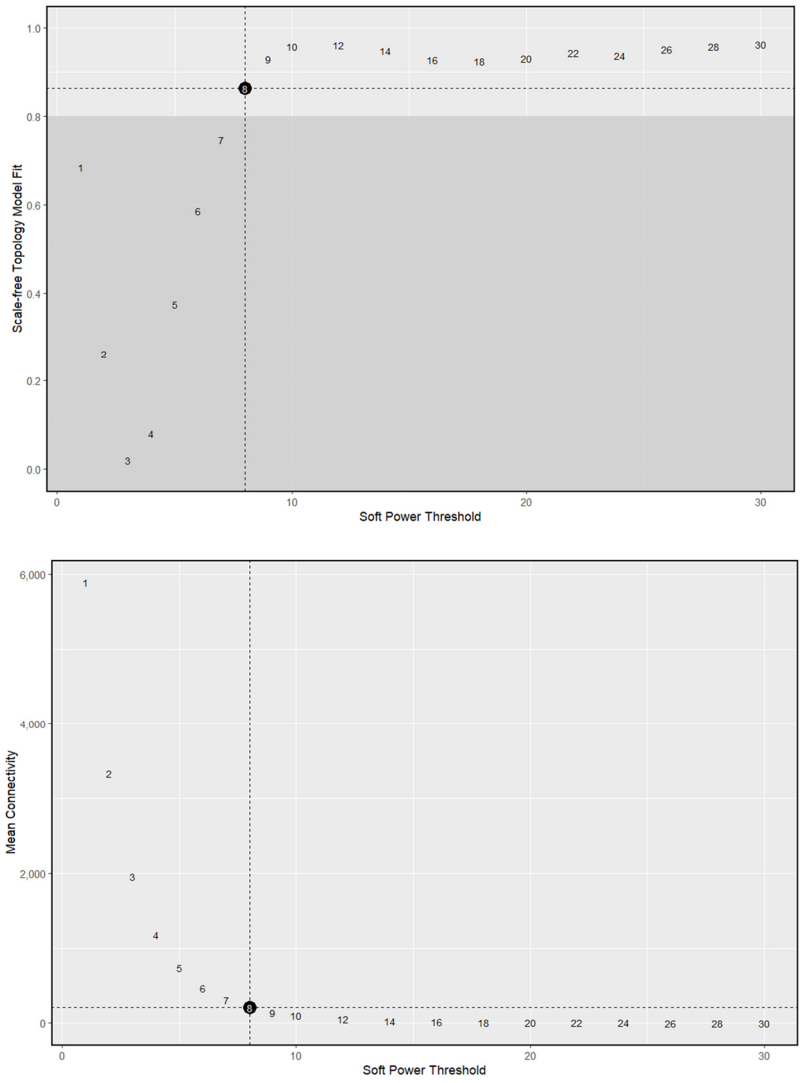
SUPPLEMENTARY FIGURES

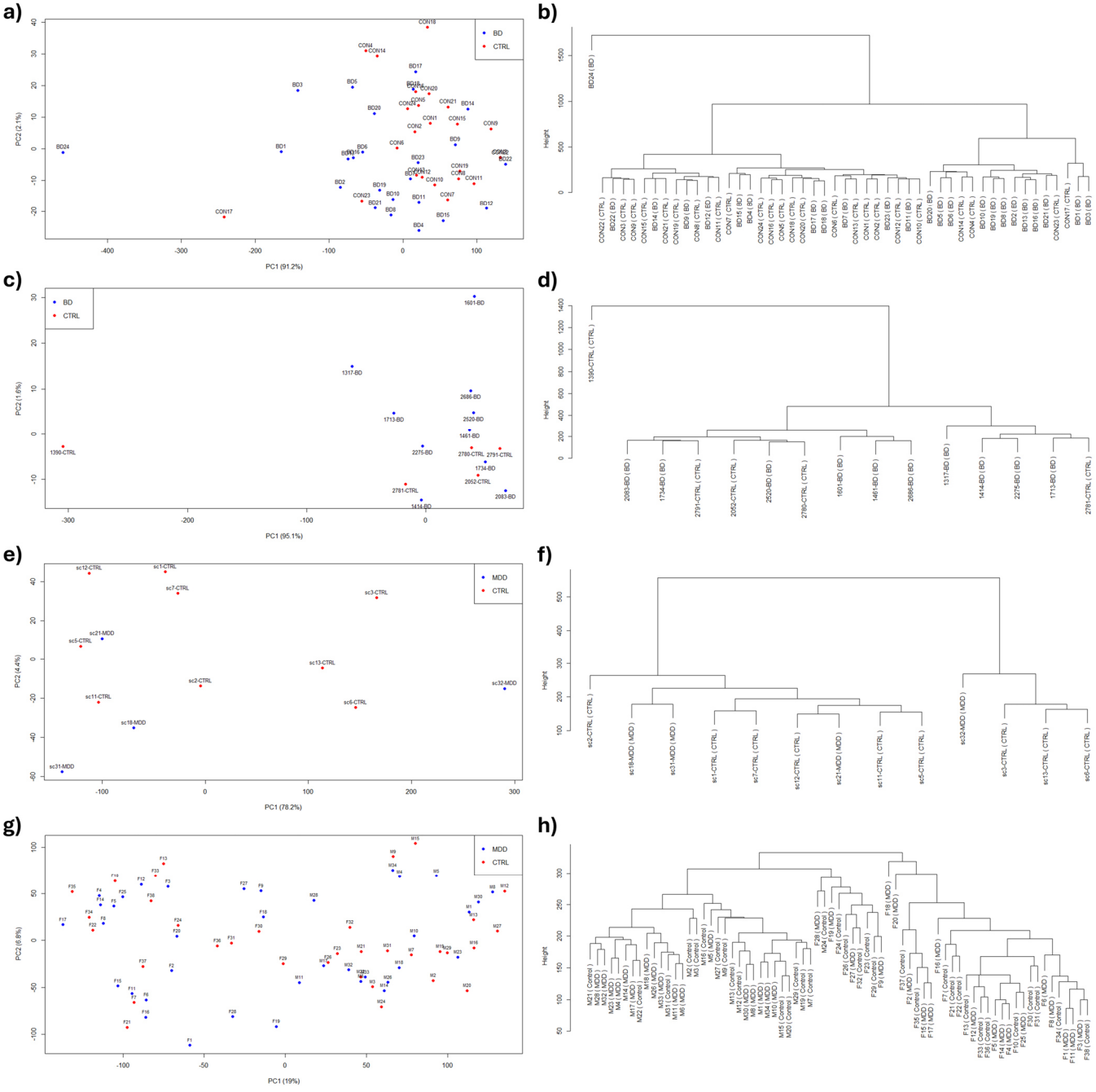
Cell-resolved cortical architecture and intercellular communication distinguish bipolar and major depressive disorders.

Giulietti et al, 2026

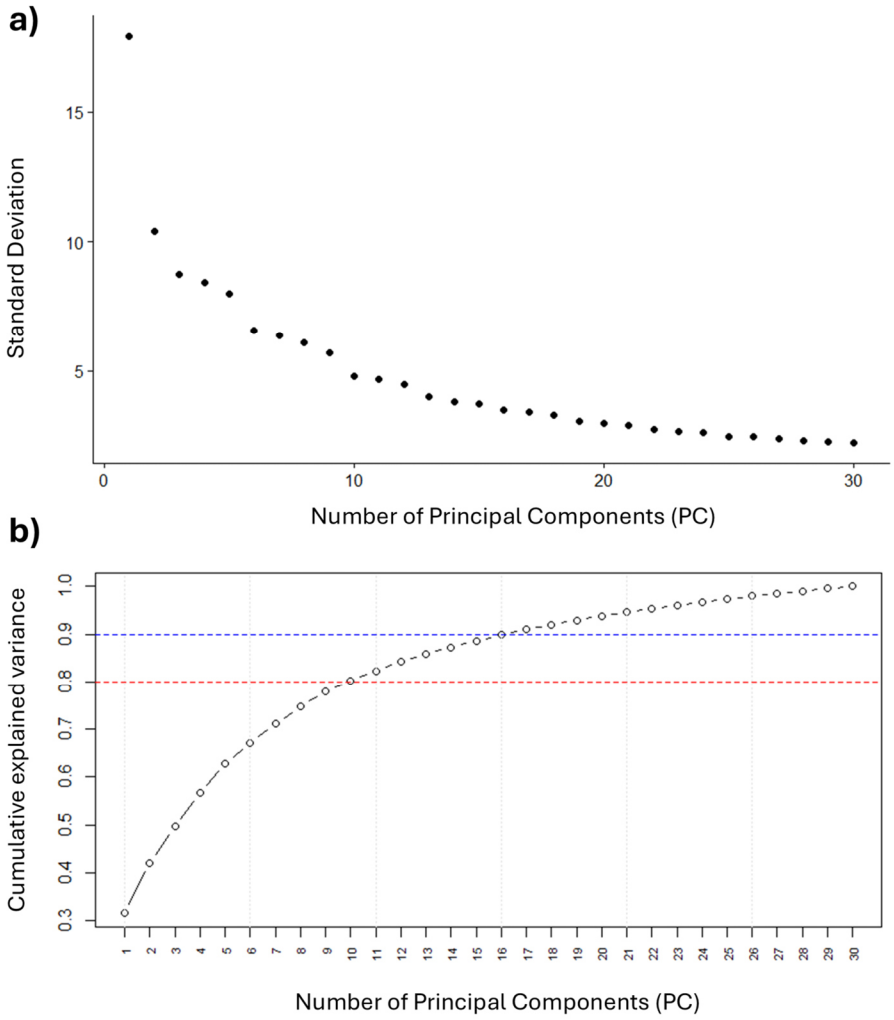
Supplementary Figure S1. Selection of the soft-thresholding power for hdWGCNA network construction. Scale-free topology analysis used to determine the optimal soft-thresholding power for network construction. The upper panel shows the relationship between soft-thresholding power and scale-free topology model fit (signed R^2), while the lower panel shows the relationship with mean connectivity. Consistent with standard WGCNA criteria, a value of β = 8 was selected as the best trade-off between achieving an approximately scale-free network topology and preserving sufficient network connectivity.



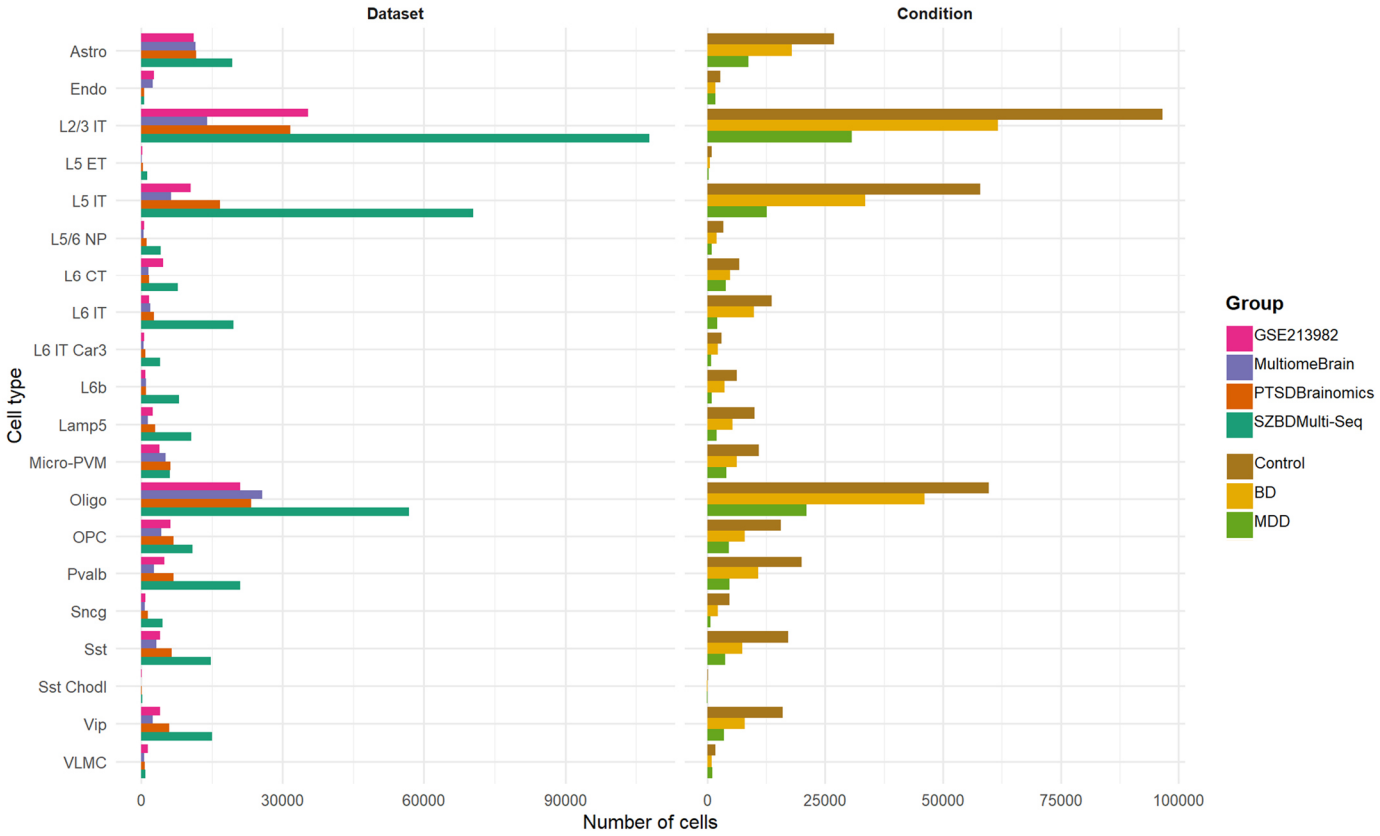
Supplementary Figure S2. ***Identification of outlier samples across datasets using pseudobulk PCA and hierarchical clustering.*** Principal component analysis (PCA; panels a, c, e, g) and hierarchical clustering (panels b, d, f, h) based on global gene expression profiles of pseudobulk data (aggregated raw counts per sample) were performed to assess sample-level variation in: (a–b) SZBDMulti-Seq, (c–d) MultiomeBrain, (e–f) PTSDBrainomics, and (g–h) GSE213982 datasets. Outlier samples BD24 in SZBDMulti-Seq (a–b) and 1390-ctrl in MultiomeBrain (c–d) were clearly distinguishable from the rest and excluded from downstream analyses. No evident outliers were detected in the PTSDBrainomics (e–f) and GSE213982 (g–h) datasets.



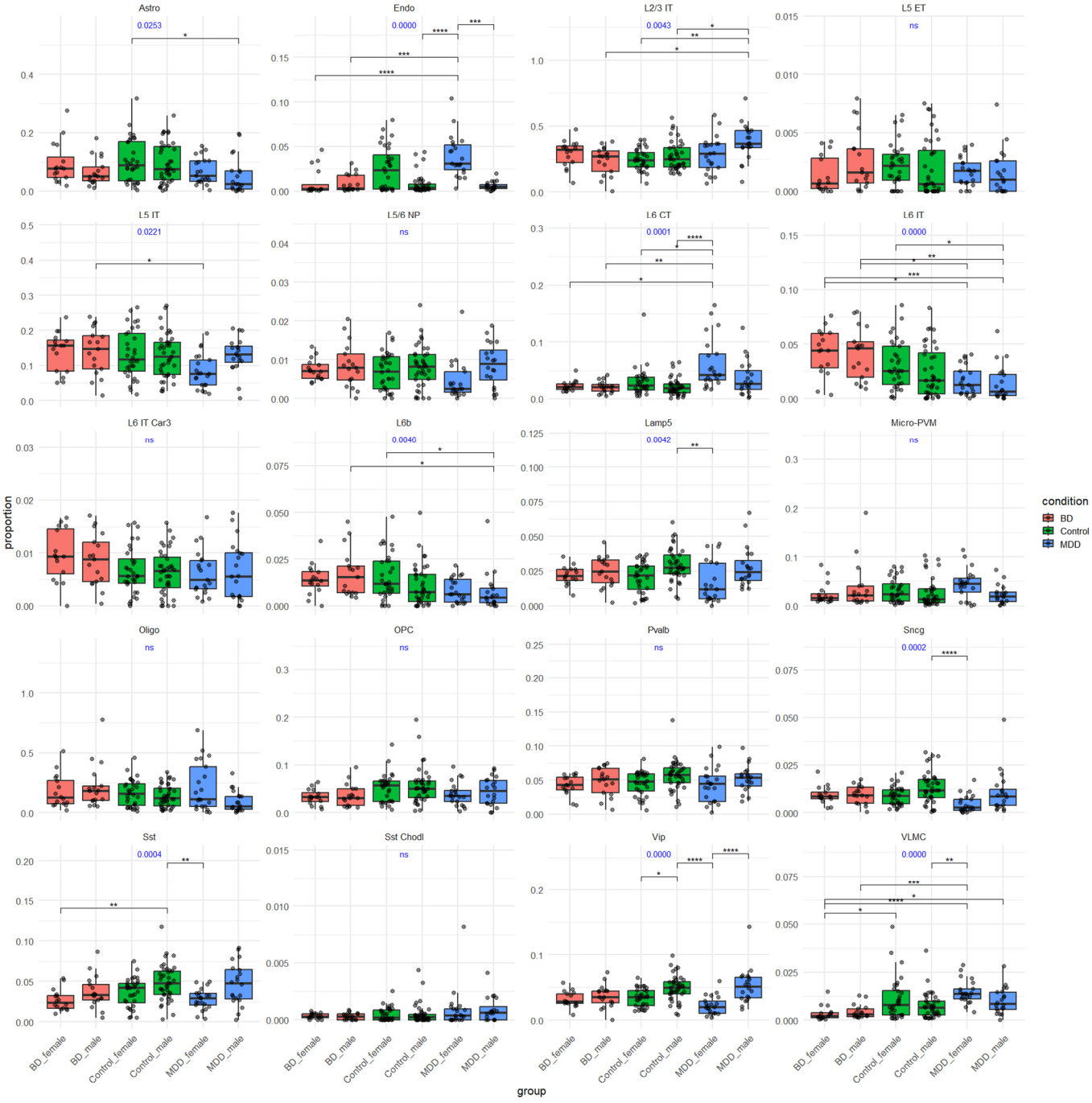
Supplementary Figure S3. (a) Elbow plot displaying the variance explained by each principal component (PC) across the dataset. This plot is used to identify the number of PCs to retain for downstream dimensionality reduction. (b) Cumulative variance explained by increasing numbers of PCs, providing a visual overview of how the dataset's total variance is distributed among components. The first 16 PCs capture approximately 90% of the total variance.



Supplementary Figure S4. Bar plot showing the number of cells per cell type, according to Allen Brain Atlas, across different datasets (left panel) and diagnostic conditions (right panel). Each bar represents the number of nuclei for a specific cell type (y-axis).

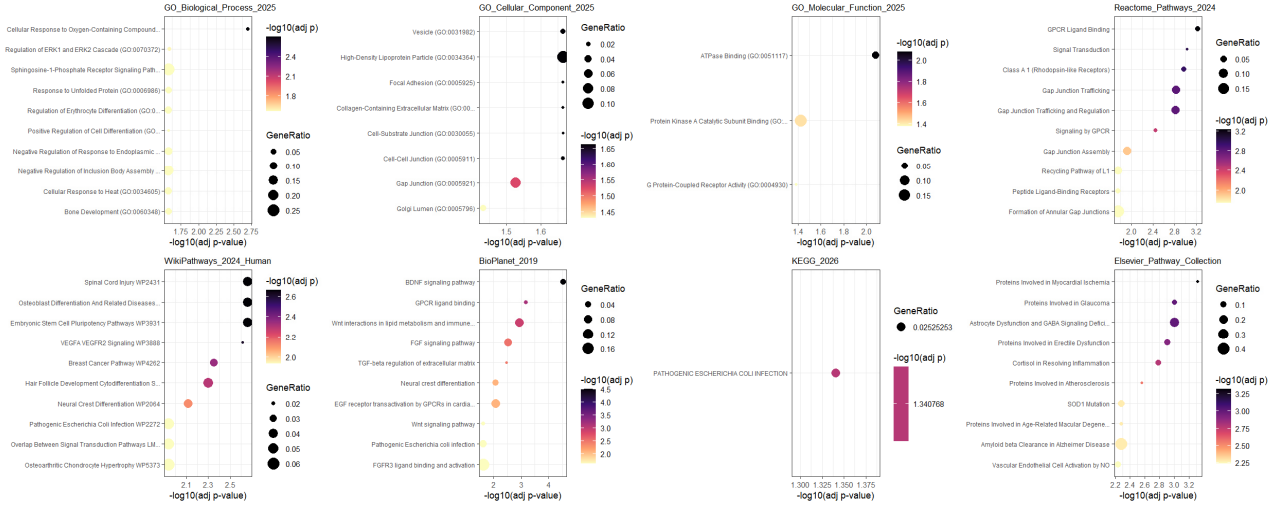


Supplementary Figure S5. Cell type proportion differences across diagnostic and sex groups (BD-female, BD-male, Control-female, Control-male, MDD-female, MDD-male). Box plots show the distribution of relative cell type proportions for each of the 20 identified cell types across the six groups defined by diagnosis and sex. Blue p-values correspond to Kruskal–Wallis tests assessing overall differences across groups. Significant pairwise comparisons from Dunn's post hoc test are indicated using the following notation: ns = not significant; * = p < 0.05; ** = p < 0.01; *** = p < 0.001; **** = p < 0.0001.

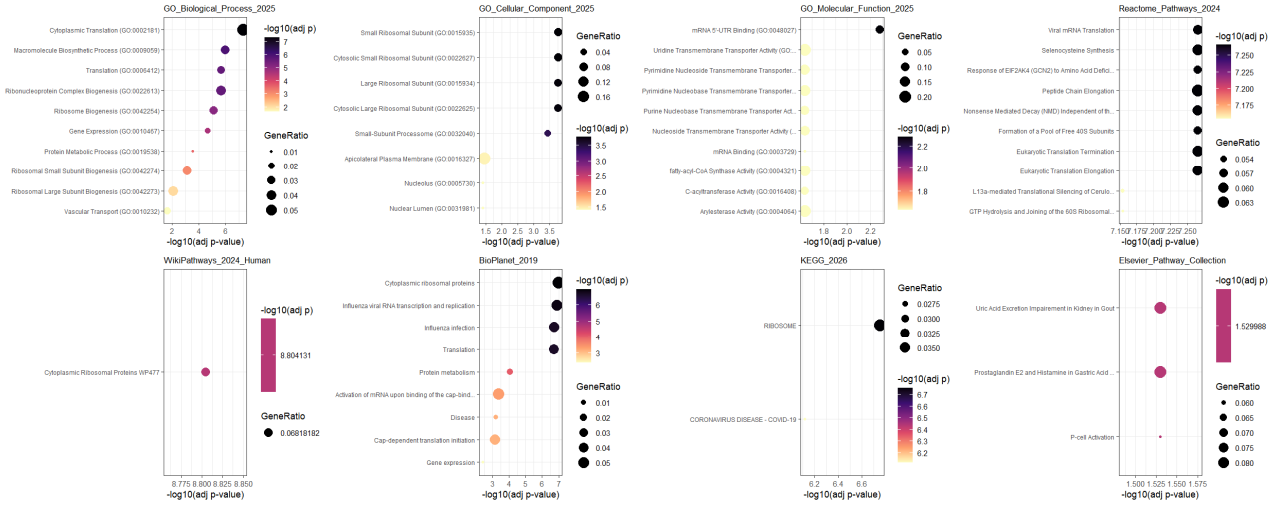


Supplementary Figure S6. Functional enrichment of (a) upregulated genes in BD vs MDD, (b) downregulated genes in BD vs MDD, and (c) downregulated genes in MDD vs CTRL. Dot plots show the top enriched terms across multiple gene set libraries for differentially expressed genes. Dot size represents the gene ratio (fraction of input genes overlapping the gene set), and color intensity corresponds to −log10-transformed adjusted p-value. Only the top 10 terms per database are shown for clarity. Enrichment was performed only for DEG lists containing at least 4 genes.

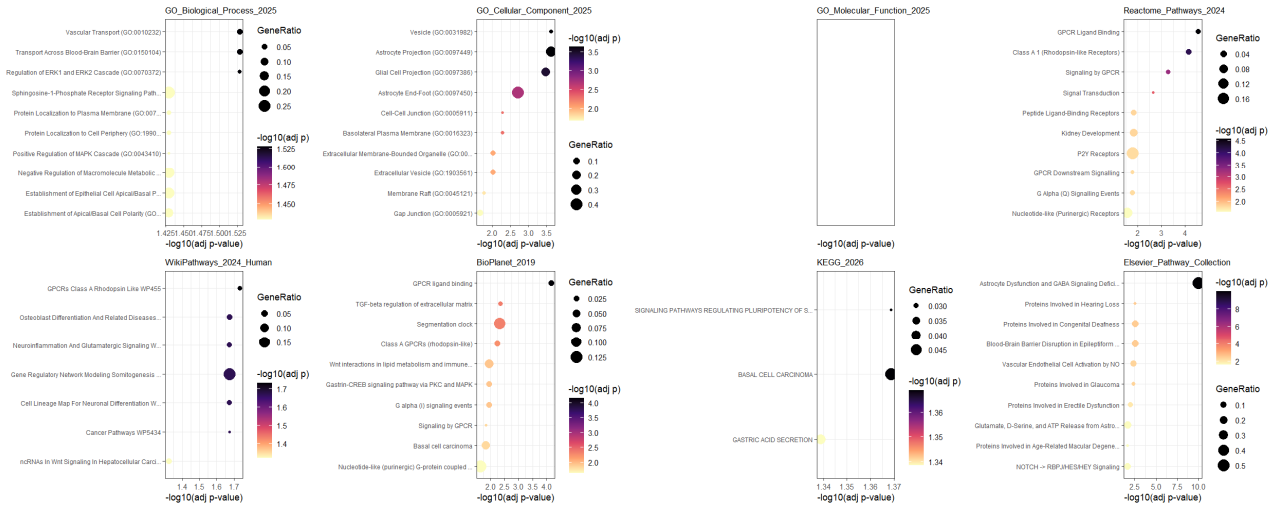
a) Functional enrichment of upregulated genes in BD vs MDD



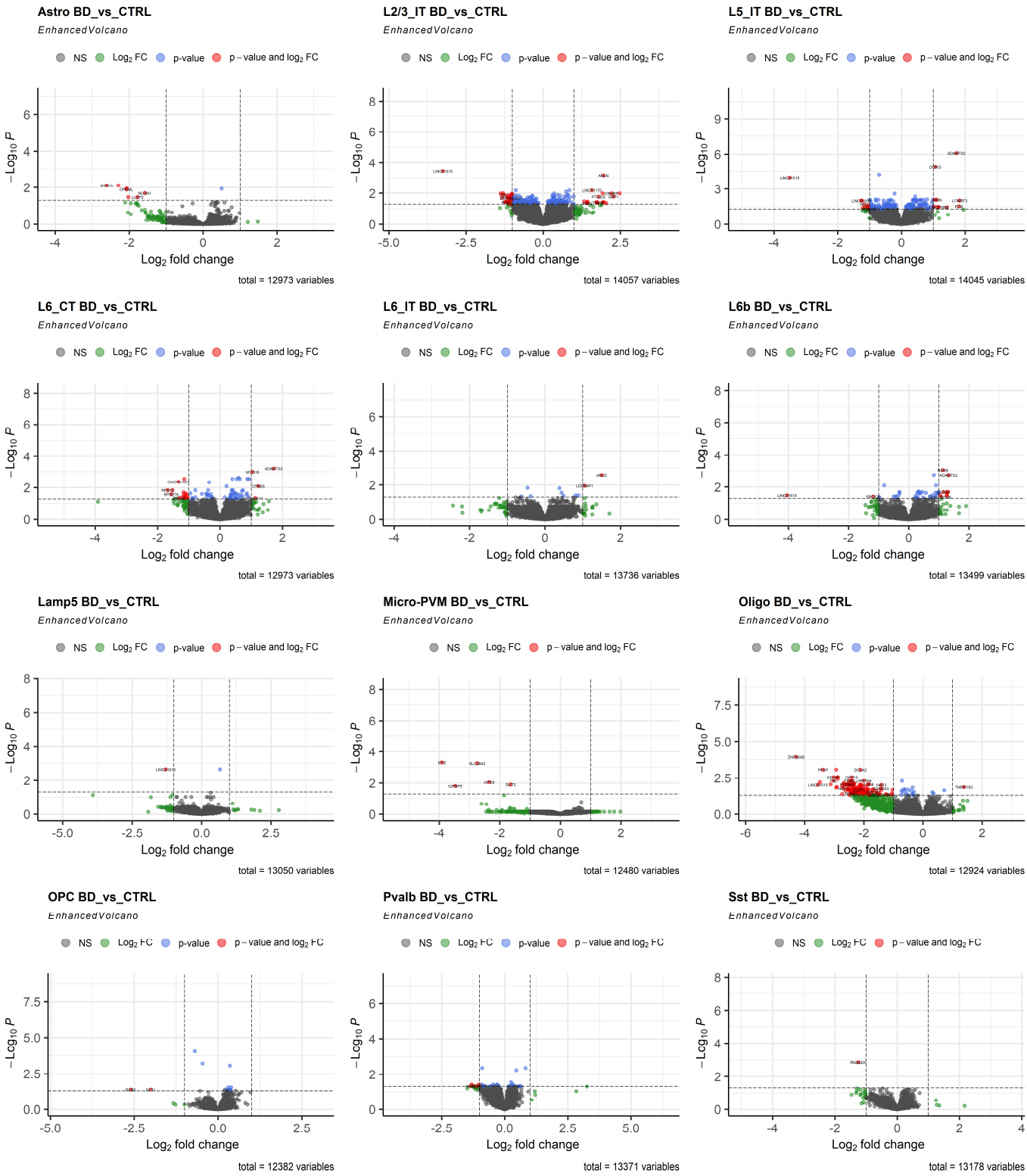
b) Functional enrichment of downregulated genes in BD vs MDD



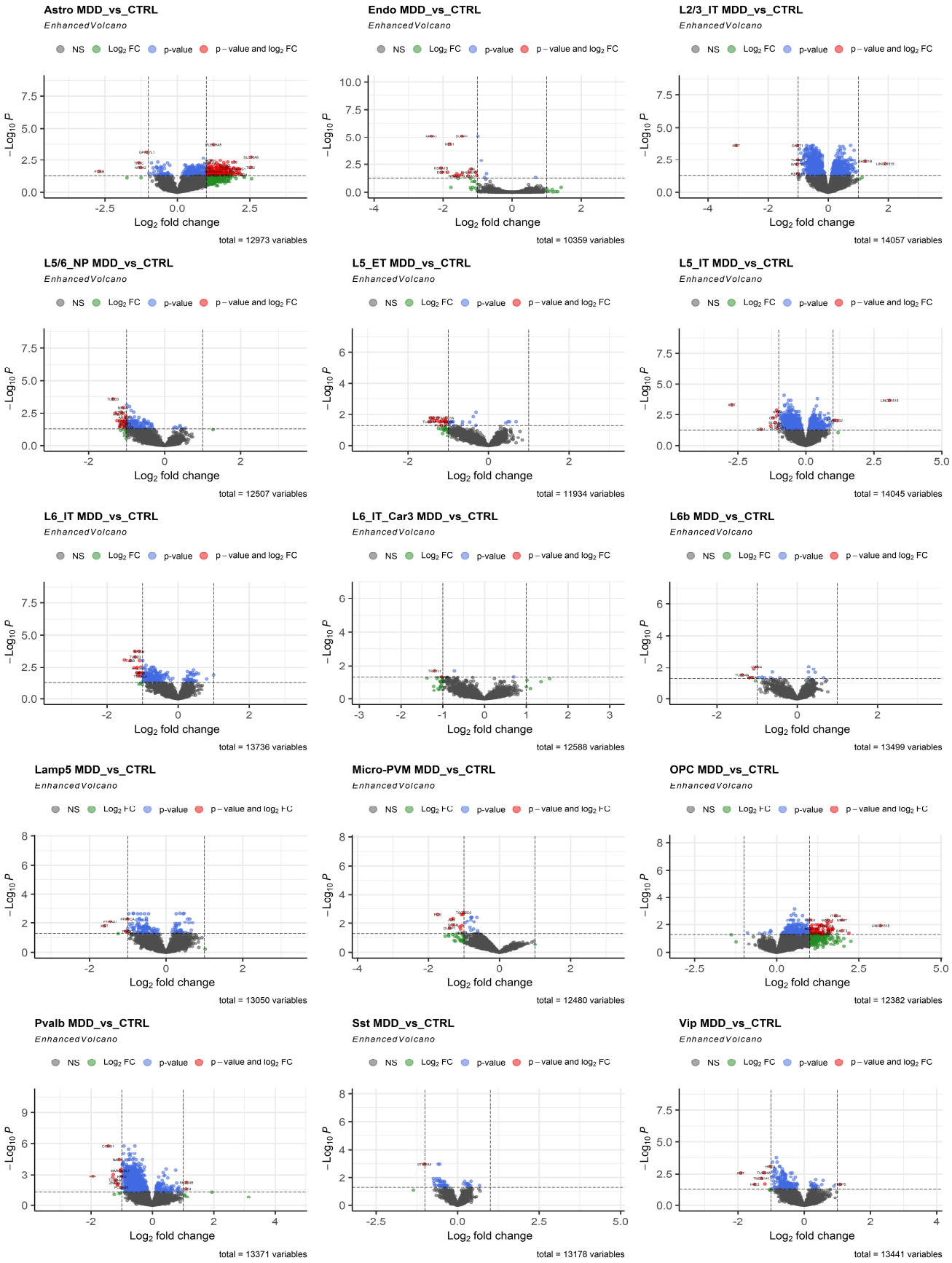
c) Functional enrichment of downregulated genes in MDD vs CTRL



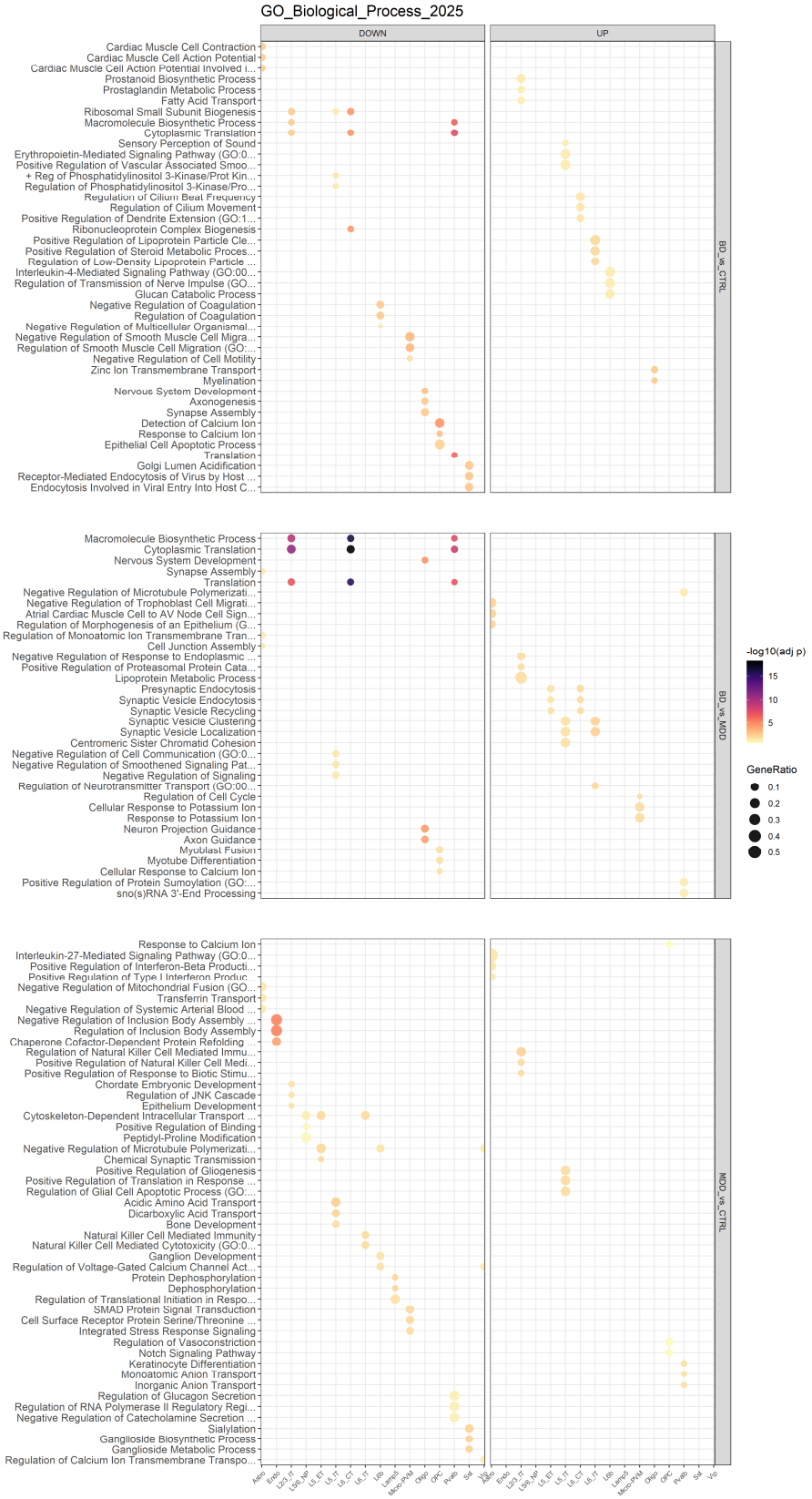
Supplementary Figure S7. Cell-type-specific volcano plots of differential gene expression in BD vs CTRL comparisons. Each point represents a gene, plotted according to its log2 fold change (x-axis) and adjusted p-value (y-axis, −log10 scale). Genes with FDR < 0.05 are highlighted. Volcano plots were generated independently for each cell type using pseudobulk counts and DESeq2-based differential expression analysis. Only comparisons with significant differential expression are shown.

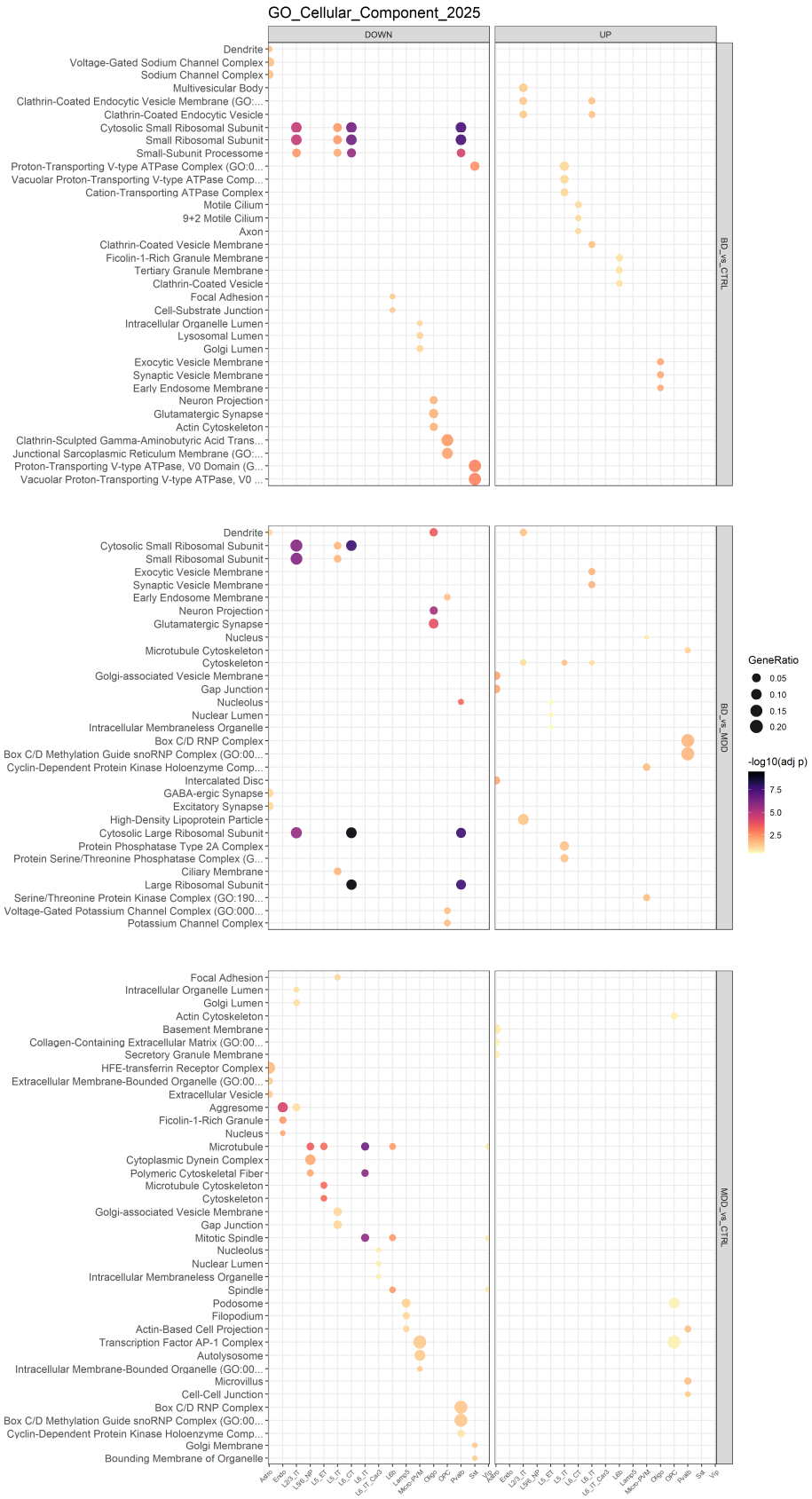


Supplementary Figure S8. Cell-type-specific volcano plots of differential gene expression in MDD vs CTRL comparisons. Each point represents a gene, plotted according to its log2 fold change (x-axis) and adjusted p-value (y-axis, −log10 scale). Genes with FDR < 0.05 are highlighted. Volcano plots were generated independently for each cell type using pseudobulk counts and DESeq2-based differential expression analysis. Only comparisons with significant differential expression are shown.

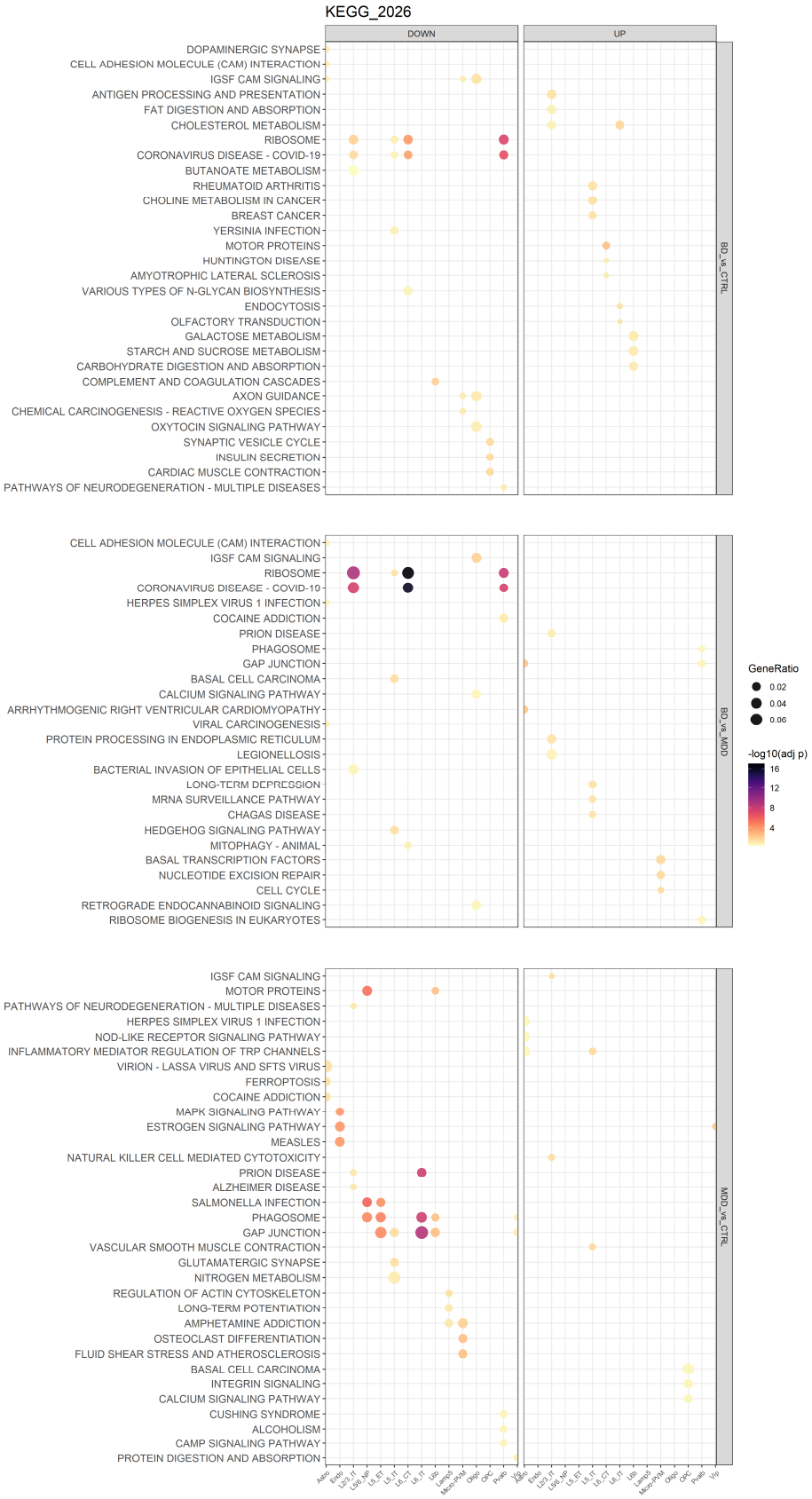


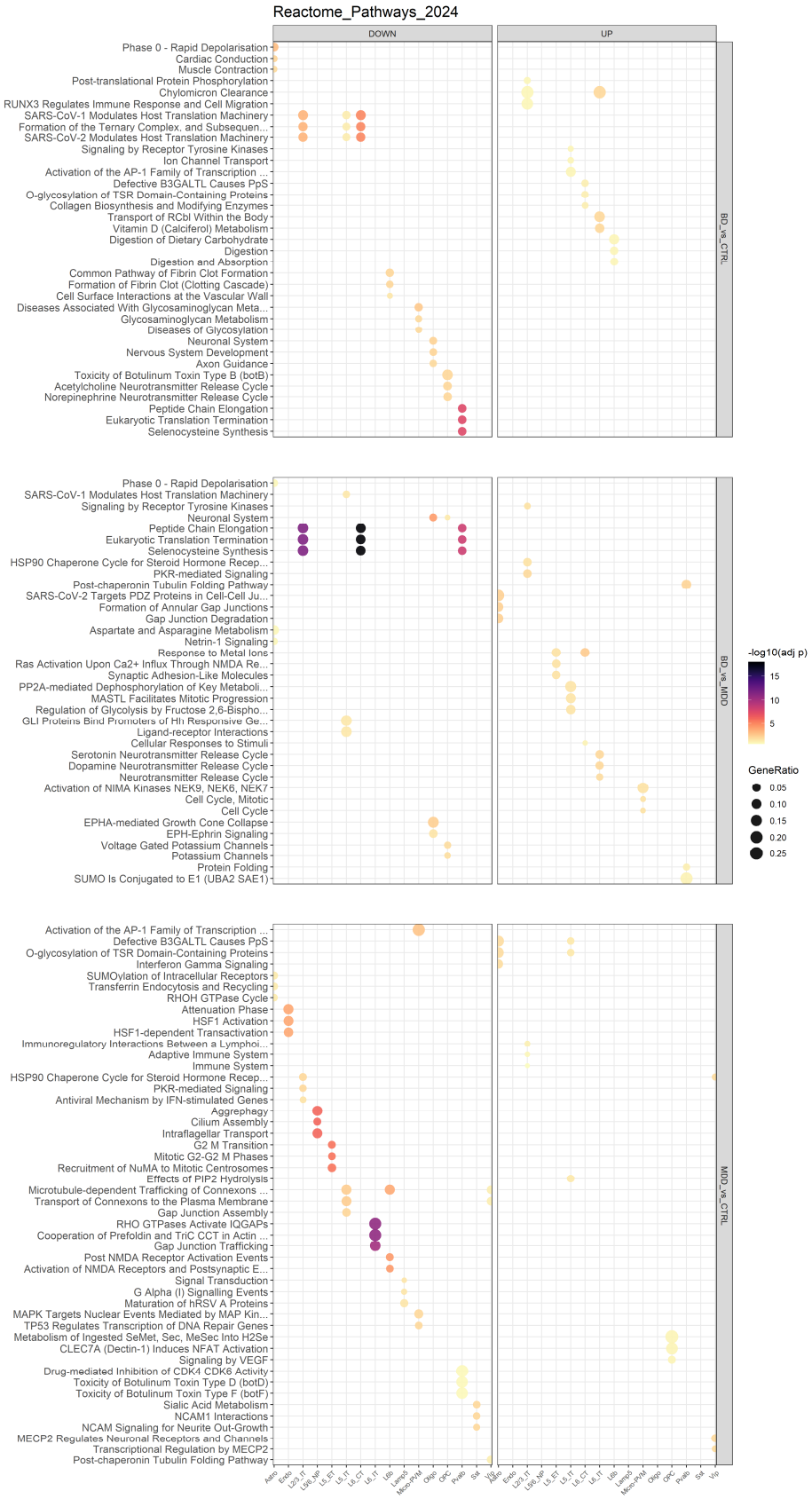
Supplementary Figure S9. Cell type-specific pathway enrichment across diagnostic contrasts in Gene Ontology Biological Process (BP), Cellular Component (GO-CC), Molecular Function (GO-MF), KEGG, Reactome, WikiPathways, BioPlanet, and the Elsevier Pathway Collection libraries. Dot plots summarizing functional enrichment results obtained from differentially expressed genes stratified by cell type, diagnostic contrast, and direction of regulation. For each comparison, only significantly enriched terms (adjusted P < 0.05) are shown, with up to the top 3 terms retained per library. The x-axis represents the −log10 adjusted P value, dot size indicates the gene ratio (overlap between input gene list and gene set), and color intensity reflects enrichment significance.




GO_Cellular_Component_2025
DOWN
UP
BD_vs_CTRL
Dendrite
Voltage-Gated Sodium Channel Complex
Sodium Channel Complex
Multivesicular Body
Clathrin-Coated Endocytic Vesicle Membrane (GO:...
Clathrin-Coated Endocytic Vesicle
Cytosolic Small Ribosomal Subunit
Small Ribosomal Subunit
Small-Subunit Processome
Proton-Transporting V-type ATPase Complex (GO:0...
Vacuolar Proton-Transporting V-type ATPase Comp...
Cation-Transporting ATPase Complex
Motile Cilium
9+2 Motile Cilium
Axon
Clathrin-Coated Vesicle Membrane
Ficolin-1-Rich Granule Membrane
Tertiary Granule Membrane
Clathrin-Coated Vesicle
Focal Adhesion
Cell-Substrate Junction
Intracellular Organelle Lumen
Lysosomal Lumen
Golgi Lumen
Exocytic Vesicle Membrane
Synaptic Vesicle Membrane
Early Endosome Membrane
Neuron Projection
Glutamatergic Synapse
Actin Cytoskeleton
Clathrin-Sculpted Gamma-Aminobutyric Acid Trans...
Junctional Sarcoplasmic Reticulum Membrane (GO:...
Proton-Transporting V-type ATPase, V0 Domain (G...
Vacuolar Proton-Transporting V-type ATPase, V0 ...
BD_vs_MDD
Dendrite
Cytosolic Small Ribosomal Subunit
Small Ribosomal Subunit
Exocytic Vesicle Membrane
Synaptic Vesicle Membrane
Early Endosome Membrane
Neuron Projection
Glutamatergic Synapse
Nucleus
Microtubule Cytoskeleton
Cytoskeleton
Golgi-associated Vesicle Membrane
Gap Junction
Nucleolus
Nuclear Lumen
Intracellular Membraneless Organelle
Box C/D RNP Complex
Box C/D Methylation Guide snoRNP Complex (GO:00...
Cyclin-Dependent Protein Kinase Holoenzyme Comp...
Intercalated Disc
GABA-ergic Synapse
Excitatory Synapse
High-Density Lipoprotein Particle
Cytosolic Large Ribosomal Subunit
Protein Phosphatase Type 2A Complex
Protein Serine/Threonine Phosphatase Complex (G...
Ciliary Membrane
Large Ribosomal Subunit
Serine/Threonine Protein Kinase Complex (GO:190...
Voltage-Gated Potassium Channel Complex (GO:000...
Potassium Channel Complex
GeneRatio
0.05
0.10
0.15
0.20
-log10(adj p)
7.5
5.0
2.5
MDD_vs_CTRL
Focal Adhesion
Intracellular Organelle Lumen
Golgi Lumen
Actin Cytoskeleton
Basement Membrane
Collagen-Containing Extracellular Matrix (GO:00...
Secretory Granule Membrane
HFE-transferrin Receptor Complex
Extracellular Membrane-Bounded Organelle (GO:00...
Extracellular Vesicle
Aggresome
Ficolin-1-Rich Granule
Nucleus
Microtubule
Cytoplasmic Dynein Complex
Polymeric Cytoskeletal Fiber
Microtubule Cytoskeleton
Cytoskeleton
Golgi-associated Vesicle Membrane
Gap Junction
Mitotic Spindle
Nucleolus
Nuclear Lumen
Intracellular Membraneless Organelle
Spindle
Podosome
Filopodium
Actin-Based Cell Projection
Transcription Factor AP-1 Complex
Autolysosome
Intracellular Membrane-Bounded Organelle (GO:00...
Microvillus
Cell-Cell Junction
Box C/D RNP Complex
Box C/D Methylation Guide snoRNP Complex (GO:00...
Cyclin-Dependent Protein Kinase Holoenzyme Comp...
Golgi Membrane
Bounding Membrane of Organelle
Astro
Endo
L2/3_IT
L5/6_NP
L5_ET
L5_IT
L6_CT
L6_IT
L6_IT_Car3
L6b
Lamp5
Micro-PVM
Oligo
OPC
Pvalb
Sst
Vip


GO_Molecular_Function_2025
DOWN
UP
BD_vs_CTRL
BD_vs_MDD
MDD_vs_CTRL
Neurexin Family Protein Binding
Voltage-Gated Sodium Channel Activity
Fibroblast Growth Factor Receptor Binding (GO:0...
E-box Binding
Phosphatidylcholine-Sterol O-acyltransferase Ac...
MHC Class II Protein Binding
Dermatan Sulfotransferase Activity
Uridine Transmembrane Transporter Activity (GO:...
Pyrimidine Nucleobase Transmembrane Transporter...
ATP-dependent Diacylglycerol Kinase Activity (G...
Metalloaminopeptidase Activity
Intracellularly Calcium-Gated Channel Activity ...
G Protein-Coupled Purinergic Nucleotide Recepto...
Prostaglandin Transmembrane Transporter Activit...
Icosanoid Transmembrane Transporter Activity (G...
Calcium-Dependent Phospholipid Binding (GO:0005...
Metalloendopeptidase Activity
Phosphatase Binding
Chondroitin Sulfotransferase Activity
mRNA 5'-UTR Binding
Clathrin Adaptor Activity
Intracellularly Calcium-Gated Chloride Channel ...
Alpha-Glucosidase Activity
Ligand-Gated Monoatomic Ion Channel Activity In...
Extracellular Ligand-Gated Monoatomic Ion Chann...
Insulin-Like Growth Factor II Binding
Oxalate Transmembrane Transporter Activity (GO:...
Sulfate Transmembrane Transporter Activity (GO:...
Zinc Ion Binding
Transition Metal Ion Binding
Transmembrane Receptor Protein Tyrosine Kinase ...
GABA-gated Chloride Ion Channel Activity (GO:00...
GABA-A Receptor Activity
Intracellularly Ligand-Gated Monoatomic Ion Cha...
Protein Kinase A Catalytic Subunit Binding (GO:...
Intracellularly Gated Calcium Channel Activity ...
Adenylate Cyclase Inhibiting G Protein-Coupled ...
Ubiquitin Protein Ligase Binding
Ubiquitin-Like Protein Ligase Binding
RNA Endonuclease Activity
Endonuclease Activity
RNA Nuclease Activity
Neurexin Family Protein Binding
mRNA 5'-UTR Binding
Zinc Ion Binding
Transmembrane Receptor Protein Tyrosine Kinase ...
Adenylate Cyclase Inhibiting G Protein-Coupled ...
Ubiquitin Protein Ligase Binding
Protein Kinase Binding
Glutathione Transmembrane Transporter Activity ...
Tripeptide Transmembrane Transporter Activity (...
Protein Kinase Regulator Activity
Wide Pore Channel Activity
Chromo Shadow Domain Binding
Dipeptidase Activity
Low-Density Lipoprotein Particle Receptor Bindi...
Lipoprotein Particle Receptor Binding
Metalloendopeptidase Inhibitor Activity (GO:000...
Adenyl Nucleotide Binding
Phospholipase Inhibitor Activity
Cuprous Ion Binding
Lipase Inhibitor Activity
Nucleosomal DNA Binding
Protein Phosphatase Regulator Activity (GO:0019...
Endopeptidase Inhibitor Activity
mRNA Binding
mRNA 3'-UTR Binding
Protein Tyrosine Kinase Binding
ATP Binding
Cyclin-Dependent Protein Serine/Threonine Kinas...
Protein Serine/Threonine Kinase Activity (GO:00...
Protein Tyrosine Kinase Activator Activity (GO:...
Voltage-Gated Monoatomic Cation Channel Activit...
Delayed Rectifier Potassium Channel Activity (G...
Cyclic Nucleotide Binding
Voltage-Gated Potassium Channel Activity (GO:00...
rRNA Methyltransferase Activity
Glutamate Receptor Activity
GeneRatio
0.05
0.10
0.15
0.20
-log10(adj p)
6
4
2
Metalloendopeptidase Activity
Ubiquitin Protein Ligase Binding
Hyaluronic Acid Binding
Diacylglycerol-Dependent Serine/Threonine Kinas...
Nuclear Glucocorticoid Receptor Binding (GO:003...
Nuclear Retinoid X Receptor Binding
Nuclear Retinoic Acid Receptor Binding (GO:0042...
DNA-binding Transcription Activator Activity, R...
Double-Stranded DNA Binding
Sequence-Specific Double-Stranded DNA Binding (...
Histone Deacetylase Binding
G Protein-Coupled Receptor Binding
Receptor Ligand Activity
GTP Binding
Guanyl Ribonucleotide Binding
Protein Kinase Binding
Protein Serine/Threonine Kinase Binding (GO:012...
Protein Serine/Threonine Kinase Inhibitor Activ...
Glutathione Transmembrane Transporter Activity ...
Tripeptide Transmembrane Transporter Activity (...
L-glutamate Transmembrane Transporter Activity ...
MHC Class I Protein Binding
Calcium Ion Binding
Transmembrane Receptor Protein Phosphatase Acti...
Transmembrane Receptor Protein Tyrosine Phospha...
Cadherin Binding Involved in Cell-Cell Adhesion...
R-SMAD Binding
Lipoprotein Particle Binding
snoRNA Binding
Peptidase Activator Activity
Chloride Channel Activity
Chloride Transmembrane Transporter Activity (GO...
Monoatomic Anion Channel Activity
Protein Kinase Regulator Activity
Protein Tyrosine/Threonine Phosphatase Activity...
Preribosome Binding
alpha-N-acetylneuraminate Alpha-2,8-Sialyltrans...
Sialyltransferase Activity
Metal Ion Binding
Actin Binding
Astro
Endo
Lin3_IT
L6/6_NP
L5_ET
L5_IT
L5_CT
L6_IT
L6_CT
L6_IT
Lamp5
Micro-PVM
Oligo
OPC
Pvalb
Sst
Vip


KEGG_2026
DOWN
UP
DOPAMINERGIC SYNAPSE
CELL ADHESION MOLECULE (CAM) INTERACTION
IGSF CAM SIGNALING
ANTIGEN PROCESSING AND PRESENTATION
FAT DIGESTION AND ABSORPTION
CHOLESTEROL METABOLISM
RIBOSOME
CORONAVIRUS DISEASE - COVID-19
BUTANOATE METABOLISM
RHEUMATOID ARTHRITIS
CHOLINE METABOLISM IN CANCER
BREAST CANCER
YERSINIA INFECTION
MOTOR PROTEINS
HUNTINGTON DISEASE
AMYOTROPHIC LATERAL SCLEROSIS
VARIOUS TYPES OF N-GLYCAN BIOSYNTHESIS
ENDOCYTOSIS
OLFACTORY TRANSDUCTION
GALACTOSE METABOLISM
STARCH AND SUCROSE METABOLISM
CARBOHYDRATE DIGESTION AND ABSORPTION
COMPLEMENT AND COAGULATION CASCADES
AXON GUIDANCE
CHEMICAL CARCINOGENESIS - REACTIVE OXYGEN SPECIES
OXYTOCIN SIGNALING PATHWAY
SYNAPTIC VESICLE CYCLE
INSULIN SECRETION
CARDIAC MUSCLE CONTRACTION
PATHWAYS OF NEURODEGENERATION - MULTIPLE DISEASES
BD_vs_CTRL
CELL ADHESION MOLECULE (CAM) INTERACTION
IGSF CAM SIGNALING
RIBOSOME
CORONAVIRUS DISEASE - COVID-19
HERPES SIMPLEX VIRUS 1 INFECTION
COCAINE ADDICTION
PRION DISEASE
PHAGOSOME
GAP JUNCTION
BASAL CELL CARCINOMA
CALCIUM SIGNALING PATHWAY
ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY
VIRAL CARCINOGENESIS
PROTEIN PROCESSING IN ENDOPLASMIC RETICULUM
LEGIONELLOSIS
BACTERIAL INVASION OF EPITHELIAL CELLS
LONG-TERM DEPRESSION
MRNA SURVEILLANCE PATHWAY
CHAGAS DISEASE
HEDGEHOG SIGNALING PATHWAY
MITOPHAGY - ANIMAL
BASAL TRANSCRIPTION FACTORS
NUCLEOTIDE EXCISION REPAIR
CELL CYCLE
RETROGRADE ENDOCANNABINOID SIGNALING
RIBOSOME BIOGENESIS IN EUKARYOTES
BD_vs_MDD
GeneRatio
0.02
0.04
0.06
-log10(adj p)
16
12
8
4
IGSF CAM SIGNALING
MOTOR PROTEINS
PATHWAYS OF NEURODEGENERATION - MULTIPLE DISEASES
HERPES SIMPLEX VIRUS 1 INFECTION
NOD-LIKE RECEPTOR SIGNALING PATHWAY
INFLAMMATORY MEDIATOR REGULATION OF TRP CHANNELS
VIRION - LASSA VIRUS AND SFTS VIRUS
FERROPTOSIS
COCAINE ADDICTION
MAPK SIGNALING PATHWAY
ESTROGEN SIGNALING PATHWAY
MEASLES
NATURAL KILLER CELL MEDIATED CYTOTOXICITY
PRION DISEASE
ALZHEIMER DISEASE
SALMONELLA INFECTION
PHAGOSOME
GAP JUNCTION
VASCULAR SMOOTH MUSCLE CONTRACTION
GLUTAMATERGIC SYNAPSE
NITROGEN METABOLISM
REGULATION OF ACTIN CYTOSKELETON
LONG-TERM POTENTIATION
AMPHETAMINE ADDICTION
OSTEOCLAST DIFFERENTIATION
FLUID SHEAR STRESS AND ATHEROSCLEROSIS
BASAL CELL CARCINOMA
INTEGRIN SIGNALING
CALCIUM SIGNALING PATHWAY
CUSHING SYNDROME
ALCOHOLISM
CAMP SIGNALING PATHWAY
PROTEIN DIGESTION AND ABSORPTION
Astro
Endo
L2/3_IT
L4/6_INP
L5_ET
L5_IT
L5_CT
L6_IT
L6b
Lamp5
Micro-PVM
Oligo
OPC
Pvalb
Vip
MDD_vs_CTRL


Reactome_Pathways_2024
DOWN
UP
BD_vs_CTR
Phase 0 - Rapid Depolarisation
Cardiac Conduction
Muscle Contraction
Post-translational Protein Phosphorylation
Chylomicron Clearance
RUNX3 Regulates Immune Response and Cell Migration
SARS-CoV-1 Modulates Host Translation Machinery
Formation of the Ternary Complex, and Subsequen...
SARS-CoV-2 Modulates Host Translation Machinery
Signaling by Receptor Tyrosine Kinases
Ion Channel Transport
Activation of the AP-1 Family of Transcription ...
Defective B3GALTL Causes PpS
O-glycosylation of TSR Domain-Containing Proteins
Collagen Biosynthesis and Modifying Enzymes
Transport of RCbl Within the Body
Vitamin D (Calciferol) Metabolism
Digestion of Dietary Carbohydrate
Digestion
Digestion and Absorption
Common Pathway of Fibrin Clot Formation
Formation of Fibrin Clot (Clotting Cascade)
Cell Surface Interactions at the Vascular Wall
Diseases Associated With Glycosaminoglycan Meta...
Glycosaminoglycan Metabolism
Diseases of Glycosylation
Neuronal System
Nervous System Development
Axon Guidance
Toxicity of Botulinum Toxin Type B (botB)
Acetylcholine Neurotransmitter Release Cycle
Norepinephrine Neurotransmitter Release Cycle
Peptide Chain Elongation
Eukaryotic Translation Termination
Selenocysteine Synthesis
BD_vs_MDD
Phase 0 - Rapid Depolarisation
SARS-CoV-1 Modulates Host Translation Machinery
Signaling by Receptor Tyrosine Kinases
Neuronal System
Peptide Chain Elongation
Eukaryotic Translation Termination
Selenocysteine Synthesis
HSP90 Chaperone Cycle for Steroid Hormone Recep...
PKR-mediated Signaling
Post-chaperonin Tubulin Folding Pathway
SARS-CoV-2 Targets PDZ Proteins in Cell-Cell Ju...
Formation of Annular Gap Junctions
Gap Junction Degradation
Aspartate and Asparagine Metabolism
Netrin-1 Signaling
Response to Metal Ions
Ras Activation Upon Ca2+ Influx Through NMDA Re...
Synaptic Adhesion-Like Molecules
PP2A-mediated Dephosphorylation of Key Metaboli...
MASTL Facilitates Mitotic Progression
Regulation of Glycolysis by Fructose 2,6-Bispho...
GLI Proteins Bind Promoters of Hh Responsive Ge...
Ligand-receptor Interactions
Cellular Responses to Stimuli
Serotonin Neurotransmitter Release Cycle
Dopamine Neurotransmitter Release Cycle
Neurotransmitter Release Cycle
Activation of NIMA Kinases NEK9, NEK6, NEK7
Cell Cycle, Mitotic
Cell Cycle
EPHA-mediated Growth Cone Collapse
EPH-Ephrin Signaling
Voltage Gated Potassium Channels
Potassium Channels
Protein Folding
SUMO Is Conjugated to E1 (UBA2 SAE1)
-log10(adj p)
15
10
5
GeneRatio
0.05
0.10
0.15
0.20
0.25
MDD_vs_CTRL
Activation of the AP-1 Family of Transcription ...
Defective B3GALTL Causes PpS
O-glycosylation of TSR Domain-Containing Proteins
Interferon Gamma Signaling
SUMOylation of Intracellular Receptors
Transferrin Endocytosis and Recycling
RHOH GTPase Cycle
Attenuation Phase
HSF1 Activation
HSF1-dependent Transactivation
Immunoregulatory Interactions Between a Lymphoi...
Adaptive Immune System
Immune System
HSP90 Chaperone Cycle for Steroid Hormone Recep...
PKR-mediated Signaling
Antiviral Mechanism by IFN-stimulated Genes
Aggrephagy
Cilium Assembly
Intraflagellar Transport
G2 M Transition
Mitotic G2-G2 M Phases
Recruitment of NuMA to Mitotic Centrosomes
Effects of PIP2 Hydrolysis
Microtubule-dependent Trafficking of Connexons ...
Transport of Connexons to the Plasma Membrane
Gap Junction Assembly
RHO GTPases Activate IQGAPs
Cooperation of Prefoldin and TriC CCT in Actin ...
Gap Junction Trafficking
Post NMDA Receptor Activation Events
Activation of NMDA Receptors and Postsynaptic E...
Signal Transduction
G Alpha (i) Signalling Events
Maturation of hRSV A Proteins
MAPK Targets Nuclear Events Mediated by MAP Kin...
TP53 Regulates Transcription of DNA Repair Genes
Metabolism of Ingested SeMet, Sec, MeSec Into H2Se
CLEC7A (Dectin-1) Induces NFAT Activation
Signaling by VEGF
Drug-mediated Inhibition of CDK4 CDK6 Activity
Toxicity of Botulinum Toxin Type D (botD)
Toxicity of Botulinum Toxin Type F (botF)
Sialic Acid Metabolism
NCAM1 Interactions
NCAM Signaling for Neurite Out-Growth
MECP2 Regulates Neuronal Receptors and Channels
Transcriptional Regulation by MECP2
Post-chaperonin Tubulin Folding Pathway
Astro
Endo
L2/3_IT
L5/6_NP
L5_ET
L5_IT
L5_CT
L6_IT
L6b
Lamp5
Micro-PVM
Oligo
OPC
Pvalb
Sst
Vip


WikiPathways_2024_Human
DOWN
UP
Serotonin And Anxiety Related Events WP3944
NRXN1 Deletion Syndrome WP5398
ADHD And Autism ASD Pathways WP5420
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TYROBP Causal Network In Microglia WP3945
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Mineralocorticoid Biosynthesis WP5279
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Gastrin Signaling WP4659
Breast Cancer Pathway WP4262
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TGF Beta In Thyroid Cells For Epithelial Mesenc...
Metabolic Pathways Of Fibroblasts WP5312
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Smith Magenis And Potocki Lupski Syndrome Copy ...
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Fatty Acids And Lipoproteins Transport In Hepat...
Vitamin A1 And A5 X Pathways WP5397
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Arrhythmogenic Right Ventricular Cardiomyopathy...
Splicing Factor NOVA Regulated Synaptic Protein...
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Disruption Of Postsynaptic Signaling By CNV WP4875
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Intracellular Trafficking Proteins Involved In ...
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GPCRs Class C Metabotropic Glutamate Pheromone ...
Parkin Ubiquitin Proteasomal System Pathway WP2359
Pathogenic Escherichia Coli Infection WP2272
Sudden Infant Death Syndrome SIDS Susceptibilit...
VEGFA VEGFR2 Signaling WP3888
Ectoderm Differentiation WP2858
Genes Targeted By miRNAs In Adipocytes WP1992
1Q21 1 Copy Number Variation Syndrome WP4905
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Hedgehog Signaling WP4249
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Synaptic Vesicle Pathway WP2267
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EPAC1 And PKA Reduction Of Retinal Inflammation...
Eukaryotic Transcription Initiation WP405
Nucleotide Excision Repair WP4753
Calcium Regulation In Cardiac Cells WP536
Neurogenesis Regulation In The Olfactory Epithe...
Cell Differentiation Expanded Index WP2023
Exercise Induced Circadian Regulation WP410
BD_vs_MDD
GeneRatio
0.05
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0.15
-log10(adj p)
15
10
5
Serotonin And Anxiety Related Events WP3944
Mammary Gland Development Pathway Puberty Stage...
Metabolic Pathways Of Fibroblasts WP5312
Type I Collagen Synthesis Osteogenesis Imperfec...
Type I Interferon Induction And Signaling SARS ...
Pathways Of Nucleic Acid Metabolism And Innate ...
Type II Interferon Signaling WP619
Corticotropin Releasing Hormone Signaling WP2355
Iron Metabolism In Placenta WP2007
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Nuclear Receptors Meta Pathway WP2882
Macrophage Stimulating Protein MSP Signaling WP...
MAPK Signaling WP382
Parkin Ubiquitin Proteasomal System Pathway WP2359
Alzheimer 39 S Disease WP5124
Alzheimer 39 S Disease And miRNA Effects WP2059
Pathogenic Escherichia Coli Infection WP2272
HDAC6 Interactions In The Central Nervous Syste...
Kisspeptin Kisspeptin Receptor System In The Ov...
Cell Lineage Map For Neuronal Differentiation W...
Neuroinflammation And Glutamatergic Signaling W...
Sudden Infant Death Syndrome SIDS Susceptibilit...
VEGFA VEGFR2 Signaling WP3888
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TGF Beta Signaling Pathway WP366
Selenium Metabolism And Selenoproteins WP28
RANKL RANK Signaling WP2018
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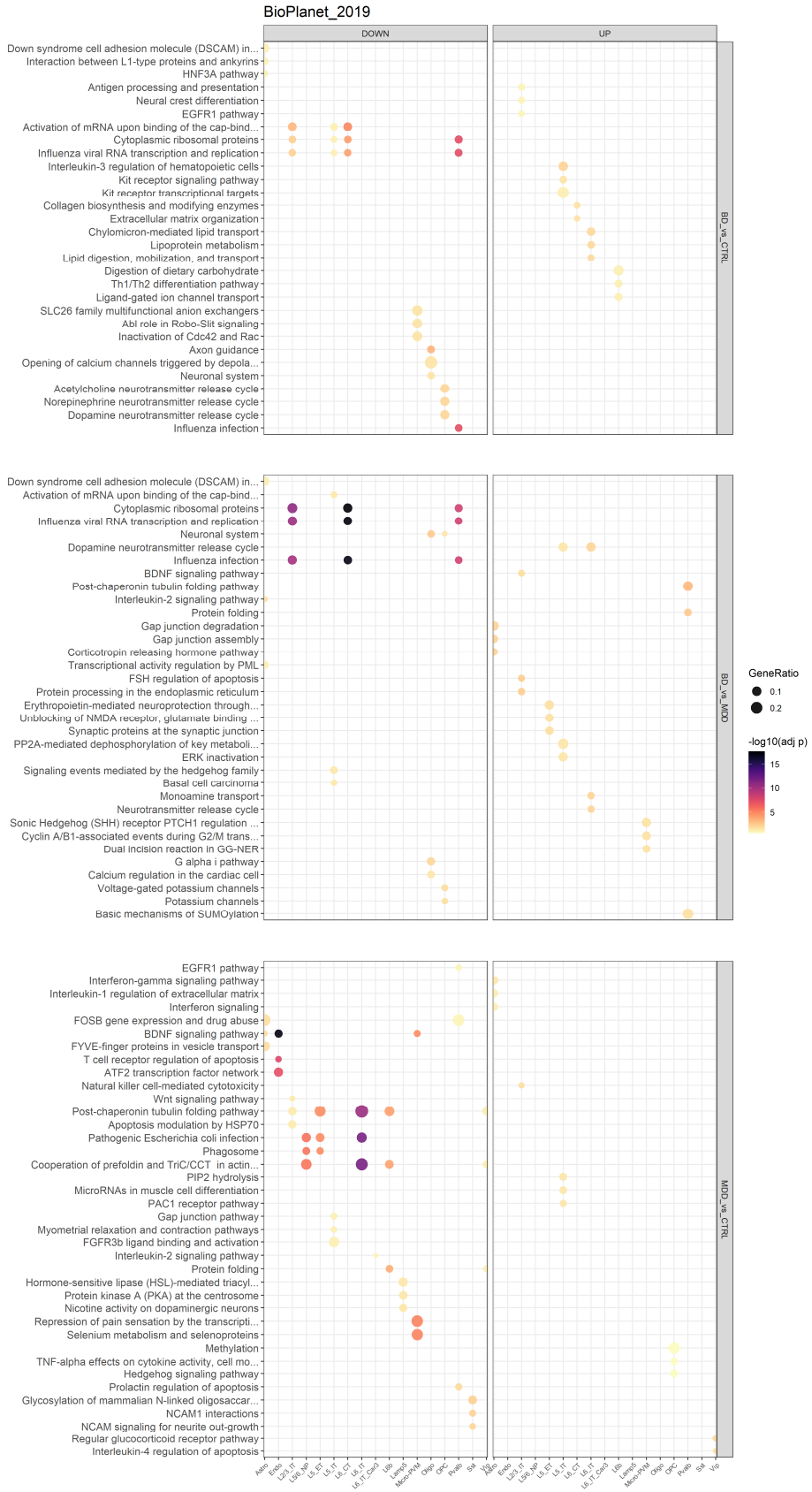
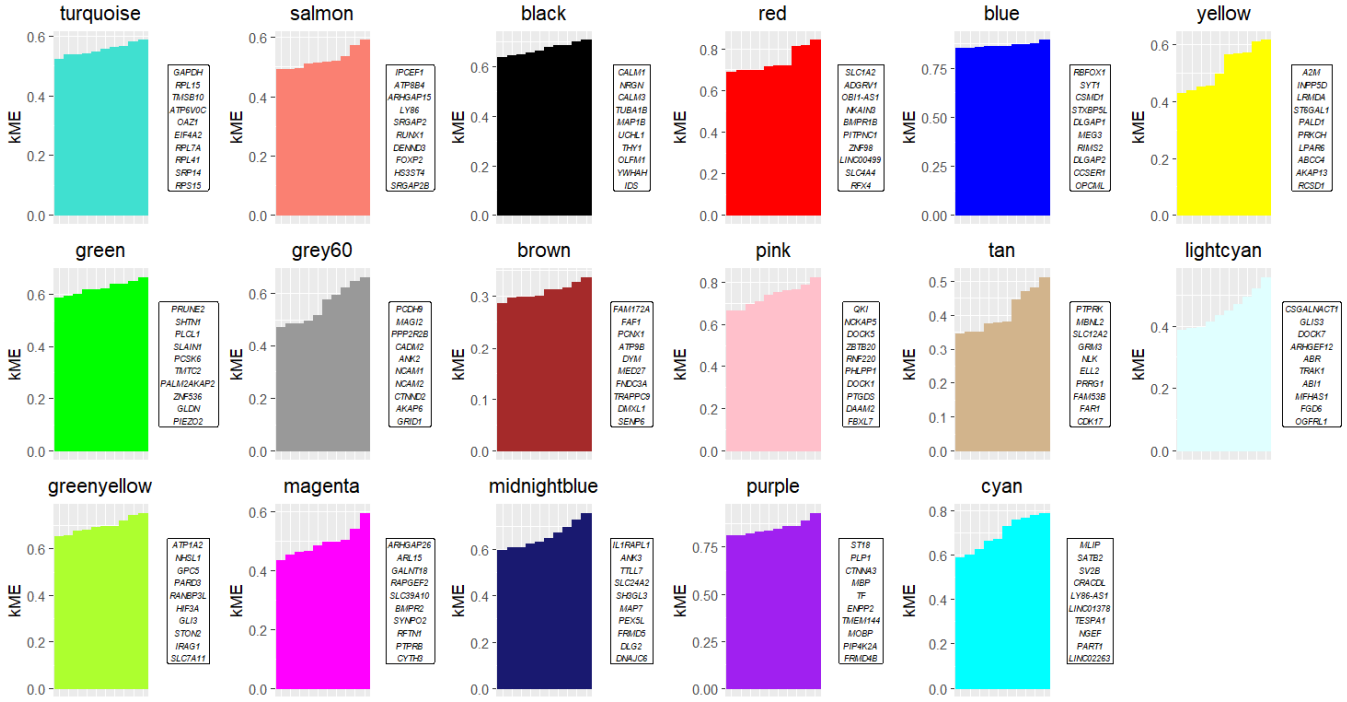
Hematopoietic SC Differentiation WP2849
Congenital Generalized Lipodystrophy WP5101
10Q22Q23 Copy Number Variation WP5402
H19 Rb E2F1 And CDK Beta Catenin In Colorectal ...
Ectoderm Differentiation WP2858
Farnesoid X Receptor Pathway WP2879
MECP2 And Associated Rett Syndrome WP3584
Androgen Receptor Network In Prostate Cancer WP...
miRNA Targets In ECM And Membrane Receptors WP2911
Histone Modifications WP2369
Astro
Endo
L2/3_IT
L6B_MP
L5_ET
L5_IT
L5_CT
L6_IT
L6_IT_Car3
Lamp5
Micro-PVM
Oligo
OPC
Pvalb
Sst
Vip
MDD_vs_CTRL

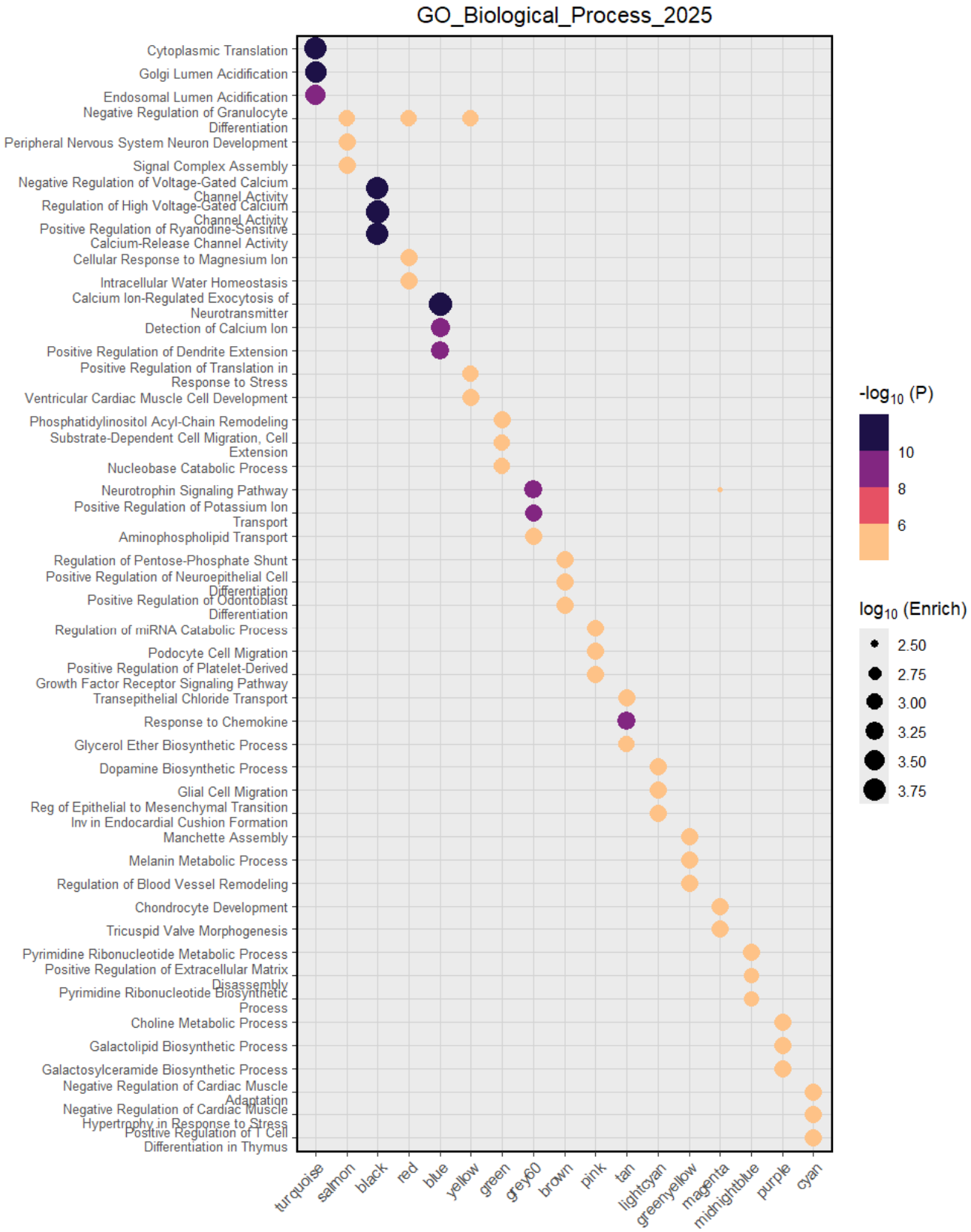

BioPlanet_2019
DOWN
UP
Down syndrome cell adhesion molecule (DSCAM) in...
Interaction between L1-type proteins and ankyrins
HNF3A pathway
Antigen processing and presentation
Neural crest differentiation
EGFR1 pathway
Activation of mRNA upon binding of the cap-bind...
Cytoplasmic ribosomal proteins
Influenza viral RNA transcription and replication
Interleukin-3 regulation of hematopoietic cells
Kit receptor signaling pathway
Kit receptor transcriptional targets
Collagen biosynthesis and modifying enzymes
Extracellular matrix organization
Chylomicron-mediated lipid transport
Lipoprotein metabolism
Lipid digestion, mobilization, and transport
Digestion of dietary carbohydrate
Th1/Th2 differentiation pathway
Ligand-gated ion channel transport
SLC26 family multifunctional anion exchangers
Abl role in Robo-Slit signaling
Inactivation of Cdc42 and Rac
Axon guidance
Opening of calcium channels triggered by depola...
Neuronal system
Acetylcholine neurotransmitter release cycle
Norepinephrine neurotransmitter release cycle
Dopamine neurotransmitter release cycle
Influenza infection
BD_vs_CTRL
Down syndrome cell adhesion molecule (DSCAM) in...
Activation of mRNA upon binding of the cap-bind...
Cytoplasmic ribosomal proteins
Influenza viral RNA transcription and replication
Neuronal system
Dopamine neurotransmitter release cycle
Influenza infection
BDNF signaling pathway
Post-chaperonin tubulin folding pathway
Interleukin-2 signaling pathway
Protein folding
Gap junction degradation
Gap junction assembly
Corticotropin releasing hormone pathway
Transcriptional activity regulation by PML
FSH regulation of apoptosis
Protein processing in the endoplasmic reticulum
Erythropoietin-mediated neuroprotection through...
Unblocking of NMDA receptor, glutamate binding ...
Synaptic proteins at the synaptic junction
PP2A-mediated dephosphorylation of key metaboli...
ERK inactivation
Signaling events mediated by the hedgehog family
Basal cell carcinoma
Monoamine transport
Neurotransmitter release cycle
Sonic Hedgehog (SHH) receptor PTCH1 regulation ...
Cyclin A/B1-associated events during G2/M trans...
Dual incision reaction in GG-NER
G alpha i pathway
Calcium regulation in the cardiac cell
Voltage-gated potassium channels
Potassium channels
Basic mechanisms of SUMOylation
BD_vs_MDD
GeneRatio
0.1
0.2
-log10(adj p)
15
10
5
EGFR1 pathway
Interferon-gamma signaling pathway
Interleukin-1 regulation of extracellular matrix
Interferon signaling
FOSB gene expression and drug abuse
BDNF signaling pathway
FYVE-finger proteins in vesicle transport
T cell receptor regulation of apoptosis
ATF2 transcription factor network
Natural killer cell-mediated cytotoxicity
Wnt signaling pathway
Post-chaperonin tubulin folding pathway
Apoptosis modulation by HSP70
Pathogenic Escherichia coli infection
Phagosome
Cooperation of prefoldin and TriC/CCT in actin...
PIP2 hydrolysis
MicroRNAs in muscle cell differentiation
PAC1 receptor pathway
Gap junction pathway
Myometrial relaxation and contraction pathways
FGFR3b ligand binding and activation
Interleukin-2 signaling pathway
Protein folding
Hormone-sensitive lipase (HSL)-mediated triacyl...
Protein kinase A (PKA) at the centrosome
Nicotine activity on dopaminergic neurons
Repression of pain sensation by the transcripti...
Selenium metabolism and selenoproteins
Methylation
TNF-alpha effects on cytokine activity, cell mo...
Hedgehog signaling pathway
Prolactin regulation of apoptosis
Glycosylation of mammalian N-linked oligosaccar...
NCAM1 interactions
NCAM signaling for neurite out-growth
Regular glucocorticoid receptor pathway
Interleukin-4 regulation of apoptosis
Astro
Endo
L2/3_IT
L4/5_IMP
L5_ET
L5_IT
L6_CT
L6_IT
L6_IT_Car3
Lamp5
Micro-PVM
Oligo
OPC
Pvalb
Sst
Vip
MDD_vs_CTRL

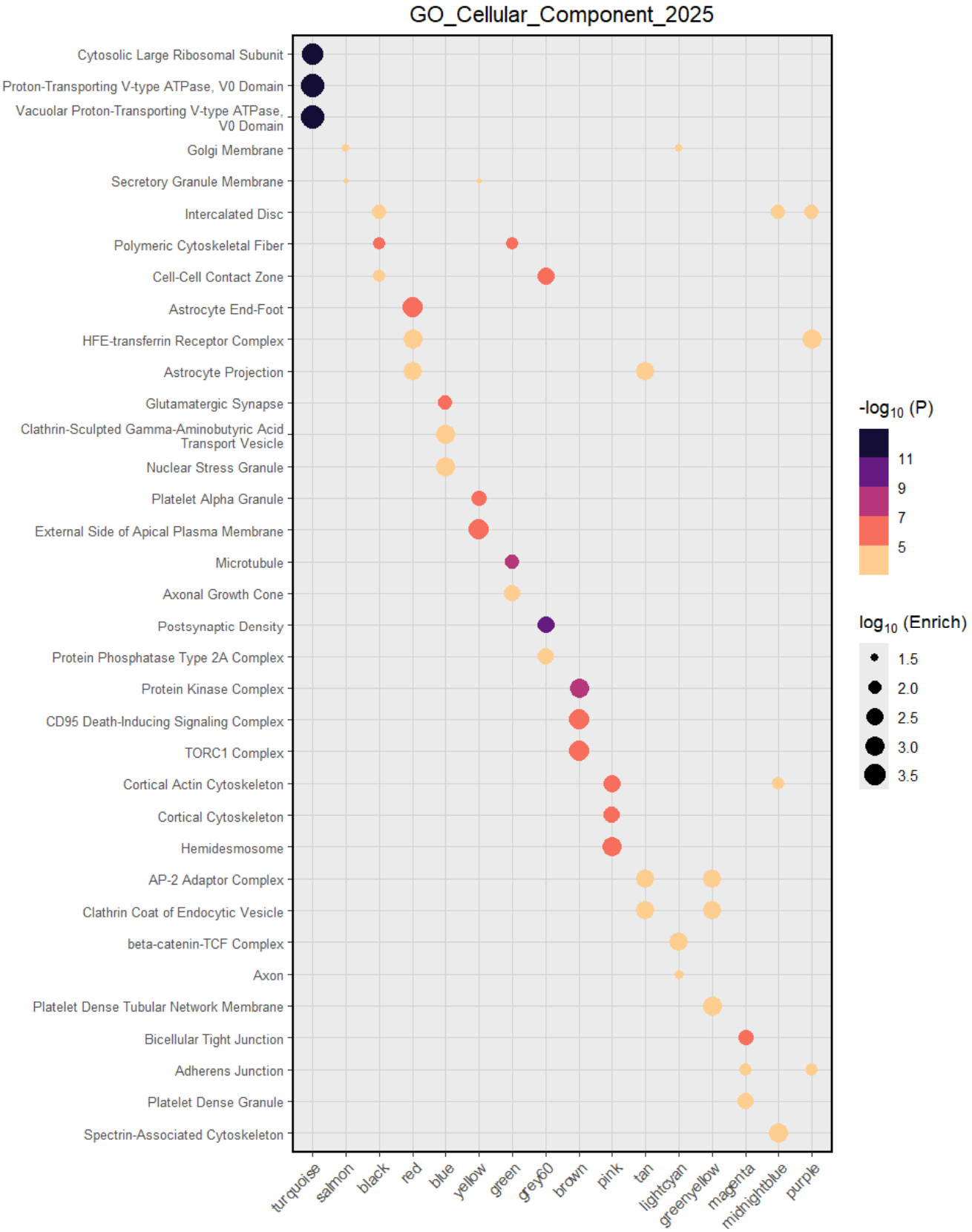

Elsevier_Pathway_Collection
DOWN
UP
Genes with Mutations Associated with Familial a...
Proteins Involved in Epilepsy
Glutamate Overdose and Aura Effect in Familial ...
Proteins Involved in Diabetic Nephropathy
Proteins Involved in Ulcerative Colitis
Proteins Involved in Presbycusis
Synovial Fibroblast Activation by Citokines in ...
Proteins Involved in Inflammatory Bowel Diseases
Proteins Involved in Endometriosis
Mast-Cell Activation without Degranulation
Acute Myeloid Leukemia
Breast Cancer
Proteins Involved in Osteoarthritis
Mast-Cells De Novo Synthesized Mediators via Ig...
Proteins Involved in Spontaneous Abortion
Sperm Motility Impairement in Testicular Male I...
Genes with Mutations Associated with Testicular...
Proteins Involved in Osteoporosis
IL7R -> STAT Signaling
IL7R -> FOXO/NF-kB Signaling
IL13R -> STAT6 Signaling
IL4R -> STAT Signaling
IL13R -> STAT Signaling
Hematopoietic Cell Lineage: B-cell
Arterial Hypertension
Vascular Endothelial Cell Activation by Growth ...
Proteins Involved in Stem Cell Exhaustion in Aging
Proteins Involved in Breast Cancer Related to I...
Genes with Mutations Associated with Retinitis ...
Glutamate Overdose and Aura Effect Caused by Mu...
Glutamate Overdose and Aura Effect Overiew
ADRA2A -> Neurotransmitter Release
Ca2+ Signaling in Dilated Cardiomyopathy
Ritonavir Induced Cardiovascular Dysfunction
GRM2-4/6-8 (Presynaptic) -> Glutamate Release A...
Proteins Involved in Hyperprolactinemia
SOD1 Mutation
BD_vs_CTRL
Proteins Involved in Epilepsy
Proteins Involved in Presbycusis
Proteins Involved in Osteoarthritis
GRM2-4/6-8 (Presynaptic) -> Glutamate Release A...
Proteins Involved in Hyperprolactinemia
Proteins Involved in Parkinson's Disease
Astrocyte Dysfunction and GABA Signaling Defici...
Proteins Involved in Huntington Disease
G0/G1 Cell Cycle Phase Transition Activation in...
Luteinizing Hormone in Oocyte Meiotic Resumption
Gap Junction Assembly
Genes with Mutations Associated with Usher Synd...
Proteins Mutated in Cochlear Hair Cell Synapse
Proteins Mutated in Photoreceptor and Retinal P...
Proteins Involved in Age-Related Macular Degene...
ER Stress (Unfolded Protein Response)
Amyloid beta Clearance in Alzheimer Disease
Extracellular Matrix Turnover
Proteins Involved in Arterial Hypertension
NMDA Receptors -> Ca2+/CREB Activation/PGE2 Syn...
CRH Secretion Regulation
Exocytosis: Vesicle Fusion
Synaptic Exocytosis in Dementia
GABA(B)R -> Postsynaptic Inhibition
TAM Receptor Signaling Activation in Cancer
Proteins Involved in Hepatocellular Carcinoma
G1/S Phase Transition
G0/G1 Phase Transition
EGFR -> ZNF259 Signaling
EGFR -> CTNND Signaling
Huntingtin Mutant Protein Toxicity Effects
Histone Sumoylation
Proteins Involved in Diabetic Neuropathy
BD_vs_MDD
GeneRatio
0.1
0.2
0.3
0.4
-log10(adj p)
5
4
3
2
1
Ritonavir Induced Cardiovascular Dysfunction
Primary Mediastinal B-cell Lymphoma (PMDL) Subtype
Proteins Involved in Myocarditis
Mucin Hyperproduction in Goblet and Mucous Cells
Oxytocin Signaling in Brain Nerve Cell (Hypothe...
Microglia Activation in Parkinson's Disease
Macrophage Related Iron Uptake and Release
Cortisol in Resolving Inflammation
TGFBR1/AP-1 Signaling
Endothelin Signaling in Arterial Hypertension
Natural Killer Cell Activation through ITSM-Con...
Protein Oxidation and Aggregation in Aging
Mitochondrial Respiratory Chain Dysfunction
SNCA in Young Onset Parkinson's Disease
Proteins Involved in Parkinson's Disease
Androgen Receptor/FKBP5 Signaling
Dexamethasone Induced Neurotoxicity
Glycolysis
SIRT2 Signaling in Aging
CGRP -> Calcium Influx
X-Linked Ichthyosis
eNOS (NOS3) Activation via Prostaglandin E2 and...
Astrocyte Dysfunction and GABA Signaling Defici...
Proteins Involved in Glaucoma
Ammonia Effects on Brain Cells
RNase L Signaling in Prostate Cancer
SWI/SNF BRM/BAF in Chromatin Remodeling
Proteins Involved in Hypothyroidism
Proteins Involved in Huntington Disease
Genes with Mutations Associated with Aging in H...
Dendritic Spine Morphogenesis and Stabilization
ERK/MAPK Canonical Signaling
G0/G1 Cell Cycle Phase Transition Activation in...
Natural Killer Cell Activation
Oxytocin Action in Mammary Gland
MPB-Related Complement Cascade Activation
Aqueous Humor Production
Cetuximab Resistance in Colorectal Cancer
Mast-Cell Activation without Degranulation thro...
Proteins Involved in Lesch Nyhan Syndrome
Proteins with Altered Expression in Prostate Ca...
Proteins Involved in Prostate Cancer
Astro
Endo
L2/3_IT
L5/6_NP
L5_ET
L5_IT
L6_CT
L6_IT
L6b
Lamp5
Micro-PVM
Oligo
OPC
Pvalb
Vip
MDD_vs_CTRL

Supplementary Figure S10. hdWGCNA module architecture and top hub genes. High-dimensional weighted gene co-expression network analysis (hdWGCNA) identified 17 non-grey co-expression modules from pseudobulked single-cell RNA-seq data aggregated by patient and macro cell type. For each module, the top hub genes were ranked according to intramodular connectivity (kME). Several modules displayed clear biological identities, including purple (oligodendroglial/myelin; e.g., *PLP1, MBP, MOBP, MOG*), red and greenyellow (astroglial/homeostatic; e.g., *SLC1A2, AQP4, ATP1A2, SLC7A11*), salmon (microglial/myeloid; e.g., *ATP8B4, ARHGAP15, LY86*), yellow (vascular/perivascular immune-interface; e.g., *A2M, INPP5D, ABCB1*), and multiple neuronal modules including black, blue, midnightblue, and cyan. These hub gene profiles indicate that hdWGCNA resolved biologically coherent co-expression systems corresponding to major cortical cell lineages and functions.



Supplementary Figure S11. Functional enrichment of hdWGCNA module hub genes across pathway libraries. Dot plots showing functional enrichment results for the top hub genes of each hdWGCNA co-expression module across eight gene set libraries: GO Biological Process, GO Cellular Component, GO Molecular Function, KEGG, Reactome, WikiPathways, BioPlanet, and the Elsevier Pathway Collection. For each module, the top three enriched terms are shown. Modules are displayed on the x-axis, and enriched terms are shown on the y-axis. Dot size represents the gene ratio, while color intensity indicates enrichment significance.

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Cytosolic Large Ribosomal Subunit
Proton-Transporting V-type ATPase, V0 Domain
Vacuolar Proton-Transporting V-type ATPase, V0 Domain
Golgi Membrane
Secretory Granule Membrane
Intercalated Disc
Polymeric Cytoskeletal Fiber
Cell-Cell Contact Zone
Astrocyte End-Foot
HFE-transferrin Receptor Complex
Astrocyte Projection
Glutamatergic Synapse
Clathrin-Sculpted Gamma-Aminobutyric Acid Transport Vesicle
Nuclear Stress Granule
Platelet Alpha Granule
External Side of Apical Plasma Membrane
Microtubule
Axonal Growth Cone
Postsynaptic Density
Protein Phosphatase Type 2A Complex
Protein Kinase Complex
CD95 Death-Inducing Signaling Complex
TORC1 Complex
Cortical Actin Cytoskeleton
Cortical Cytoskeleton
Hemidesmosome
AP-2 Adaptor Complex
Clathrin Coat of Endocytic Vesicle
beta-catenin-TCF Complex
Axon
Platelet Dense Tubular Network Membrane
Bicellular Tight Junction
Adherens Junction
Platelet Dense Granule
Spectrin-Associated Cytoskeleton
turquoise
salmon
black
red
blue
yellow
green
grey60
brown
pink
tan
lightcyan
greenyellow
magenta
midnightblue
purple
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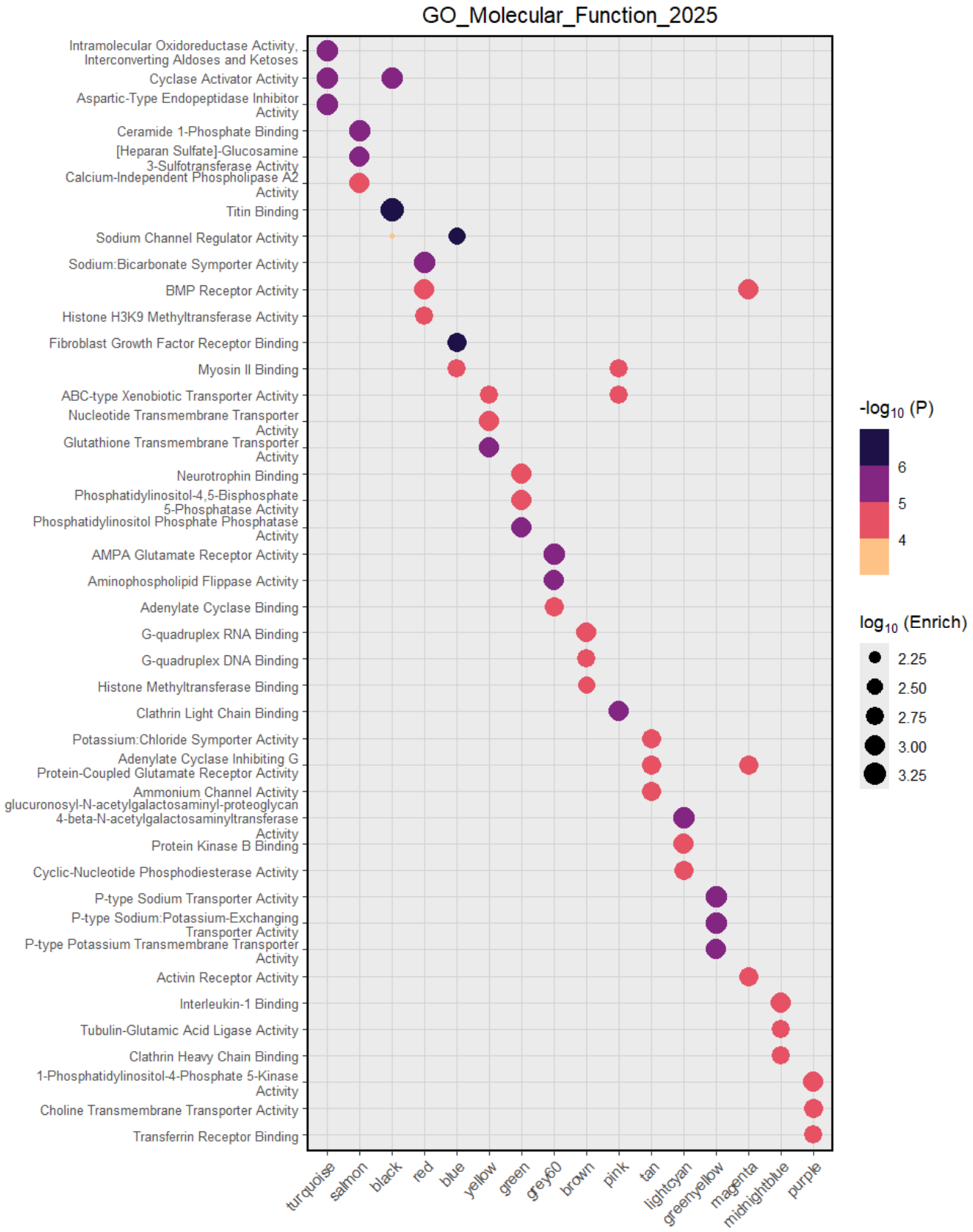
11
9
7
5
log10 (Enrich)
1.5
2.0
2.5
3.0
3.5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Intramolecular Oxidoreductase Activity, Interconverting Aldoses and Ketoses
Cyclase Activator Activity
Aspartic-Type Endopeptidase Inhibitor Activity
Ceramide 1-Phosphate Binding
[Heparan Sulfate]-Glucosamine 3-Sulfotransferase Activity
Calcium-Independent Phospholipase A2 Activity
Titin Binding
Sodium Channel Regulator Activity
Sodium:Bicarbonate Symporter Activity
BMP Receptor Activity
Histone H3K9 Methyltransferase Activity
Fibroblast Growth Factor Receptor Binding
Myosin II Binding
ABC-type Xenobiotic Transporter Activity
Nucleotide Transmembrane Transporter Activity
Glutathione Transmembrane Transporter Activity
Neurotrophin Binding
Phosphatidylinositol-4,5-Bisphosphate 5-Phosphatase Activity
Phosphatidylinositol Phosphate Phosphatase Activity
AMPA Glutamate Receptor Activity
Aminophospholipid Flippase Activity
Adenylate Cyclase Binding
G-quadruplex RNA Binding
G-quadruplex DNA Binding
Histone Methyltransferase Binding
Clathrin Light Chain Binding
Potassium:Chloride Symporter Activity
Adenylate Cyclase Inhibiting G Protein-Coupled Glutamate Receptor Activity
Ammonium Channel Activity
glucuronosyl-N-acetylgalactosaminyl-proteoglycan 4-beta-N-acetylgalactosaminyltransferase Activity
Protein Kinase B Binding
Cyclic-Nucleotide Phosphodiesterase Activity
P-type Sodium Transporter Activity
P-type Sodium:Potassium-Exchanging Transporter Activity
P-type Potassium Transmembrane Transporter Activity
Activin Receptor Activity
Interleukin-1 Binding
Tubulin-Glutamic Acid Ligase Activity
Clathrin Heavy Chain Binding
1-Phosphatidylinositol-4-Phosphate 5-Kinase Activity
Choline Transmembrane Transporter Activity
Transferrin Receptor Binding
turquoise
salmon
black
red
blue
yellow
green
grey60
brown
pink
tan
lightcyan
greenyellow
magenta
midnightblue
purple
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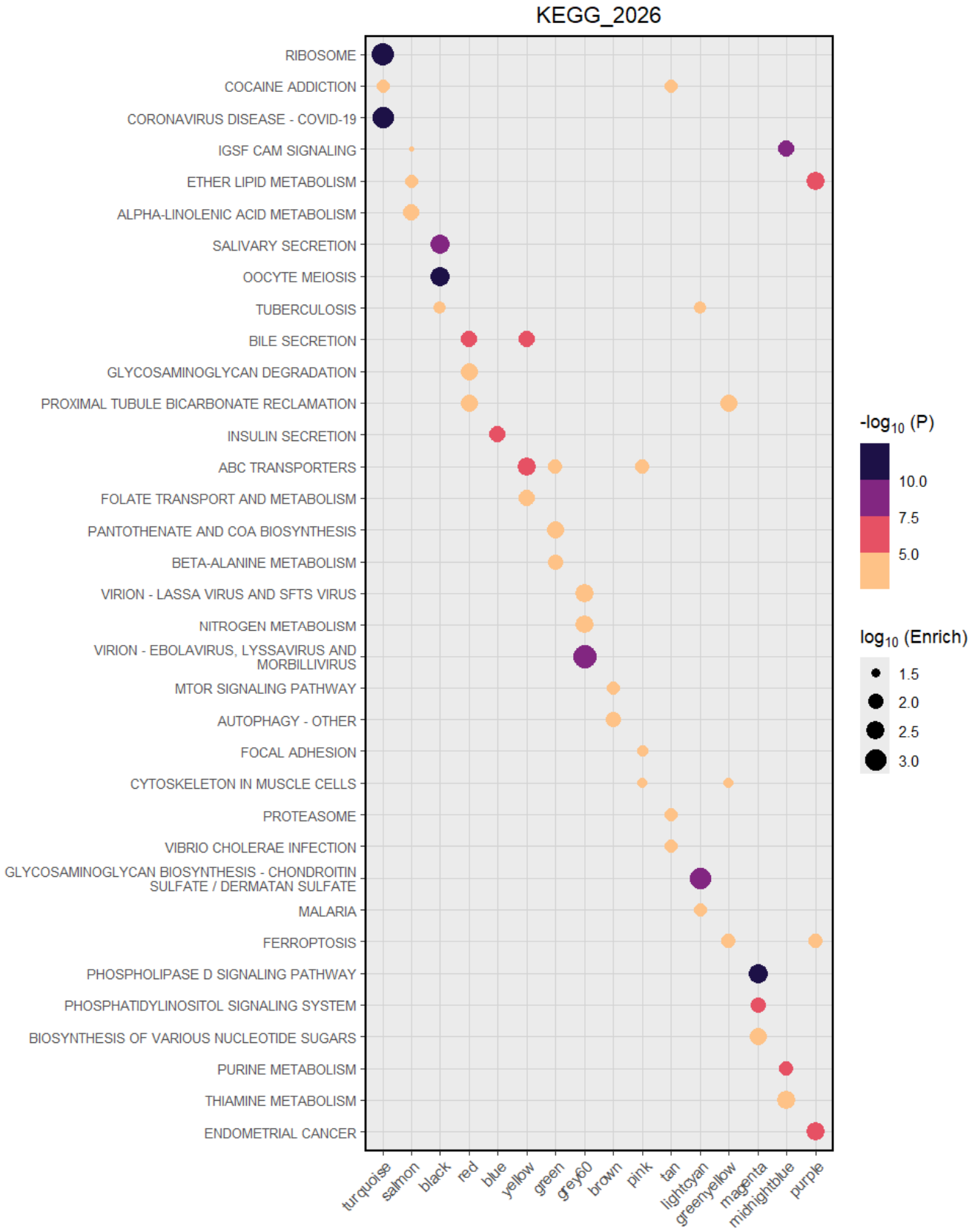
6
5
4
log10 (Enrich)
2.25
2.50
2.75
3.00
3.25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COCAINE ADDICTION
CORONAVIRUS DISEASE - COVID-19
IGSF CAM SIGNALING
ETHER LIPID METABOLISM
ALPHA-LINOLENIC ACID METABOLISM
SALIVARY SECRETION
OOCYTE MEIOSIS
TUBERCULOSIS
BILE SECRETION
GLYCOSAMINOGLYCAN DEGRADATION
PROXIMAL TUBULE BICARBONATE RECLAMATION
INSULIN SECRETION
ABC TRANSPORTERS
FOLATE TRANSPORT AND METABOLISM
PANTOTHENATE AND COA BIOSYNTHESIS
BETA-ALANINE METABOLISM
VIRION - LASSA VIRUS AND SFTS VIRUS
NITROGEN METABOLISM
VIRION - EBOLAVIRUS, LYSSAVIRUS AND MORBILLIVIRUS
MTOR SIGNALING PATHWAY
AUTOPHAGY - OTHER
FOCAL ADHESION
CYTOSKELETON IN MUSCLE CELLS
PROTEASOME
VIBRIO CHOLERAE INFECTION
GLYCOSAMINOGLYCAN BIOSYNTHESIS - CHONDROITIN SULFATE / DERMATAN SULFATE
MALARIA
FERROPTOSIS
PHOSPHOLIPASE D SIGNALING PATHWAY
PHOSPHATIDYLINOSITOL SIGNALING SYSTEM
BIOSYNTHESIS OF VARIOUS NUCLEOTIDE SUGARS
PURINE METABOLISM
THIAMINE METABOLISM
ENDOMETRIAL CANCER
turquoise
salmon
black
red
blue
yellow
green
grey60
brown
pink
tan
lightcyan
greenyellow
magenta
midnightblue
purple
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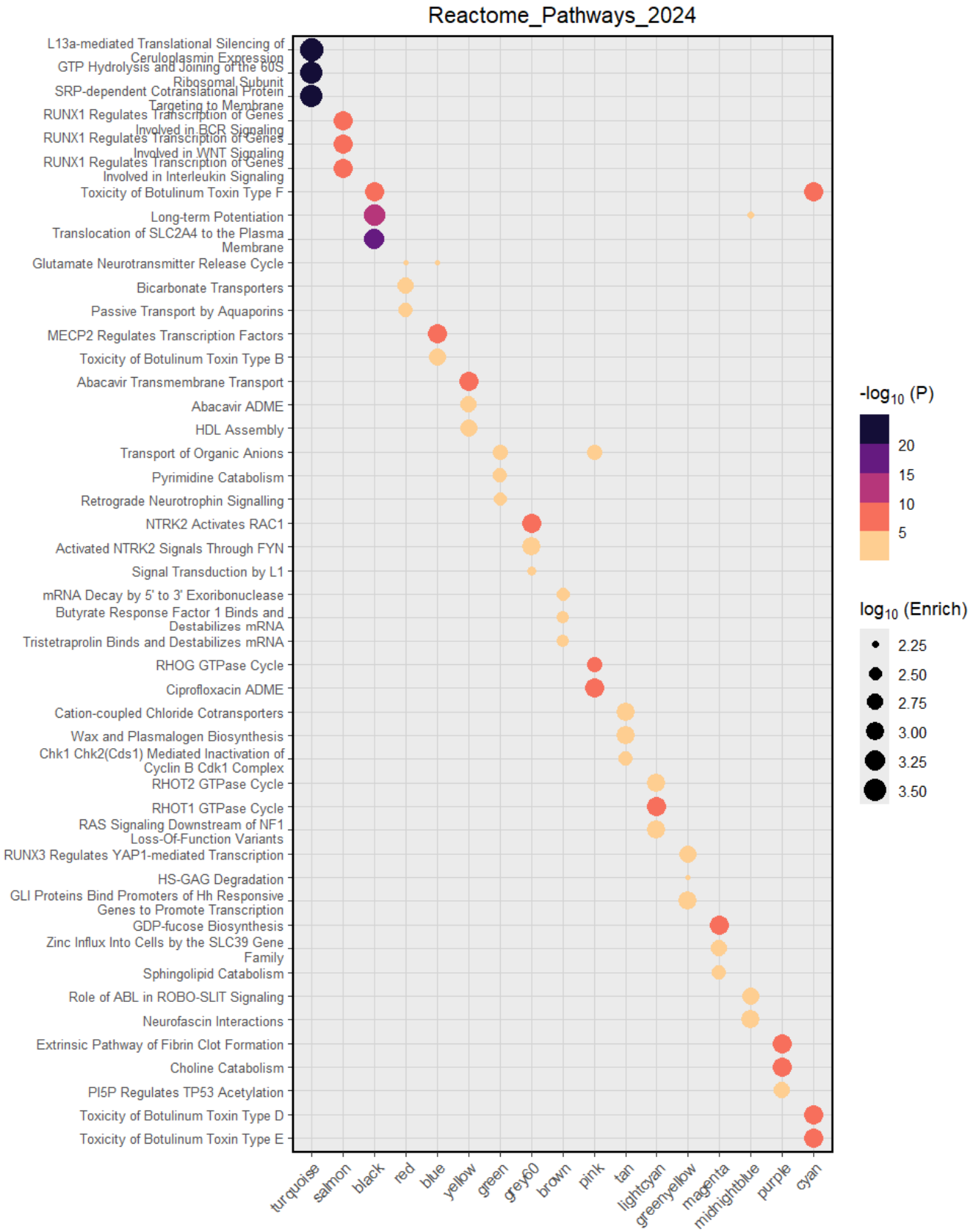
10.0
7.5
5.0
log10 (Enrich)
1.5
2.0
2.5
3.0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L13a-mediated Translational Silencing of Ceruloplasmin Expression
GTP Hydrolysis and Joining of the 60S Ribosomal Subunit
SRP-dependent Cotranslational Protein Targeting to Membrane
RUNX1 Regulates Transcription of Genes Involved in BCR Signaling
RUNX1 Regulates Transcription of Genes Involved in WNT Signaling
RUNX1 Regulates Transcription of Genes Involved in Interleukin Signaling
Toxicity of Botulinum Toxin Type F
Long-term Potentiation
Translocation of SLC2A4 to the Plasma Membrane
Glutamate Neurotransmitter Release Cycle
Bicarbonate Transporters
Passive Transport by Aquaporins
MECP2 Regulates Transcription Factors
Toxicity of Botulinum Toxin Type B
Abacavir Transmembrane Transport
Abacavir ADME
HDL Assembly
Transport of Organic Anions
Pyrimidine Catabolism
Retrograde Neurotrophin Signalling
NTRK2 Activates RAC1
Activated NTRK2 Signals Through FYN
Signal Transduction by L1
mRNA Decay by 5' to 3' Exoribonuclease
Butyrate Response Factor 1 Binds and Destabilizes mRNA
Tristetraprolin Binds and Destabilizes mRNA
RHOG GTPase Cycle
Ciprofloxacin ADME
Cation-coupled Chloride Cotransporters
Wax and Plasmalogen Biosynthesis
Chk1 Chk2(Cds1) Mediated Inactivation of Cyclin B Cdk1 Complex
RHOT2 GTPase Cycle
RHOT1 GTPase Cycle
RAS Signaling Downstream of NF1 Loss-Of-Function Variants
RUNX3 Regulates YAP1-mediated Transcription
HS-GAG Degradation
GLI Proteins Bind Promoters of Hh Responsive Genes to Promote Transcription
GDP-fucose Biosynthesis
Zinc Influx Into Cells by the SLC39 Gene Family
Sphingolipid Catabolism
Role of ABL in ROBO-SLIT Signaling
Neurofascin Interactions
Extrinsic Pathway of Fibrin Clot Formation
Choline Catabolism
PI5P Regulates TP53 Acetylation
Toxicity of Botulinum Toxin Type D
Toxicity of Botulinum Toxin Type E
turquoise
salmon
black
red
blue
yellow
green
grey60
brown
pink
tan
lightcyan
greenyellow
magenta
midnightblue
purple
cyan
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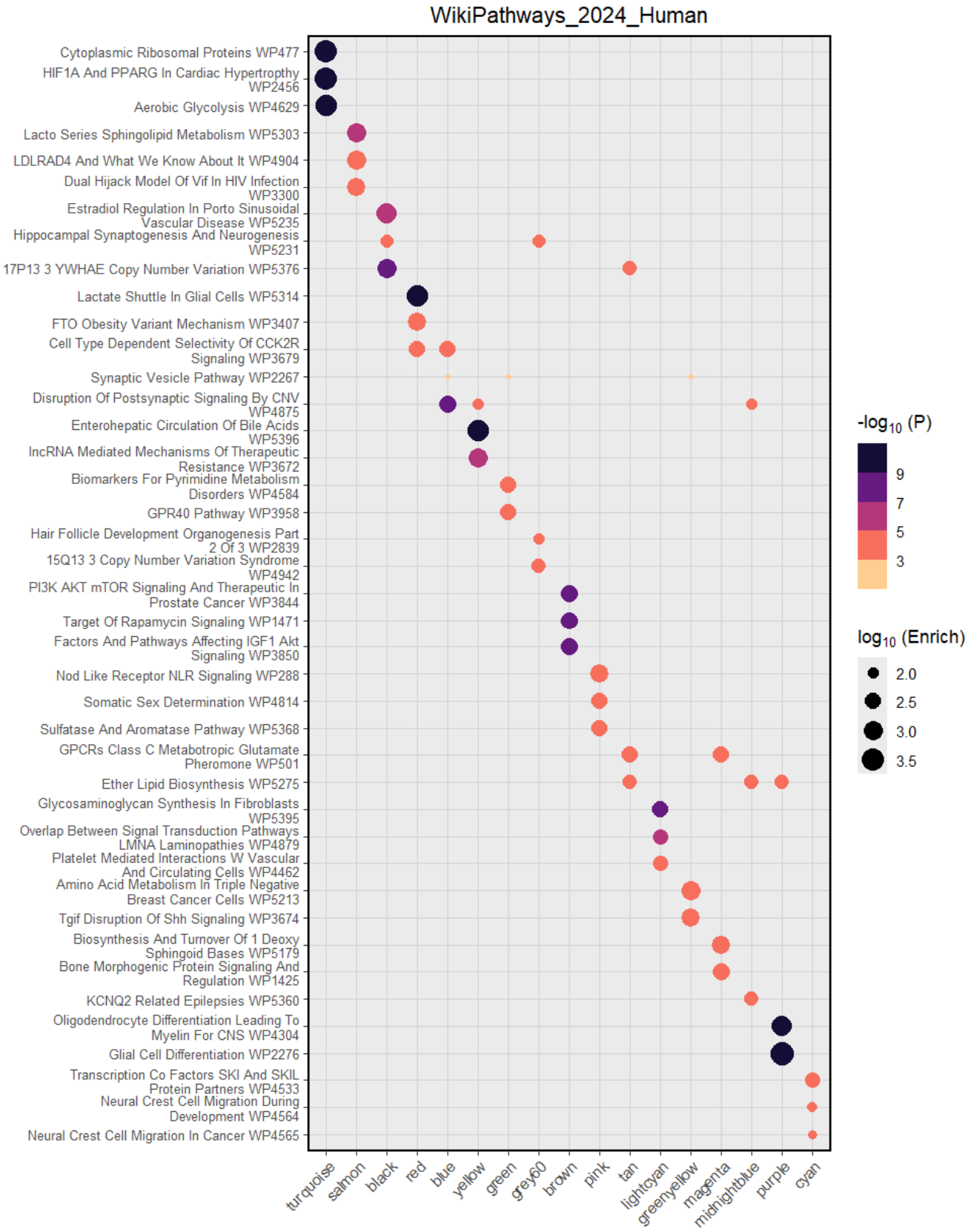
log10 (Enrich)
2.25
2.50
2.75
3.00
3.25
3.50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Cytoplasmic Ribosomal Proteins WP477
HIF1A And PPARG In Cardiac Hypertrophy WP2456
Aerobic Glycolysis WP4629
Lacto Series Sphingolipid Metabolism WP5303
LDLRAD4 And What We Know About It WP4904
Dual Hijack Model Of Vif In HIV Infection WP3300
Estradiol Regulation In Porto Sinusoidal Vascular Disease WP5235
Hippocampal Synaptogenesis And Neurogenesis WP5231
17P13 3 YWHAE Copy Number Variation WP5376
Lactate Shuttle In Glial Cells WP5314
FTO Obesity Variant Mechanism WP3407
Cell Type Dependent Selectivity Of CCK2R Signaling WP3679
Synaptic Vesicle Pathway WP2267
Disruption Of Postsynaptic Signaling By CNV WP4875
Enterohepatic Circulation Of Bile Acids WP5396
lncRNA Mediated Mechanisms Of Therapeutic Resistance WP3672
Biomarkers For Pyrimidine Metabolism Disorders WP4584
GPR40 Pathway WP3958
Hair Follicle Development Organogenesis Part 2 Of 3 WP2839
15Q13 3 Copy Number Variation Syndrome WP4942
PI3K AKT mTOR Signaling And Therapeutic In Prostate Cancer WP3844
Target Of Rapamycin Signaling WP1471
Factors And Pathways Affecting IGF1 Akt Signaling WP3850
Nod Like Receptor NLR Signaling WP288
Somatic Sex Determination WP4814
Sulfatase And Aromatase Pathway WP5368
GPCRs Class C Metabotropic Glutamate Pheromone WP501
Ether Lipid Biosynthesis WP5275
Glycosaminoglycan Synthesis In Fibroblasts WP5395
Overlap Between Signal Transduction Pathways LMNA Laminopathies WP4879
Platelet Mediated Interactions W Vascular And Circulating Cells WP4462
Amino Acid Metabolism In Triple Negative Breast Cancer Cells WP5213
Tgif Disruption Of Shh Signaling WP3674
Biosynthesis And Turnover Of 1 Deoxy Sphingoid Bases WP5179
Bone Morphogenic Protein Signaling And Regulation WP1425
KCNQ2 Related Epilepsies WP5360
Oligodendrocyte Differentiation Leading To Myelin For CNS WP4304
Glial Cell Differentiation WP2276
Transcription Co Factors SKI And SKIL Protein Partners WP4533
Neural Crest Cell Migration During Development WP4564
Neural Crest Cell Migration In Cancer WP4565
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red
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yellow
green
grey60
brown
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magenta
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-log10 (P)
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7
5
3
log10 (Enrich)
2.0
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3.0
3.5


BioPlanet_2019
Translation
Cytoplasmic ribosomal proteins
Cap-dependent translation initiation
Nephrin interactions
Hydrolysis of lysophosphatidylcholine
Acyl chain remodeling of cardiolipin
Calcium/calmodulin-dependent protein kinase activation
Insulin regulation of blood glucose
Dopamine neurotransmitter release cycle
Bicarbonate transporters
Passive transport by aquaporins
BMP signaling and regulation
Acetylcholine neurotransmitter release cycle
Norepinephrine neurotransmitter release cycle
Abacavir transmembrane transport
Codeine and morphine metabolism
Transport of organic anions
Pyrimidine catabolism
Retrograde neurotrophin signaling
Prion diseases
Interaction between L1-type proteins and ankyrins
TOR signaling
eIF4E release
S6K1 signaling
Bone mineralization regulation
Recycling of bile acids and salts
Peroxisomal lipid metabolism
Cation-coupled chloride cotransporters
PIK3C1/B pathway
Chondroitin sulfate biosynthesis
PDGF genes and receptors
Gene expression regulation by hypoxia-inducible factor
Sonic Hedgehog pathway
TGF-beta receptor signaling in EMT
Zinc influx into cells by the SLC39 gene family
Class C GPCRs
Synaptic proteins at the synaptic junction
Neurofascin interactions
Cell to cell adhesion signaling
FYVE-finger proteins in vesicle transport
CDC42 activity regulation
Ephrin receptor A forward pathway
RAC1 activity regulation
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log10 (Enrich)
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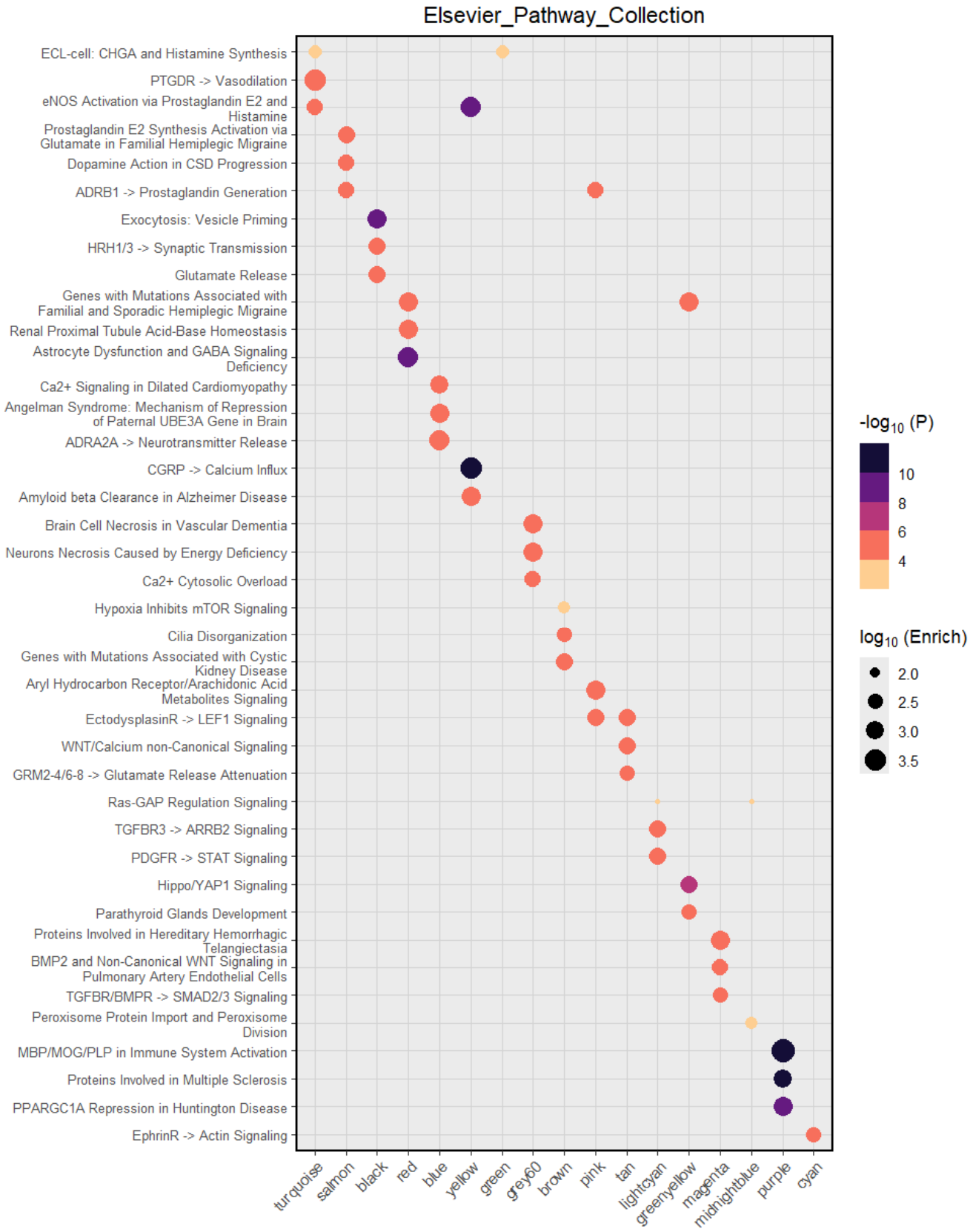
Elsevier_Pathway_Collection
ECL-cell: CHGA and Histamine Synthesis
PTGDR -> Vasodilation
eNOS Activation via Prostaglandin E2 and Histamine
Prostaglandin E2 Synthesis Activation via Glutamate in Familial Hemiplegic Migraine
Dopamine Action in CSD Progression
ADRB1 -> Prostaglandin Generation
Exocytosis: Vesicle Priming
HRH1/3 -> Synaptic Transmission
Glutamate Release
Genes with Mutations Associated with Familial and Sporadic Hemiplegic Migraine
Renal Proximal Tubule Acid-Base Homeostasis
Astrocyte Dysfunction and GABA Signaling Deficiency
Ca2+ Signaling in Dilated Cardiomyopathy
Angelman Syndrome: Mechanism of Repression of Paternal UBE3A Gene in Brain
ADRA2A -> Neurotransmitter Release
CGRP -> Calcium Influx
Amyloid beta Clearance in Alzheimer Disease
Brain Cell Necrosis in Vascular Dementia
Neurons Necrosis Caused by Energy Deficiency
Ca2+ Cytosolic Overload
Hypoxia Inhibits mTOR Signaling
Cilia Disorganization
Genes with Mutations Associated with Cystic Kidney Disease
Aryl Hydrocarbon Receptor/Arachidonic Acid Metabolites Signaling
EctodysplasinR -> LEF1 Signaling
WNT/Calcium non-Canonical Signaling
GRM2-4/6-8 -> Glutamate Release Attenuation
Ras-GAP Regulation Signaling
TGFBR3 -> ARRB2 Signaling
PDGFR -> STAT Signaling
Hippo/YAP1 Signaling
Parathyroid Glands Development
Proteins Involved in Hereditary Hemorrhagic Telangiectasia
BMP2 and Non-Canonical WNT Signaling in Pulmonary Artery Endothelial Cells
TGFBR/BMPR -> SMAD2/3 Signaling
Peroxisome Protein Import and Peroxisome Division
MBP/MOG/PLP in Immune System Activation
Proteins Involved in Multiple Sclerosis
PPARGC1A Repression in Huntington Disease
EphrinR -> Actin Signaling
turquoise
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log10 (Enrich)
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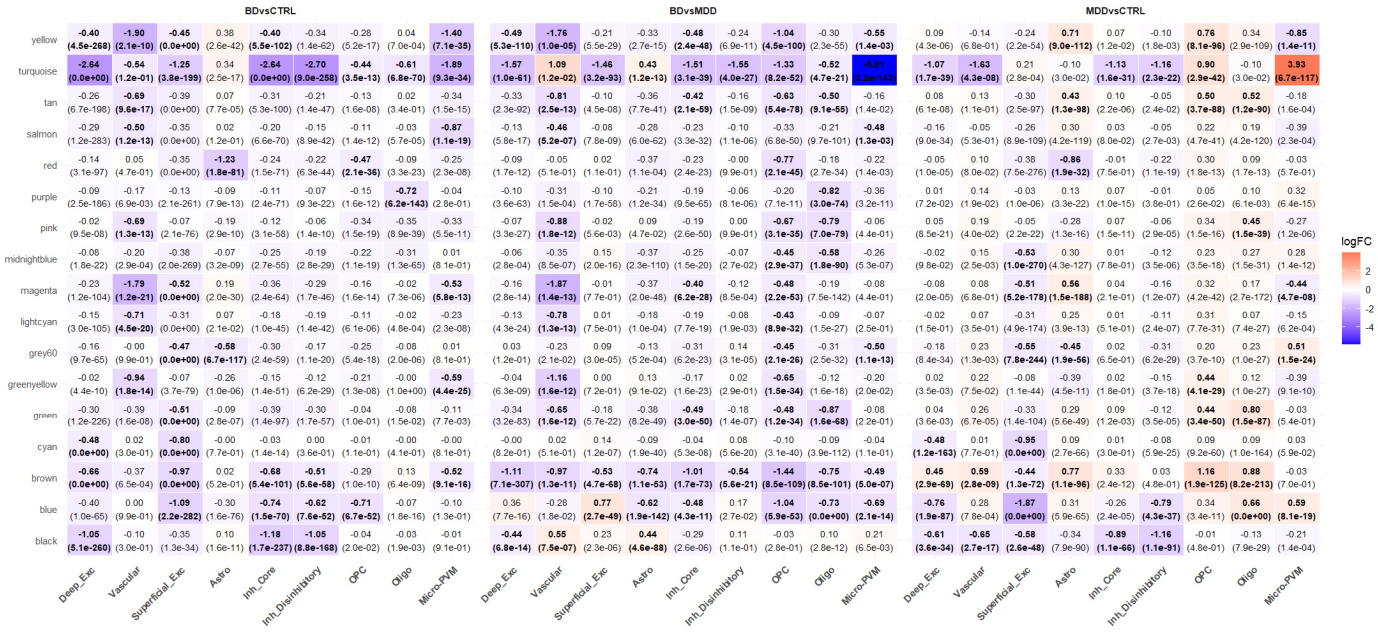
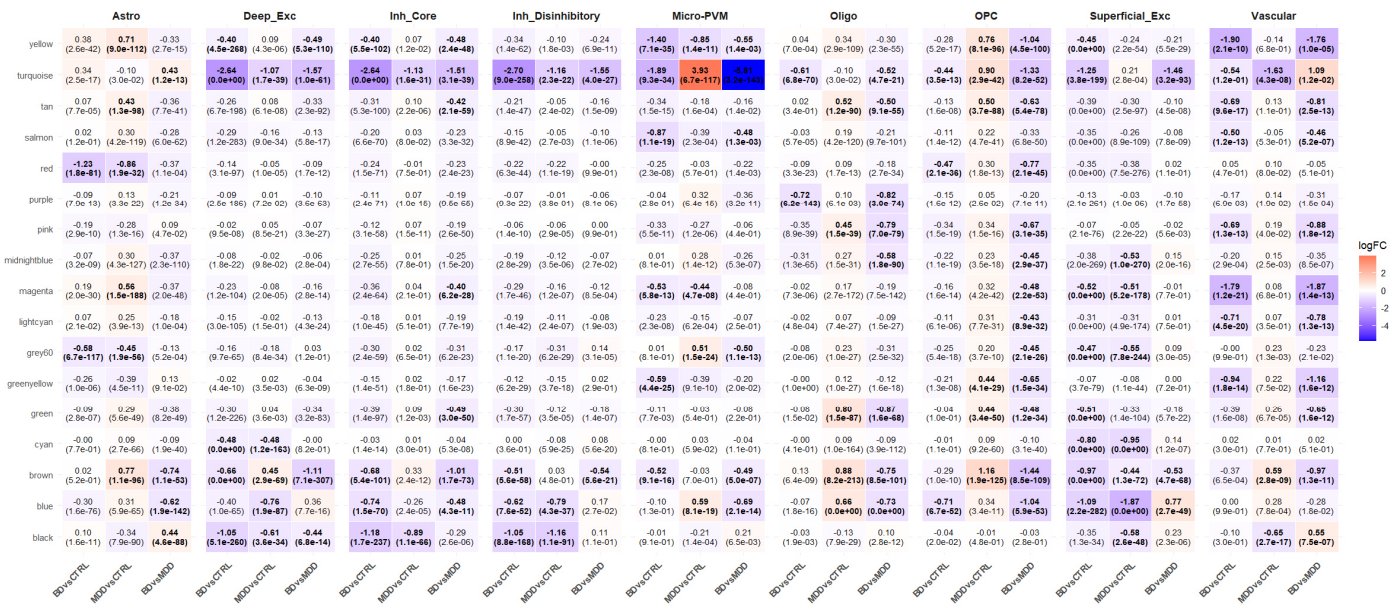
Supplementary Figure S12. Cell type–specific differential module eigengene activity across diagnostic groups. Heatmap showing differential hdWGCNA module eigengene activity within each macro cell type across the three diagnostic contrasts (BD vs CTRL, MDD vs CTRL, and BD vs MDD). Values represent model-derived log fold changes for each module within each cellular compartment, with associated adjusted *P* values shown in parentheses. For interpretive clarity, modules with |logFC| > 0.4 were highlighted in bold. Panels a) and b) show the same data organized differently: panel a) groups the data by diagnostic contrast, whereas panel b) groups them by cell type.

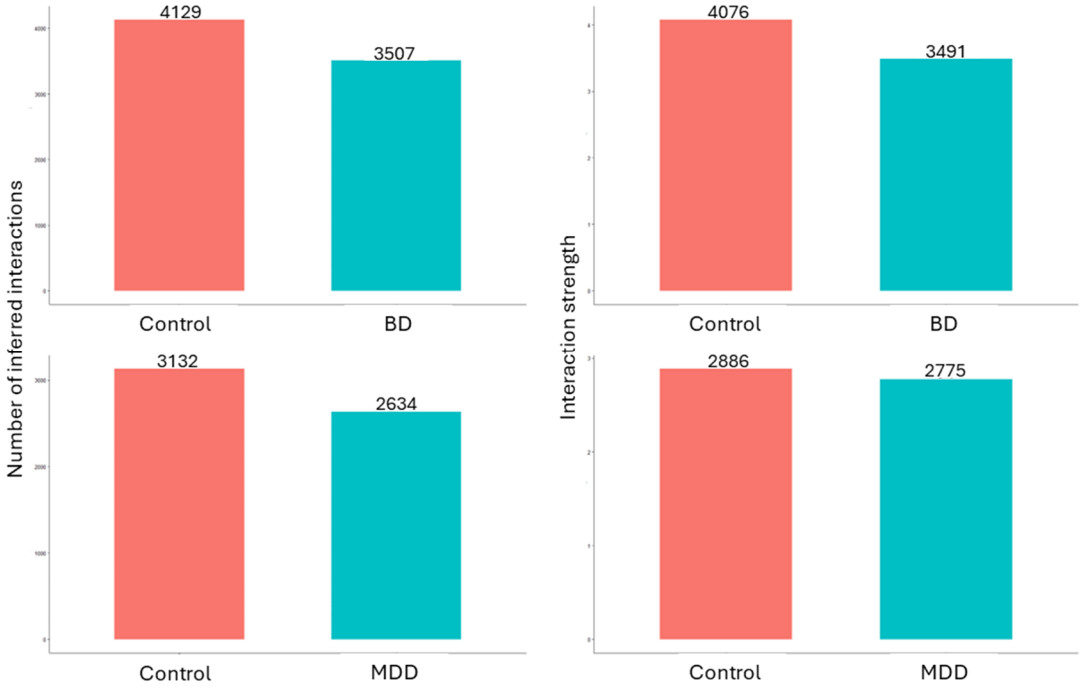
a)



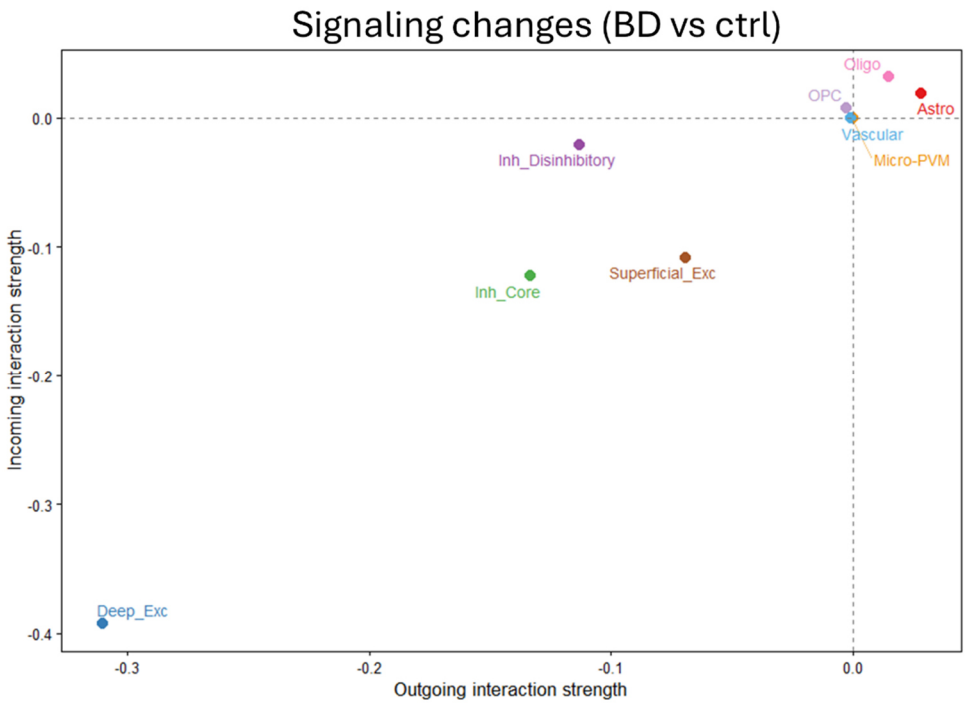
b)

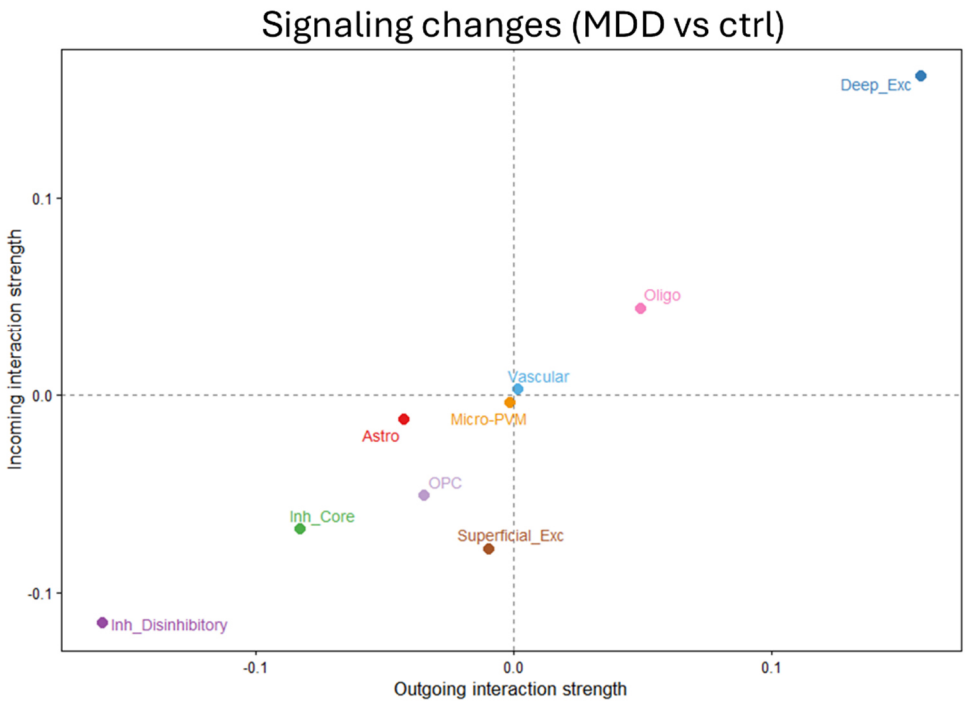


Supplementary Figure S13. Global number of inferred CellChat interactions and their strength in BD, MDD and matched controls. Bar plot showing the total number of inferred CellChat interactions and the total interaction strength in BD, MDD samples and matched controls. Interaction counts and interaction strength were calculated from the aggregated CellChat network using macro cell-type annotations.

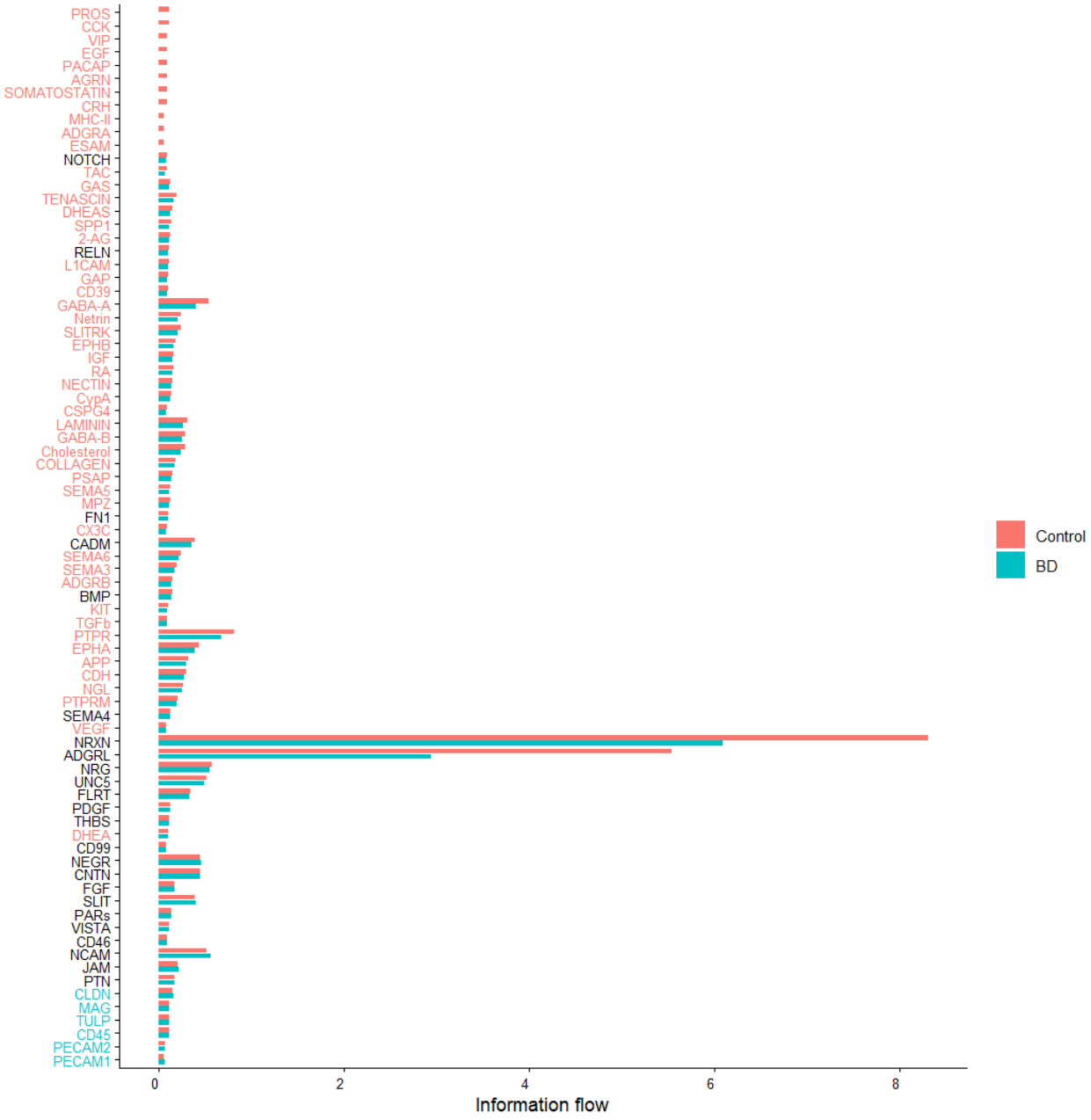


Supplementary Figure S14. Differential sender and receiver signaling roles in BD and MDD. Scatter plot showing differential outgoing and incoming CellChat signaling roles for each macro cell type in BD and MDD relative to matched controls. The x-axis represents changes in outgoing signaling strength, and the y-axis represents changes in incoming signaling strength.





Supplementary Figure S15. Pathway-level CellChat information flow in BD and matched controls. Bar plot showing pathway-level CellChat information flow in BD samples and dataset-matched controls. Each bar represents the total inferred information flow for a CellChat signaling pathway.



Supplementary Figure S16. Pathway-level CellChat information flow in MDD and matched controls. Bar plot showing pathway-level CellChat information flow in MDD samples and dataset-matched controls. Each bar represents the total inferred information flow for a CellChat signaling pathway.