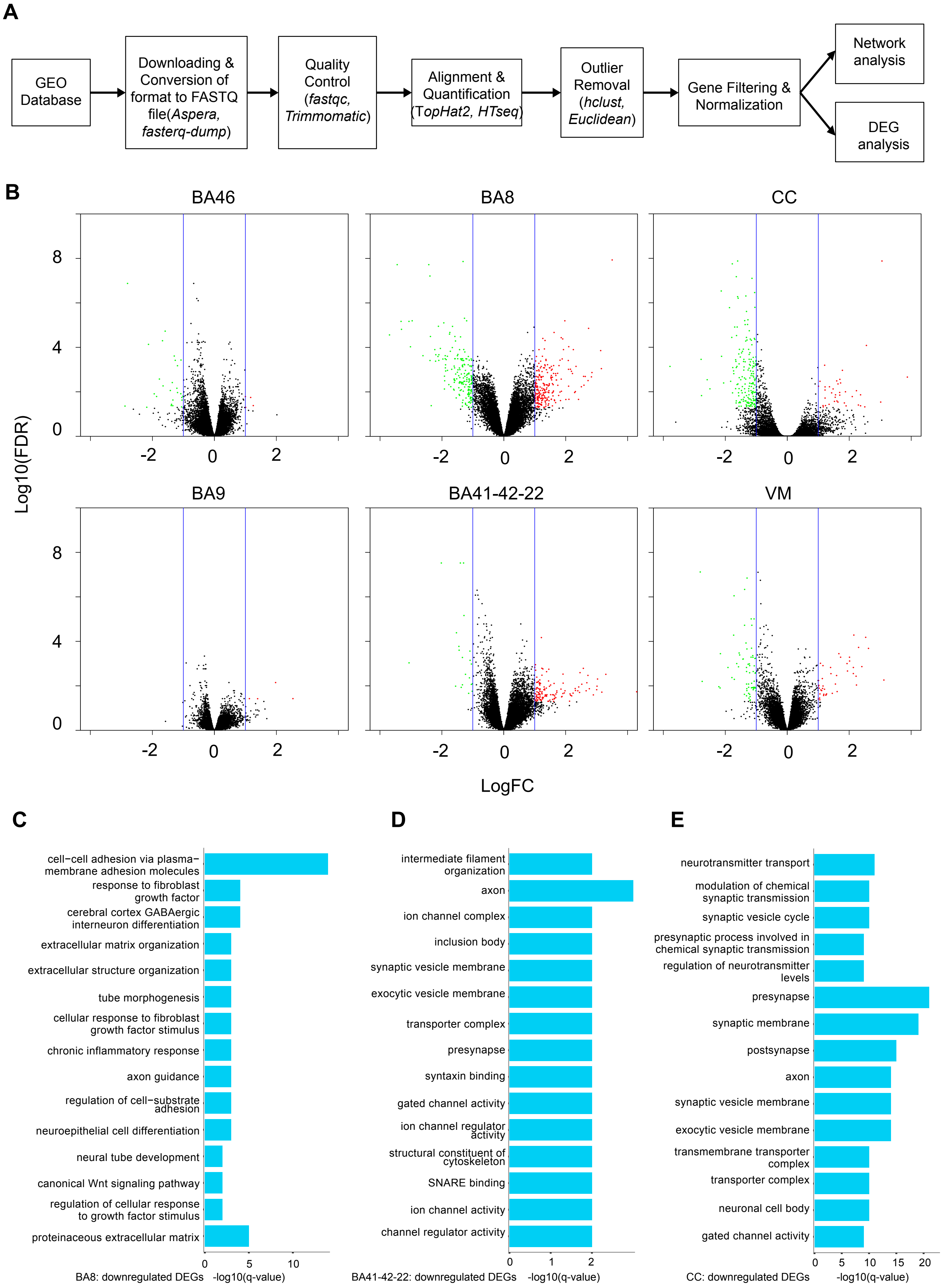


Figure S1. Transcriptome data and GO enrichment analysis of downregulated DEGs in the different brain regions. (A) Pipeline of RNA-Seq raw data analysis. (B) Volcano plot of gene expression analysis in different brain areas. Red indicates upregulated DEGs, and green indicates downregulated DEGs. The x-axis specifies the log2(fold change, FC), and the y-axis specifies the FDR negative logarithm in base 10. (C) Top 15 enriched GO terms foe the downregulated genes in BA8. (D) Top 15 enriched GO termS for the downregulated genes in BA41-42-22. (E) Top 15 enriched GO terms for the downregulated genes in CC. The x-axis shows the –log(q-value), and the y-axis shows the GO terms.

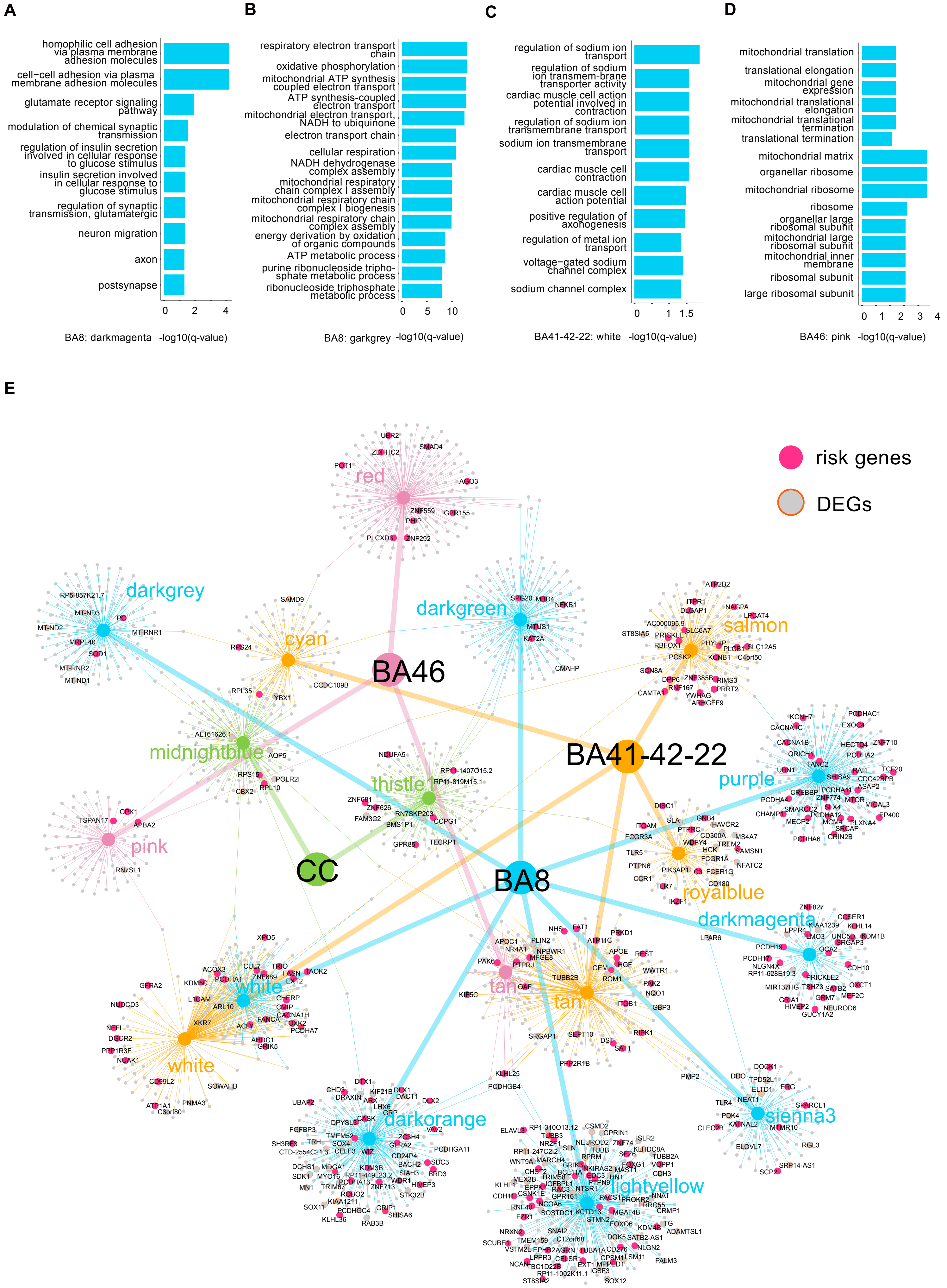

A
homophilic cell adhesion via plasma membrane adhesion molecules
cell−cell adhesion via plasma membrane adhesion molecules
glutamate receptor signaling pathway
modulation of chemical synaptic transmission
regulation of insulin secretion involved in cellular response to glucose stimulus
insulin secretion involved in cellular response to glucose stimulus
regulation of synaptic transmission, glutamatergic
neuron migration
axon
postsynapse
0
2
4
BA8: darkmagenta
-log10(q-value)
B
respiratory electron transport chain
oxidative phosphorylation
mitochondrial ATP synthesis coupled electron transport
ATP synthesis-coupled electron transport
mitochondrial electron transport, NADH to ubiquinone
electron transport chain
cellular respiration
NADH dehydrogenase complex assembly
mitochondrial respiratory chain complex I assembly
mitochondrial respiratory chain complex I biogenesis
mitochondrial respiratory chain complex assembly
energy derivation by oxidation of organic compounds
ATP metabolic process
purine ribonucleoside triphosphate metabolic process
ribonucleoside triphosphate metabolic process
0
5
10
BA8: garkgrey
-log10(q-value)
C
regulation of sodium ion transport
regulation of sodium ion transmem-brane transporter activity
cardiac muscle cell action potential involved in contraction
regulation of sodium ion transmembrane transport
sodium ion transmembrane transport
cardiac muscle cell contraction
cardiac muscle cell action potential
positive regulation of axonogenesis
regulation of metal ion transport
voltage−gated sodium channel complex
sodium channel complex
0
1
1.5
BA41-42-22: white
-log10(q-value)
D
mitochondrial translation
translational elongation
mitochondrial gene expression
mitochondrial translational elongation
mitochondrial translational termination
translational termination
mitochondrial matrix
organellar ribosome
mitochondrial ribosome
ribosome
organellar large ribosomal subunit
mitochondrial large ribosomal subunit
mitochondrial inner membrane
ribosomal subunit
large ribosomal subunit
0
1
2
3
4
BA46: pink
-log10(q-value)
E
risk genes
DEGs
BA46
BA41-42-22
BA8
CC
red
darkgrey
darkgreen
cyan
salmon
midnightblue
thistle1
purple
pink
royalblue
darkmagenta
white
tan
tan
white
darkorange
lightyellow
sienna3
UBR2
SMAD4
ZDHHC2
POT1
AGO3
ZNF559
GPR155
PHIP
PLCXD3
ZNF292
RP5-857K21.7
MT-ND3
PC
MT-ND2
MT-RNR1
MRPL40
SOD1
MT-RNR2
MT-ND1
SAMD9
RPS24
CCDC109B
RPL35
YBX1
AL161626.1
AQP5
RPS15
POLR2I
RPL10
CBX2
SPG20
MBD4
NFKB1
MTUS1
KAT2A
CMAHP
ATP2B2
ITPR1
DLGAP1
NAGPA
LPCAT4
AC000095.9
SLC6A7
ST8SIA5
PRICKLE1
PHYHIP
RBFOX1
PLCB1
SLC12A5
PCSK2
KCNB1
C4orf50
SCN8A
DPP6
ZNF385B
RIMS3
RNF167
PRRT2
CAMTA1
YWHAG
ARHGEF9
NDUFA5
RP11-1407O15.2
RP11-819M15.1
ZNF681
ZNF626
FAM3C2
RN7SKP203
BMS1P1
CCPG1
GPR85
TECRP1
GPX1
TSPAN17
APBA2
RN7SL1
KCNH7
PCDHAC1
CACNA1C
EXOC4
CACNA1B
HECTD4
ZNF710
QRICH1
PCDHA2
TANC2
UBN1
RAI1
TCF20
SHISA9
CDC42BPB
ASAP2
CREBBP
PCDHA11
PCDHA4
ZNF774
MTOR
MICAL3
SMARCC2
SLX4
CHAMP1
PCDHA12
EP400
MECP2
MCM4
PLXNA4
SRCAP
PCDHA6
GRIN2B
DISC1
ITGAM
SLA
GNB4
PTPRC
HAVCR2
FCGR3A
CD300A
MS4A7
WDFY4
TREM2
TLR5
HCK
SAMSN1
FCGR1A
PTPN6
NFATC2
PIK3AP1
C3
FCER1G
CCR1
CD180
TLR7
IKZF1
ZNF827
CCSER1
LPPR4
KIAA1239
KLHL14
LMO3
UNC5D
KDM1B
LPAR6
SRGAP3
PCDH19
OCA2
PCDH17
NLGN4X
CDH10
RP11-628E19.3
PRICKLE2
MIR137HG
TSHZ3
SATB2
OXCT1
GRIA1
GRM7
MEF2C
HIVEP2
NEUROD6
GUCY1A2
XPO5
ACOX3
CUL7
TRIO
FASN
TAOK2
PCDHA1
ZNF689
EXT2
KDM5C
GFRA2
L1CAM
ARL10
CHERP
CMIP
CACNA1H
NUDCD3
XKR7
FANCA
FOXK2
ACLY
PCDHA7
NEFL
DGCR2
AHDC1
GRIK5
PPP1R3F
NUAK1
CD99L2
SOWAHB
ATP1A1
PNMA3
C3orf80
NHS
FAT1
PRKD1
APOC1
PLIN2
ATP11C
NR4A1
NPBWR1
APOE
REST
MFGE8
PAK6
PTPRJ
GEM
HGF
WWTR1
TUBB2B
ROM1
OAF
PAK2
KIF5C
NQO1
ITGB1
GBP3
SRGAP1
SEPT10
DST
RIPK1
SAT1
PPP2R1B
KLHL25
PCDHGB4
PMP2
DDO
DOCK1
TPD52L1
ELTD1
ERG
NEAT1
TLR4
SPARCL1
PDK4
CLEC2B
KATNAL2
MTMR10
ELOVL7
RGL3
SRP14-AS1
SCP2
CHD3
DTX1
KIF21B
DLX1
DRAXIN
ARX
DACT1
DLX2
UBAP2
LHX6
GRP
DPYSL3
CASK
VAV2
FGFBP3
TMEM52
ZC3H4
SH3RF3
TRH
SOX4
GLRA2
CTD-2554C21.3
CELF3
WIZ
PCDHGA11
CD24P4
DCHS1
MDGA1
KDM3B
BACH2
SDC3
SDK1
MYO16
RP11-449L23.2
SIAH3
BRD3
MN1
TRIM67
PCDHA13
ZNF713
WDR1
HIVEP3
ROBO2
STK32B
SOX11
KIAA1211
GRIP1
PCDHGC4
SHISA6
KLHL36
RAB3B
ELAVL3
RP1-310O13.12
CSMD2
TUBB3
GPRIN1
NR2F1
NEUROD2
ZNF74
ISLR2
RP11-247C2.2
SLN
TUBB
KLHDC8A
SEZ6
TUBB2A
WNT9A
MARCH4
RPRM
CHST2
BCL11A
GRIK3
NKIRAS2
FOXG1
VOPP1
MEX3B
TRIM58
EDC3
MAST1
CDH3
KLHL1
EPPK1
IGFBPL1
PTPN9
HN1
RAC3
NTSR1
CDH11
CSNK1E
GPR161
PACS1
PROKR2
NNAT
RNF40
NCOA6
LRRC55
FZR1
SOSTDC1
KCTD13
MGAT4B
CRMP1
STMN2
FOXO6
NRXN2
SNAI2
KDM4B
TG
SCUBE1
TMEM159
C12orf68
DOK5
SATB2-AS1
ADAMTSL1
VSTM2L
EPHB2
AGRN
TUBA1A
CD276
NLGN2
NCAN
LPPR3
CELSR1
GPSM1
LSM11
TBC1D22B
EXT1
MPPED1
PALM3
RP11-1002K11.1
IGSF3
ST8SIA2
SOX12

Figure S2. Functional enrichment analysis of SCMs and network quality assessment. (A-D) GO enrichment analysis of genes in the SCMs of brain regions. e Overlap between the ASD risk gene set and SCMs. The magenta nodes in the SCMs represent the reported pathogenic genes of ASD. The red nodes represent the region-specific DEGs.

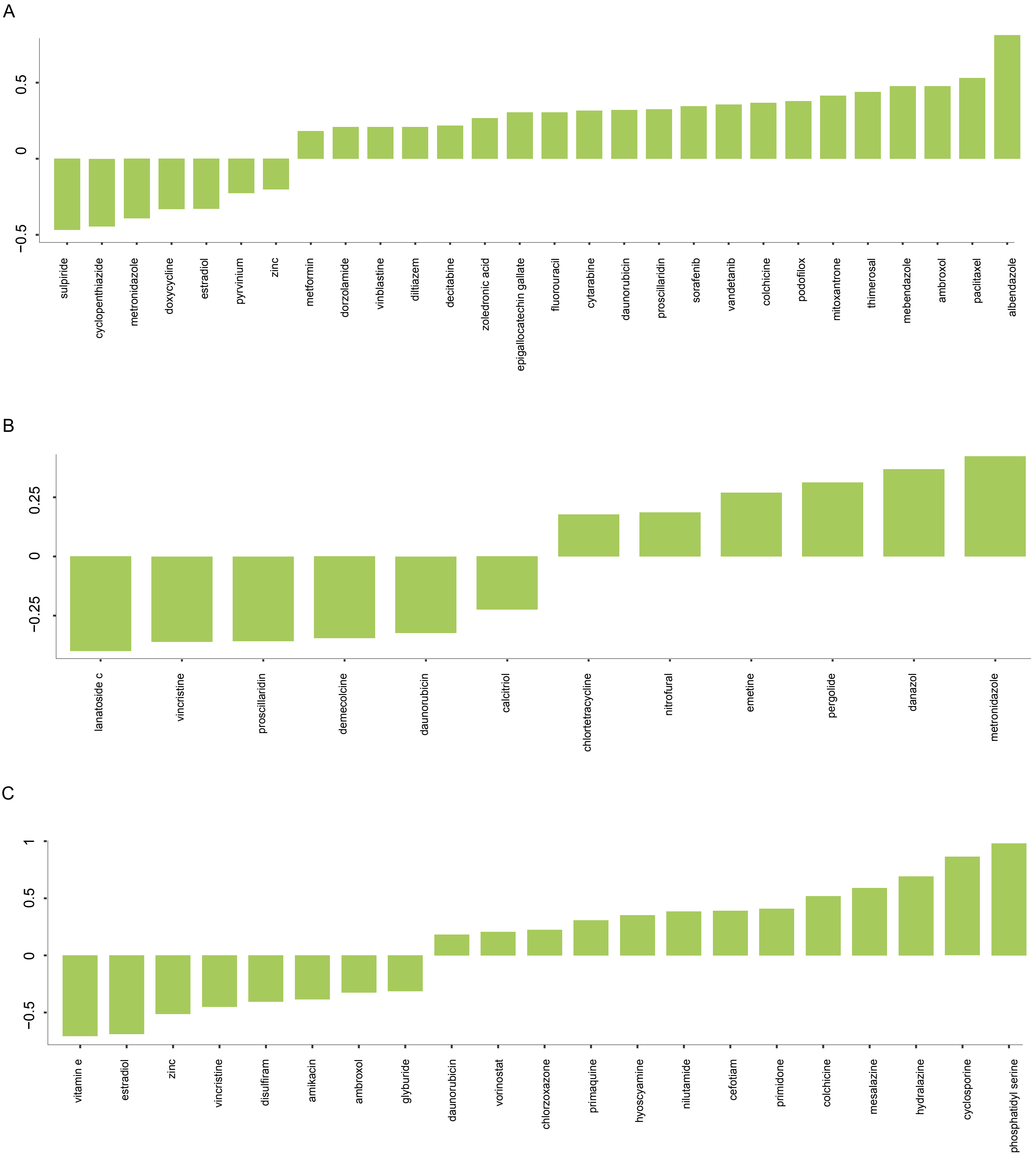


Figure S3. Significant dtNESs from other brain regions. (A) Drug candidate dtNESs from BA8. (B) Drug candidate dtNESs from BA46. (C) Drug candidate dtNESs from CC. The y-axis shows the positive dtNES -1 and negative dtNES + 1, and the x-axis shows the drug name. The vertical bars indicate the computationally predicted therapeutic scores for the drugs based on comparison of the gene expression signatures of the drugs with the NCGs. A negative score means that a drug exhibits an expression pattern that is oppositional to the disease; such, drugs are potential therapeutic drugs.

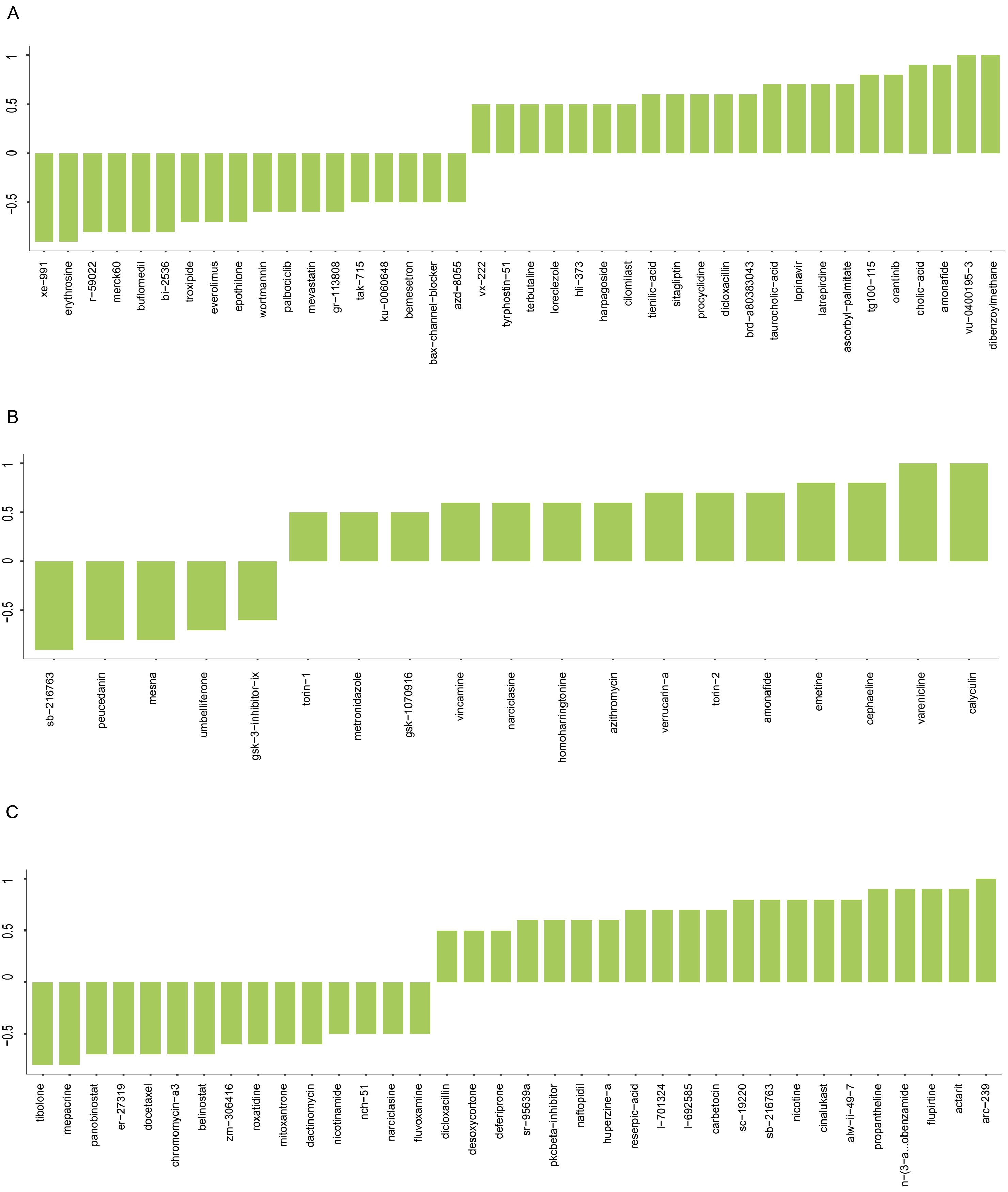
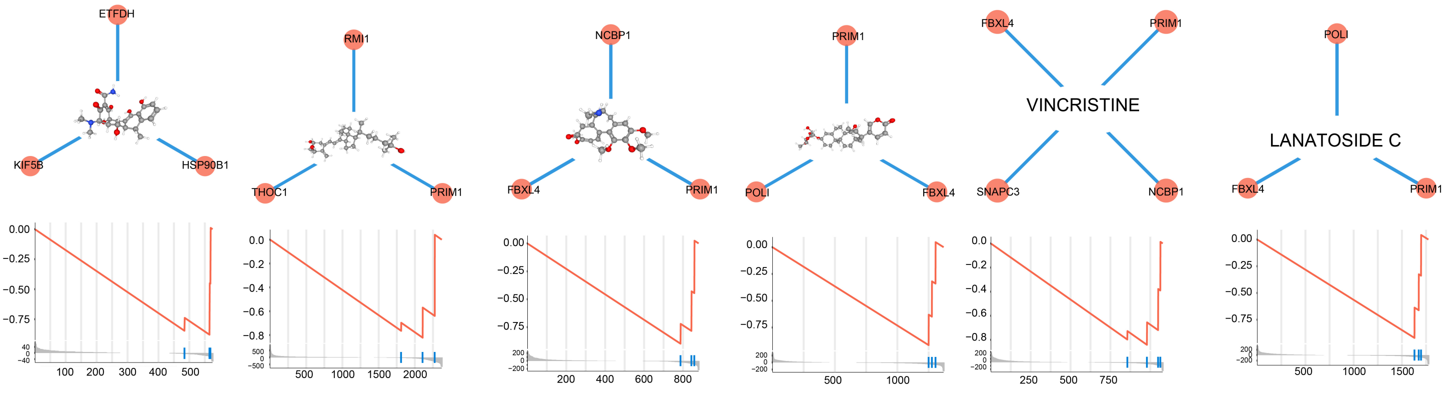
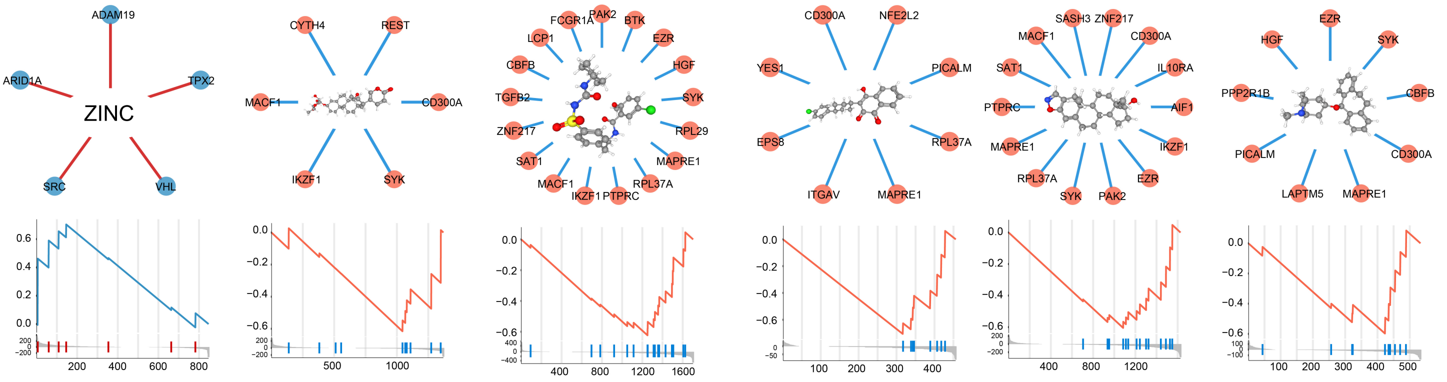


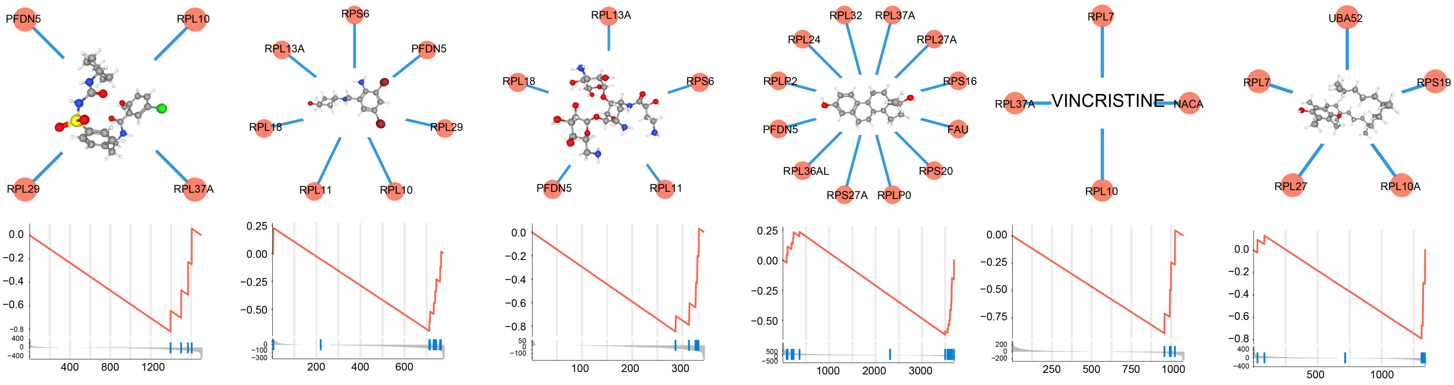
Figure S4. Significant CMap connectivity scores from other brain regions. (A) Drug candidate score from BA8. (B) Drug candidate scores from BA46. (C) Drug candidate scores from CC. The y-axis shows the scores ((positive score - 95)/10 and (negative score + 95)/10) and the x-axis shows the names of the drugs. The vertical bars indicate the computationally predicted therapeutic scores for the drugs based on comparison of the gene expression signatures of the drugs with the NCGs. A negative score indicates that a drug exhibits an expression pattern that is oppositional to the disease; such, drugs are potential therapeutic drugs.



BA8: doxycycline BA46: calcitriol BA46: demecolcine BA46: proscillaridin BA46: vincristine BA46: lanatoside c

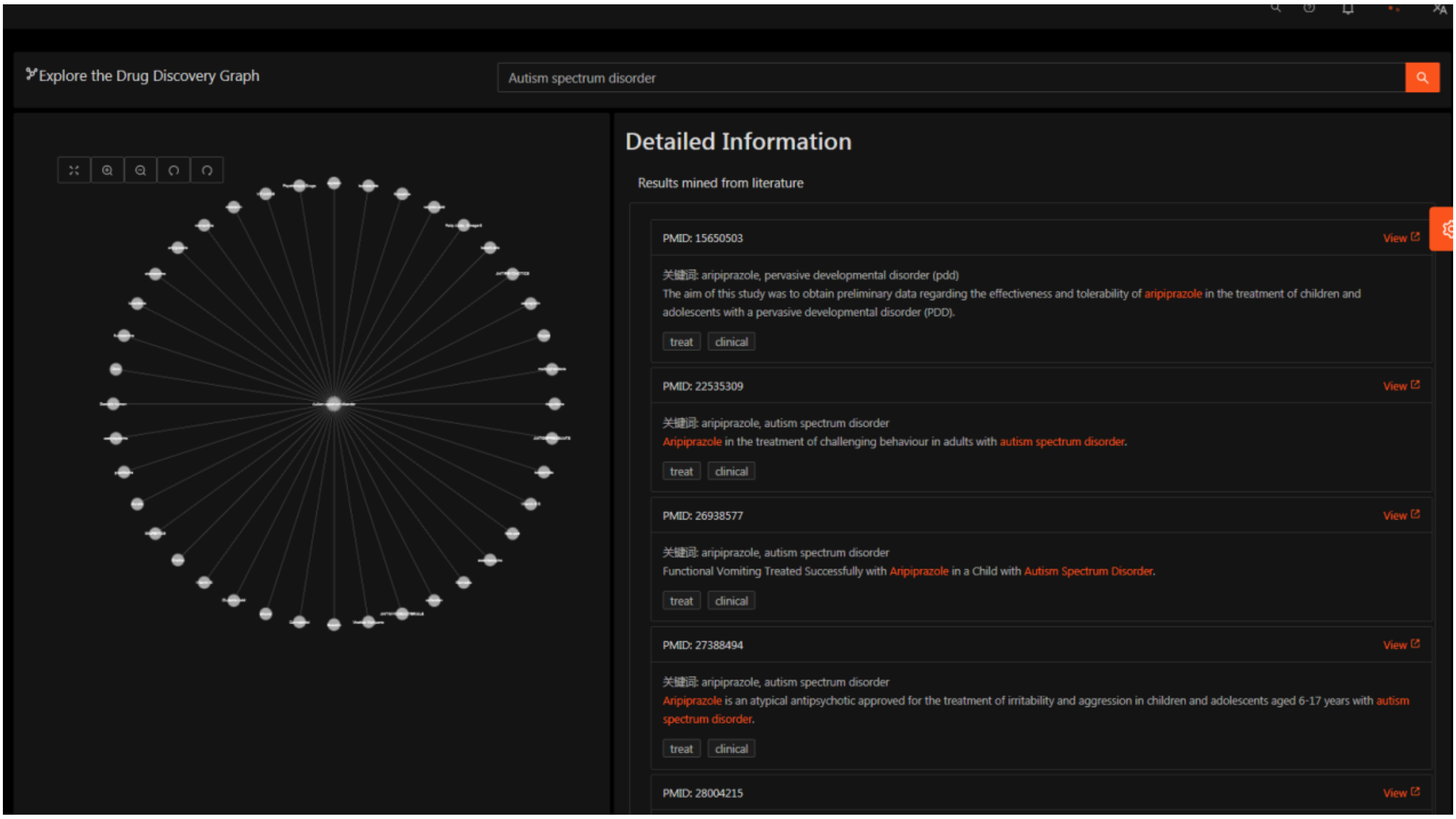


BA8: zinc BA41-42-22: proscillaridin BA41-42-22: glyburide BA41-42-22: atovaquone BA41-42-22: danazol BA41-42-22: deptropine



CC: glyburide CC: ambroxol CC: amikacin CC: estradiol CC: vincristine CC: vitamin e

Figure S5. Target NCGs and GSEA results of other drug candidates that identified by dtGSEA.



Autism spectrum disorder

Detailed Information

Results mined from literature

PMID: 15650503

关键词: aripiprazole, pervasive developmental disorder (pdd)
The aim of this study was to obtain preliminary data regarding the effectiveness and tolerability of aripiprazole in the treatment of children and adolescents with a pervasive developmental disorder (PDD).

treat clinical

PMID: 22535309

关键词: aripiprazole, autism spectrum disorder
Aripiprazole in the treatment of challenging behaviour in adults with autism spectrum disorder.

treat clinical

PMID: 26938577

关键词: aripiprazole, autism spectrum disorder
Functional Vomiting Treated Successfully with Aripiprazole in a Child with Autism Spectrum Disorder.

treat clinical

PMID: 27388494

关键词: aripiprazole, autism spectrum disorder
Aripiprazole is an atypical antipsychotic approved for the treatment of irritability and aggression in children and adolescents aged 6-17 years with autism spectrum disorder.

treat clinical

PMID: 28004215

Figure S6. MCKG visualize in the AskBob platform. The nodes in the outer circle represent compounds, the middle node the disease. Click on each edge to pop up related articles information on the right side of the interface.

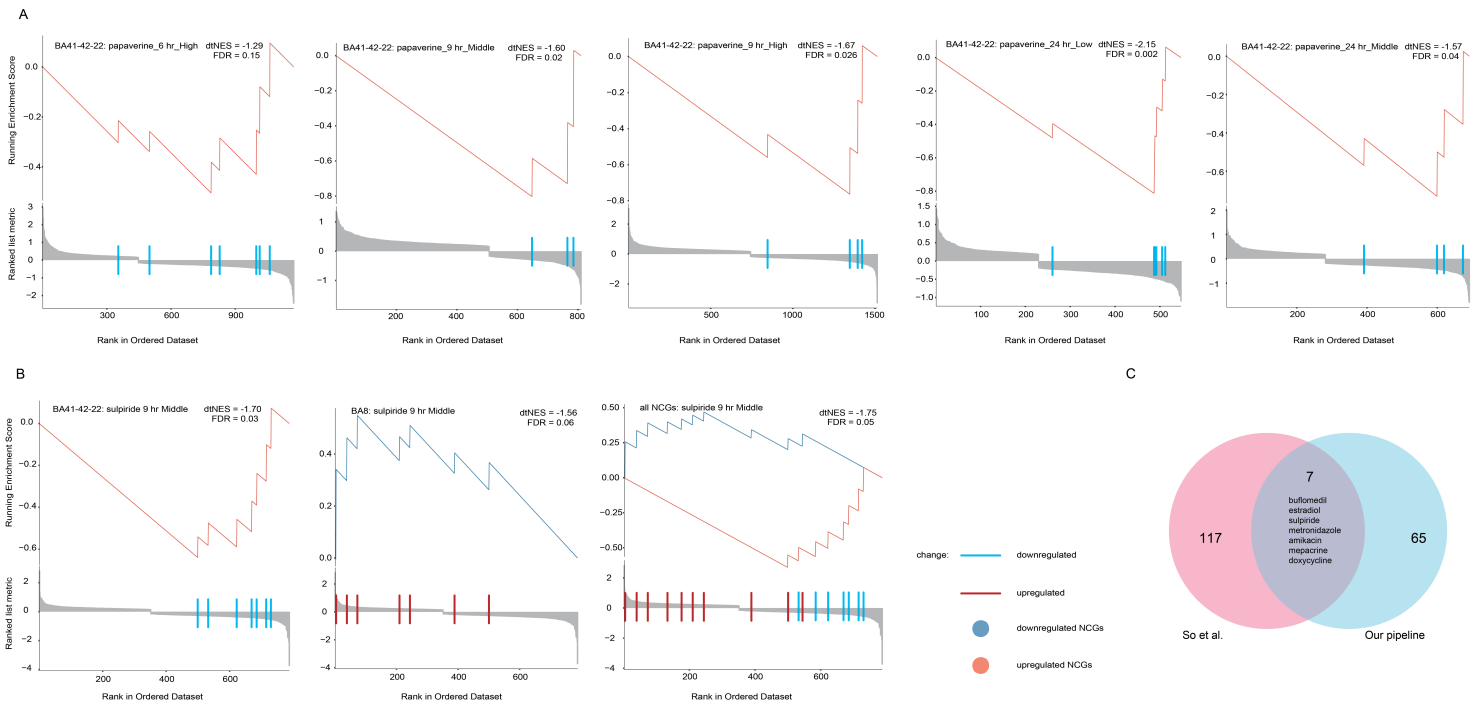


Figure S7. The result of NCGS expression was reversed in toxicogenomic data. a GSEA results of papaverine in rat in vivo transcriptomics data. b GSEA results of sulpiride in rat in vivo transcriptomics data. c Venn diagram.