

## Top 10 pathways for GSEA and hypergeometric tests (see Methods, main text).

Shown for each pathway is the name and description, the gene symbols for all genes in the pathway with nominal  $p < 0.05$  in univariate testing of association with MDD (on normalized expression data and with correction of additional covariates as described in Methods), the number of genes in the pathway that had adequate expression in this study to be analyzed (for GSEA); and the nominal  $p$ -value and  $q$ -value (FDR) for the pathway by permutation testing.

### GSEA enrichment test

#### Pathway\_name (description)

#### Genes with nominal $p < .05$

#### N(expressed genes); p; q

REACTOME\_INTERFERON\_ALPHA\_BETA\_SIGNALING (interferon-induced genes)

MX1,OAS1,IFIT3,PTPN6,ADAR,IRF7,IFIT1,USP18,ISG15,OAS2,IRF8,IFIT2,OAS3,MX2,IRF9,IFI6,OASL,XAF1,IFI35,IFNAR2

N=49;  $p=2.25E-05$ ;  $q=0.0298$

MIPS\_LARC\_COMPLEX (nucleosome remodeling)

MBD2,DPF2,MTA2,SMARCC2,SMARCD2,GATAD2B,ACTB

N=19;  $p=0.0005$ ;  $q=0.314$

MIPS\_SMN\_COMPLEX (cytoplasmic assembly of small nuclear ribonucleoproteins)

GEMIN5,SNRPF,GEMIN7,GEMIN4

N=13;  $p=0.0014$ ;  $q=0.498$

MIPS\_EMERIN\_COMPLEX\_25 (Cellular signaling and RNA processing)

YWHAE,ACTB

N=15;  $p=0.0017$ ;  $q=0.498$

MIPS\_NCOR1\_COMPLEX (transcriptional repression through recruiting histone deacetylases)

SF3A1,SMARCC2,SF3B3

N=10;  $p=0.0021$ ;  $q=0.498$

BIOCARTA\_RANKL\_PATHWAY ("receptor activator of NF- $\kappa$ B ligand, complex involved in bone remodeling")

IRF9,EIF2AK2,FOSL1,IFNAR2

N=13;  $p=0.0023$ ;  $q=0.498$

MIPS\_HDAC1\_ASSOCIATED\_CORE\_COMPLEX\_CII (Histone deacetylase complex)

MBD2,MTA2,CHD3,GATAD2B

N=9;  $p=0.0034$ ;  $q=0.565$

REACTOME\_COPI\_MEDIATED\_TRANSPORT (transport within the early secretory pathway)

COPG,COPB2,ARCN1

N=10;  $p=0.0041$ ;  $q=0.565$

MIPS\_ESCRT\_III\_COMPLEX (endosomal cargo transport)

CHMP5,CHMP2A,CHMP6

N=8;  $p=0.0042$ ;  $q=0.565$

REACTOME\_PROLACTIN\_RECEPTOR\_SIGNALING (genes involved in Prolactin receptor signaling)

PRLR,STAT5B

N=11;  $p=0.0043$ ;  $q=0.565$

**Hypergeometric enrichment test (among top 500 univariate genes)**

**Pathway\_name (description)**

**Genes with nominal  $p < .05$**

**p; q**

REACTOME\_INTERFERON\_ALPHA\_BETA\_SIGNALING (Interferon induced)

MX1,OAS1,IFIT3,PTPN6,ADAR,IRF7,IFIT1,USP18,ISG15,OAS2,IRF8,IFIT2,OAS3,MX2,IRF9,IFI6,OASL,XAF1,IFI35,IFNAR2  
N=49;p=0; q=0

REACTOME\_ANTIVIRAL\_MECHANISM\_BY\_IFN\_STIMULATED\_GENES (interferon gamma)

MX1,IFIT1,USP18,ISG15,NUP153,MX2,HERC5,EIF2AK2,NUP88,EIF4E2,ARIH1,NUP188,EIF4G3,NUP107,EIF4A3,FLNB  
N=65;p=0.0001; q=0.068

MIPS\_LARC\_COMPLEX (neuclosome remodeling)

MBD2,DPF2,MTA2,SMARCC2,SMARCD2,GATAD2B,ACTB  
N=19;p=0.0005; q=0.174

MIPS\_C\_COMPLEX\_SPLICEOSOME (RNA splicing)

SYF2,SNRNP40,PRPF19,SF3A1,SF3A2,XAB2,HNRNPA1,HNRNPU,SNRPF,CDC40,EFTUD2,HNRNPA2B1,EIF4A3,SF3B3  
N=79;p=0.0005; q=0.174

REACTOME\_INTERFERON\_GAMMA\_SIGNALING (interferon gamma)

OAS1,PTPN6,IRF7,OAS2,IRF8,OAS3,IRF9,OASL,PIAS1,SUMO1  
N=56; p=0.0008; q=0.222

MIPS\_ESCRT\_III\_COMPLEX (endosomal cargo transport)

CHMP5,CHMP2A,CHMP6  
N=8;p=0.0023; q=0.504

MIPS\_BRM\_SIN3A\_HDAC\_COMPLEX (histone modificaiton)

PRMT5,SMARCC2,SMARCD2  
N=12;p=0.0081; q=1

SA\_G1\_AND\_S\_PHASES ("CDK2, cell cycle checkpoint and transition")

NXT1,E2F2,CDK4  
N=14; p=0.0126; q=1

MIPS\_BRG1\_SIN3A\_COMPLEX (histone modification)

PRMT5,SMARCC2,SMARCD2  
N=14;p=0.0126; q=1

MIPS\_BRM\_SIN3A\_COMPLEX (histone modification)

PRMT5,SMARCC2,SMARCD2  
N=15;p=0.0154; q=1