An integrated network pharmacology, molecular docking, molecular dynamics simulation, and experimental validation study to investigate the potential mechanism of isoliquiritigenin in the treatment of ischemic stroke

Hang Yuan [1,2], Yuting Hou[1,2], Yuan Jiao[1,2], Xin Lu[1,2] and Liang Liu[1,2,*]

1 Institute of Translational Medicine, Medical College, Yangzhou University, Yangzhou 225009, China

2 Key Laboratory of the Jiangsu Higher Education Institutions for Integrated Traditional Chinese and Western Medicine in Senile Diseases Control (Yangzhou University), Yangzhou, 225009, PR China

* Correspondence: enjoyyz@163.com (L.L.).

Table S1. Target Prediction Datasets.

IS targets	ISL targets	Overlapping targets
HDAC1	AKR1B1	CHRNA7
F2	CHRNA7	EGFR
ITGA4	EGFR	TERT
PLG	TERT	ABCG2
NMDAR2B	ABCG2	APP
PROC	APP	CYP19A1
BDKRB2	CYP19A1	MAOA
HCAR2	MAOA	F3
CPB2	F3	NOS2
TACR3	NOS2	SNCA
VWF	SNCA	ALDH2
F11	ALDH2	ALOX5
TARDBP	KCNA3	PTGS2
PDE1	BACE1	ABCB1
NMDAR	ALOX5	ESR1
OPR	PTGS2	ESR2
PARP	MAOB	ACHE
F5	PDPK1	PDE4D
STRK1	ABCB1	KCNMA1
NOS3	ESR1	IGF1R
ALOX5AP	ESR2	XDH
GP1BA	ACHE	CDK6
ACE	TLR9	CSNK2A1
THPH2	HSD17B2	CYP1B1
THPH1	HSD17B1	TYR
FLAP	PDE4D	IGFBP3
BSS	TUBB1	ALOX15
DCP1	KCNMA1	CDK1
RPRGL1	PTPRS	MMP12
RPRGL2	AMY1A	ARG1
BDPLT1	GRK6	MAPK14
ACE1	CTSL	GSTP1

VWDP	IGF1R	PDE5A
MVCD3	PTPN1	NLRP3
BDPLT3	NOX4	CXCL12
ICH	XDH	
MTHFR	FLT3	
NOTCH3	CCNB3	
COL4A1	CDK6	
MT-TL1	ABCC1	
GLA	CSNK2A1	
ADA2	CFTR	
HTRA1	CYP1B1	
BDNF-AS	TNKS2	
ITGB3	TNKS	
SERPINC1	ALOX12	
APOE	STS	
COL4A2	DHODH	
APP	FNTA	
CST3	TYR	
JAK2	AHR	
F7	IGFBP3	
PRKCH	PIM1	
FBN1	CBR1	
ENG	AKR1C3	
ABCC6	KDM4E	
CRP	ALOX15	
F13A1	CDK1	
MYH11	GLO1	
TREX1	MMP12	
FGB	CD38	
PDE4D	TOP1	
POLG	ARG1	
IL6	GSTA1	
APOB	SLC22A12	
RNF213	CDK2	
SERPINE1	MGAM	
TTR	ESRRB	
TNF	CCNB1	
FLNA	CCNB2	

HBB	FNTB
ITGA2B	MAPK14
LDLR	BCHE
KCNQ1	CDK5R1
ACVRL1	GSTP1
MT-TK	HCK
MT-ND1	CES1
F10	PDE5A
CDKN2B-AS1	CA2
GUCY1A1	AKR1B10
MALAT1	CA12
MIAT	CA14
CBS	CA1
MT-CYB	CA3
PLAT	CA4
MT-TS1	CA5A
KRIT1	CA5B
SLC2A10	CA6
SH2B3	CA7
IL10	CA9
MT-ND5	CYP1A2
MMP9	MYOC
PIK3CA	NLRP3
PDE3A	CXCL12
CFH	
FGA	
NPPA	
SMARCAL1	
CPS1	
PMM2	
HABP2	
PRKAG2	
MT-TI	
BDNF	
MEG3	
ALPL	
NPPB	
SELP	

ACTA2
MT-TL2
WFS1
IL1B
OTC
SOST
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HLA-DQB1
EPOR
POLGARF
STIM1
MT-CO1
PNP
PCNT
MT-TP
APOA1
VHL
MMUT
IGF1
MT-CO3
FGFR1
CD36
PON1
TP53
ASS1
SLC19A2
PCCA
MT-ND4
XYLT1
H19
IVD
MT-ND6
AGTR1
GYS1
ACAD9
ACSL4
MT-CO2
TRAPPC11

ELMO2
PCCB
INS
APOH
AGT
ERF
ZSWIM6
RBM8A
GFAP
GAS5
SPARC
PRF1
JAM3
PRKCG
EOGT
TMEM127
XYLT2
USP18
CFHR1
CFHR3
SCN5A
LPL
SNX14
RAB27A
SAMD9
ATRIP
MAX
SMAD4
MAPT
MT-ATP6
PPARG
TLR4
NDUFS1
HIF1A
HOTAIR
XRCC4
PIK3R5
F3

GALK1
ESR1
SELE
ICAM1
LMNA
CHD1
EBF3
PTGS2
ADIPOQ
SMAD2
THBD
CYP2C19
TNNI3
ADAMTS13
PTEN
NLRP3
CXCL8
EDN1
KRAS
LPA
CCL2
MIR155
VEGFA
CTLA4
ITGA2
ATRIP-TREX1
IL1A
KCNJ5
ACTB
AKT1
TGFBR1
TGFB1
LOX
SOD2-OT1
GRN
TGFBR2
RPL36A-HNRNPH2
SOD1

IL4
MIR125A
ELN
CERNA3
SLC2A1
MMP3
HLA-B
TNNT2
ALB
BMP7
MYBPC3
TUG1
ENO2
MIR146A
MIR140
MTR
CXCL12
IL18
SMAD3
MIR133B
BRAF
TNFRSF1A
FAS
IL1RN
SLC6A4
MIR21
CTNNB1
CASP3
REN
CSF1R
PDGFRB
HDAC9
COL3A1
KAT6B
MYLK
TREM2
MMP2
MIR126

CACNA1A
PLA2G7
MIR223
CDKN2A
XRCC1
MAPK1
VCAM1
MAPK3
CXCR4
MIR320A
MTRR
CALR
LTA
F12
IGF1R
NOTCH1
MTOR
TWIST1
JAG1
CCR5
HMGB1
ABCC9
ABCB1
NDE1
CCM2
CYP2C9
HMGCR
MYH7
ARG1
ADRB2
BCL2
SPP1
TTN
CDKN2B
TH
MIR143
MIR499A
S100B

FTO
VDR
TGFB3
MGP
PCSK9
MIR145
EPO
PRKG1
LAMP2
DNMT3A
PSEN1
RAF1
GBA1
KNG1
IL17A
UBE3A
MIR146B
PECAM1
FGF2
LEP
NOS2
HRAS
EGF
TIMP1
PITX2
MIR216A
B2M
TGFB2
MIR150
KDR
EIF2AK2
MAPK8IP1
NF1
GRIN2B
NKX2-5
PIK3C2A
ATP7B
CD40LG

MYH6
PVT1
CAV1
APOC3
SNHG12
MIR27B
PSEN2
ALDH2
CACNA1C
GP6
VKORC1
CETP
PTH
THPO
FGG
ENPP1
GATA6
RET
TMX2-CTNND1
MAP2K1
MIR144
ABCC8
SERPINA3
MIR17
NRAS
CREB1
UCP2
MIR451A
COMT
FGFR2
ABCA1
LINC01672
MIR149
ARSA
GRIP1
COG2
PARP1
MPO

MIR210
EPHX2
FADD
MMP1
MIR34C
COL5A1
MIR221
CD14
SLC1A3
MEFV
RYR2
HSPB1
DIAPH1
SLC1A2
SERPINA1
NOS1
MIR34A
HSPA4
PRTN3
GJA1
CBL
FGF23
LIPC
EP300
MIR29A
CDC42
HMOX1
GATA3
HTR1A
TNFRSF11B
F8
AKT2
PF4
PON2
SDHB
PHACTR1
PTGIS
PRNP

ITGB1
PRKN
EIF2AK3
FGFR3
MIR125B1
SERPINI1
CSF3
ZFHX3
CYCS
ROBO1
GATA4
CDK6
CYP11B2
PDCD10
APOA5
ALOX5
STAT3
TLR2
BRD4
FGF8
MIR211
XIST
EZH2
ACHE
PRKAR1A
CSF2
HGF
ACTC1
TET2
NAGA
SCN1B
RNF213-AS1
CRKL
FGF17
MIR532
SMAD5-AS1
HP
NPY

FLT1
CDC5L
PTGS1
ARHGEF6
MIR142
IL2
ANXA5
TSPO
AHSG
NGF
CD40
VPS11
MAPK8IP2
IL13
LRP1
SRC
SKI
PLA2G6
YAP1
GDF2
SDHA
MIR141
PPBP
KCNJ2
VCP
KCNMA1
SMARCA4
GCH1
MIR200B
IFNG
COL1A1
FOS
SLC9A1
NR3C2
TEK
BRCA2
DNAH8
OLR1

CCND2
SOX4
THBS1
CHAT
MAOA
SON
P2RY12
SLC17A5
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CCR2
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SCN3B
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CALM1
MPL
SOX2
SOS1
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CYP4F2
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AGER
PDGFB

GNAS
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COL2A1
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ACTG1
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NFE2L2
EIF4E
CYP17A1
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FASN
MIR342
PWAR1
NFKB1
CTSA
ERBB4
SQSTM1
GNAQ
SLIT2
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ACE2
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FOLR1
ASTN2
MIR130A
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EDNRA
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PLOD1
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CACNA1D
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ABCG2
ATP7A
KCNE2
SNCA
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MIR24-1
CHRNA7
TLR7
DHFR
DAPK1
FLVCR2
MIRLET7E
PRRT2
TRPM6
GNB3
ADAMTS2
TERT
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SLC6A3
AMACR
MIR214
F2R
MIR100
ITPR1
PIK3CG
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BIRC5
GABRG2
PKD1
MAT2A

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TANGO2
SLC6A1

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BAX
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HMBS
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RHOA
GPX3
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PTPN22
ABL1
GCK
TYROBP

ST3GAL3
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MBL2
CYP2J2
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GSN
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ITLN1
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ARMS2
FASLG
PVALB
CCL5
KCNA5
GZMB

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BMP4
HEY2
GSTP1
JAK1
IDH1
SEC24D
SUCLG1
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FCGR3A
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NLGN1

ANXA2
VIM
SELL
TLR3
MOCS2
KCNH2
IL5RA
MAP2K2
ALDH5A1
SCN9A
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TBX18
PROCR
EXTL3
NDUFS4
STAT5A
LARS2
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BCL2L11
FUCA1
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NBAS
TRAF6
BGLAP
ASPA
CD4
TGIF1
IL12A
CUL3
PTX3
MIR330
SCARB2
CPT1A
DSG2
COQ8A
CYP27B1

SLC39A8
SLC25A3
CAMTA1
METTL3
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GLUL
IKBKG
KLF4
TAF1
VCL
NEU1
MC2R
PSPH
COG7
CKB
GNRH1
CDH15
PACS2
ARVCF
SOX17
OPA1
MCCC2
SCN8A
PYGM
PKP2
ASXL2
KIT
G6PC1
CYP3A5
GNPTAB
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CDR1-AS
GRM1
C5
PIGQ
PCNA

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SURF1
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GATM
EXT2
MVK
SNHG7
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GPT2
PEX10
NFIA
GJC2
KCNJ6
ABCG8
SRSF3
MYL3
HADH
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MAFB
TTC21B
WDR19
DNMT1
JMJD1C
RELA
HAVCR2
CCK
CASP7
LYZ
DOCK8
PDYN
MFSD8
EPRS1
SOX9
SLC12A1

MIRLET7C
ALG13
PINK1
WRN
GPC3
POMT2
FOXO1
PROM1
IFNB1
FUT8
ALG12
MYT1L
POLG2
SMARCB1
MIR545
RPIA
HTR3A
ATP5F1A
CFLAR
DOLK
IGF2BP2
MAN2B1
CXCL1
NAGLU
ADORA1
AP3D1
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MAP2
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COL13A1
SPTBN4
ACOT7
TBCD
PIGG
WDR37
MYO7B
MDH2

MIR106A
CEP164
ERCC2
SLC4A1
CYP2D6
HMGCL
TBX5
GNA11
XIAP
GABRA1
MTPAP
AIF1
LRP2
PRDM8
MIR502
CXCL10
MAP1B
FAM111A
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TBXA2R
KLKB1
DOCK7
MIR19B1
IL9
NT5E
STAMBP
CCBE1
SNORD15A
PPP3CA
CYP4A11
DIP2B
HDAC3
MIR127
GBE1
KAT2B
FASTKD2
CD86
GP5

CARS2
TFPI
REEP1
FH
ALMS1
PCDH19
TYMS
LYRM7
MIR424
FOXP3
TFRC
ARCN1
FKRP
APAF1
CNR1
CDKN3
FABP3
ATP2A2
CX3CR1
ATP5F1E
TNXB
TBL1XR1
GABRD
SLC9A6
PEX2
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ANGPT2
DGUOK
PI4KA
ABO
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SRCAP
COL11A1
CD8A
NCF1
MIR137
MIR1246
MIR200A

LZTR1
PTCH1
CALCA
COL6A2
TUBGCP6
IL1F10
COL4A5
SCGB1A1
CALM3
MIR378A
MTRFR
CCND1
CCR1
MTHFD1
NAMPT
ANK3
TYR
CHRNB2
IL12B
PGK1
F13B
AQP1
ABAT
MPDZ
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FGF10
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RMST
SERPIND1
GNAI1
GRIA3
TBX1
ROCK1
TBCE
FGD1
PLK4

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LOC107133510
GTPBP3
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SCN3A
SORT1
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GPX4
NLRP12
ADRB3
MYOCD
SPAST
MC4R
FLI1
CLU
CREBBP
MIR590
CHD8
MIR224
TWNK
CCL3
NOL3
UPF3B
NUS1
NR2F1
GABBR1
PIK3CB
TXN2
BCR
TPM1
MIR370
MIR154
SNAP25
ATAD3A

COQ8B
PPP2CA
FGF7
ZEB1
RNLS
ERCC8
SNAP29
MIR506
FBN2
MTM1
PLAU
PCDH7
MIR744
COL9A2
AMPD1
DDC
KATNB1
EDNRB
CRHR1
DPYD
NES
MIR133A1
MYL2
SLC12A5
GCG
AFF2
RRM2B
NDUFS6
EPG5
TMEM126B
DENND2B
CHD3
SOX5
RILP
SMPD1
EBP
PPOX
STAT1

GNB1
VLDLR
ROGDI
PTK2
GSTM1
CACNB4
GABRB1
ANKH
EPHB4
SARS2
MIR17HG
MIR615
ATP6AP2
DNM1
SNX10
MED23
B4GALT7
AXL
EDN3
PAH
CEACAM5
PEX5
PEX16
GLP1R
MIR582
MUC1
MIR302A
PC
COL11A2
MIR30C1
MIR135A1
MIR301A
MIR187
MIR520A
MIR654
MIR876
MIR518A1
MIR363

MIR509-1
MIR625
PIGL
MIR873
MIR513A1
PROS1
IDH2
FGF4
CDKN1A
IL2RA
CRPPA
MIR616
PNPO
RORA
ARNT2
AUTS2
ARNT
KCNA2
GP1BB
TUBB
MCCC1
SNRPN
CEP152
SLC12A2
MSX2
SOX10
CDH11
PXDNL
PHGDH
GNS
CEP290
POGZ
MCEE
QARS1
LAMA2
TRA-TGC7-1
CUX1
RAD21

MMAA
PDCD1
NFU1
SDCCAG8
BOLA3
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SUFU
CHIT1
LDHA
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EZR

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KIRREL3
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ACER3
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JPH2
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VAMP2

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DANCR
CDH2
RBFOX1
GLDC
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BSCL2
MIR92B
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SC5D
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DPM1
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ALG9
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B4GAT1
CCDC115
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RXYLT1
PGAP2
NPHP1
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AGO2
ALX4
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SHANK2
DROSHA
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CSTB
MAF
ATN1
CERS1
RPGRIP1L
POLR3A
PHF6
KLRC4
UBAC2
PLK1
GDF15
TRIT1
FGF13

RB1
CIT
KCNJ1
CACNA1E
KCNQ3
PNKP
FOXG1
COPB2
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MCPH1
STIL
WDR62
LTF
APOA4
SMARCE1
RARS2
SAA1
MIR651
PAPPA
APTX
CALM2
WEE1
PIGF
NRP1
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AGK
FOXM1
PLCB1
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DHCR24
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ALDH3A2
KCNJ10
PTS
FA2H
PMPCA
SPG7
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CHD2
ARHGAP31
DNM3
IL1RL1
SERPINF2
POLR1C
WWOX
DNMT3B

Table S2. GO enrichment of the 35 selected targets.

GO Category	Term	Name	Count	Genes	PValue	FDR
Biological Process (139)	GO:0007165	signal transduction	12	CXCL12, CDK6, CSNK2A1, CHRNA7, PDE4D, NLRP3, PDE5A, MAPK14, ESR1, EGFR, ESR2, IGF1R	8.14E-06	7.31E-03
	GO:0050727	regulation of inflammatory response	5	ALOX5, ALOX15, NLRP3, PTGS2, ESR1	2.80E-05	1.18E-02
	GO:0071392	cellular response to estradiol stimulus	4	ESR1, EGFR, ESR2, IGF1R	3.93E-05	1.18E-02
	GO:1900015	regulation of cytokine production involved in inflammatory response	3	NOS2, ALOX5, MAPK14	1.61E-04	2.89E-02
	GO:0010629	negative regulation of gene expression	6	APP, TERT, NOS2, CDK1, ESR1, XDH	1.88E-04	2.89E-02
	GO:0019372	lipoxygenase pathway	3	ALOX5, ALOX15, PTGS2	1.93E-04	2.89E-02
	GO:0043065	positive regulation of apoptotic process	6	APP, IGFBP3, KCNMA1, CYP1B1, PTGS2, SNCA	2.45E-04	3.14E-02
	GO:0071222	cellular response to lipopolysaccharide	5	NOS2, GSTP1, NLRP3, MAPK14, PTGS2	3.37E-04	3.78E-02

GO:0043410	positive regulation of MAPK cascade	5	APP, CHRNA7, IGFBP3, EGFR, IGF1R	4.24E-04	4.04E-02
GO:0032355	response to estradiol	4	CYP1B1, PTGS2, ESR1, CYP19A1	4.50E-04	4.04E-02
GO:0042759	long-chain fatty acid biosynthetic process	3	ALOX5, ALOX15, PTGS2	6.08E-04	4.55E-02
GO:0032930	positive regulation of superoxide anion generation	3	APP, GSTP1, EGFR	6.08E-04	4.55E-02
GO:2000379	positive regulation of reactive oxygen species metabolic process	3	CYP1B1, MAPK14, XDH	1.70E-03	1.17E-01
GO:0019369	arachidonate metabolic process	3	ALOX5, ALOX15, CYP1B1	2.10E-03	1.35E-01
GO:0042307	positive regulation of protein import into nucleus	3	CDK1, MAPK14, PTGS2	2.55E-03	1.39E-01
GO:0045766	positive regulation of angiogenesis	4	TERT, CHRNA7, CYP1B1, F3	2.75E-03	1.39E-01
GO:0032691	negative regulation of interleukin-1 beta production	3	CHRNA7, GSTP1, NLRP3	2.79E-03	1.39E-01
GO:0033138	positive regulation of peptidyl-serine phosphorylation	3	APP, EGFR, SNCA	2.79E-03	1.39E-01

GO:0045429	positive regulation of nitric oxide biosynthetic process	3	APP, PTGS2, ESR1	3.04E-03	1.44E-01
GO:0001666	response to hypoxia	4	CXCL12, NOS2, CHRNA7, KCNMA1	3.65E-03	1.45E-01
GO:0008344	adult locomotory behavior	3	APP, CXCL12, SNCA	3.71E-03	1.45E-01
GO:0000086	G2/M transition of mitotic cell cycle	3	APP, ABCB1, CDK1	3.71E-03	1.45E-01
GO:0048146	positive regulation of fibroblast proliferation	3	CDK6, ESR1, EGFR	3.71E-03	1.45E-01
GO:0048661	positive regulation of smooth muscle cell proliferation	3	PTGS2, EGFR, IGF1R	4.00E-03	1.50E-01
GO:0006915	apoptotic process	6	APP, CSNK2A1, IGFBP3, CDK1, NLRP3, MAPK14	5.29E-03	1.85E-01
GO:0050808	synapse organization	3	APP, CHRNA7, SNCA	5.40E-03	1.85E-01
GO:0070374	positive regulation of ERK1 and ERK2 cascade	4	APP, CHRNA7, ALOX15, EGFR	5.55E-03	1.85E-01
GO:0007611	learning or memory	3	APP, CHRNA7, EGFR	6.09E-03	1.95E-01

GO:0008285	negative regulation of cell population proliferation	5	APP, CDK6, IGFBP3, CYP1B1, PTGS2	6.59E-03	2.04E-01
GO:1905906	regulation of amyloid fibril formation	2	APP, CHRNA7	6.96E-03	2.08E-01
GO:0018105	peptidyl-serine phosphorylation	3	CSNK2A1, CDK1, MAPK14	7.97E-03	2.30E-01
GO:0043124	negative regulation of canonical NF-kappaB signal transduction	3	CHRNA7, GSTP1, ESR1	8.38E-03	2.30E-01
GO:0071260	cellular response to mechanical stimulus	3	PTGS2, EGFR, IGF1R	8.58E-03	2.30E-01
GO:0032310	prostaglandin secretion	2	NOS2, PTGS2	8.70E-03	2.30E-01
GO:0009410	response to xenobiotic stimulus	4	ABCB1, CDK1, PTGS2, SNCA	9.84E-03	2.40E-01
GO:0010628	positive regulation of gene expression	5	APP, CDK6, CDK1, MAPK14, F3	1.00E-02	2.40E-01
GO:0007613	memory	3	APP, CHRNA7, PTGS2	1.01E-02	2.40E-01
GO:1990962	xenobiotic transport across blood-brain barrier	2	ABCB1, ABCG2	1.04E-02	2.40E-01

GO:0006527	arginine catabolic process	2	NOS2, ARG1	1.04E-02	2.40E-01
GO:0043066	negative regulation of apoptotic process	5	GSTP1, CDK1, EGFR, IGF1R, SNCA	1.20E-02	2.43E-01
GO:0071393	cellular response to progesterone stimulus	2	CYP1B1, IGF1R	1.22E-02	2.43E-01
GO:0034440	lipid oxidation	2	ALOX5, ALOX15	1.22E-02	2.43E-01
GO:0002674	negative regulation of acute inflammatory response	2	GSTP1, NLRP3	1.22E-02	2.43E-01
GO:0098815	modulation of excitatory postsynaptic potential	2	APP, CHRNA7	1.22E-02	2.43E-01
GO:0098586	cellular response to virus	3	MMP12, NLRP3, MAPK14	1.22E-02	2.43E-01
GO:0030335	positive regulation of cell migration	4	CXCL12, F3, EGFR, IGF1R	1.36E-02	2.65E-01
GO:0051122	hepoxilin biosynthetic process	2	GSTP1, ALOX15	1.39E-02	2.65E-01
GO:1903426	regulation of reactive oxygen species biosynthetic process	2	ALOX5, SNCA	1.56E-02	2.92E-01

GO:0050729	positive regulation of inflammatory response	3	APP, NLRP3, SNCA	1.63E-02	2.94E-01
GO:0045944	positive regulation of transcription by RNA polymerase II	7	MMP12, APP, NLRP3, MAPK14, ESR1, EGFR, ESR2	1.68E-02	2.94E-01
GO:0009624	response to nematode	2	ARG1, PTGS2	1.73E-02	2.94E-01
GO:0070633	transepithelial transport	2	ABCB1, ABCG2	1.73E-02	2.94E-01
GO:0140115	export across plasma membrane	2	ABCB1, ABCG2	1.73E-02	2.94E-01
GO:0006805	xenobiotic metabolic process	3	ABCB1, GSTP1, CYP1B1	1.92E-02	3.19E-01
GO:0001934	positive regulation of protein phosphorylation	3	APP, CHRNA7, EGFR	2.03E-02	3.19E-01
GO:0034121	regulation of toll-like receptor signaling pathway	2	APP, ESR1	2.08E-02	3.19E-01
GO:0050730	regulation of peptidyl-tyrosine phosphorylation	2	APP, EGFR	2.08E-02	3.19E-01
GO:0032754	positive regulation of interleukin-5 production	2	PDE4D, NLRP3	2.08E-02	3.19E-01

GO:0006979	response to oxidative stress	3	APP, PTGS2, EGFR	2.10E-02	3.19E-01
GO:0071872	cellular response to epinephrine stimulus	2	PDE4D, SNCA	2.25E-02	3.31E-01
GO:0038083	peptidyl-tyrosine autophosphorylation	2	EGFR, IGF1R	2.25E-02	3.31E-01
GO:0051000	positive regulation of nitric-oxide synthase activity	2	TERT, ESR1	2.42E-02	3.45E-01
GO:0000122	negative regulation of transcription by RNA polymerase II	6	MMP12, APP, CDK6, ESR1, ESR2, SNCA	2.42E-02	3.45E-01
GO:0044849	estrous cycle	2	CYP1B1, IGF1R	2.76E-02	3.64E-01
GO:1904645	response to amyloid-beta	2	MMP12, CHRNA7	2.76E-02	3.64E-01
GO:0048169	regulation of long-term neuronal synaptic plasticity	2	APP, SNCA	2.76E-02	3.64E-01
GO:0019395	fatty acid oxidation	2	ALOX15, MAPK14	2.76E-02	3.64E-01
GO:0090336	positive regulation of brown fat cell differentiation	2	MAPK14, PTGS2	2.76E-02	3.64E-01

GO:0050728	negative regulation of inflammatory response	3	ALOX5, CHRNA7, NLRP3	2.95E-02	3.84E-01
GO:0016125	sterol metabolic process	2	CYP1B1, CYP19A1	3.10E-02	3.92E-01
GO:0048143	astrocyte activation	2	APP, EGFR	3.10E-02	3.92E-01
GO:0071391	cellular response to estrogen stimulus	2	ESR1, ESR2	3.27E-02	3.96E-01
GO:0060065	uterus development	2	ESR1, CYP19A1	3.27E-02	3.96E-01
GO:0033280	response to vitamin D	2	TYR, PTGS2	3.27E-02	3.96E-01
GO:0043651	linoleic acid metabolic process	2	GSTP1, ALOX15	3.44E-02	4.11E-01
GO:2000406	positive regulation of T cell migration	2	APP, CXCL12	3.77E-02	4.46E-01
GO:0030520	estrogen receptor signaling pathway	2	ESR1, ESR2	3.94E-02	4.48E-01
GO:1900273	positive regulation of long-term synaptic potentiation	2	APP, CHRNA7	3.94E-02	4.48E-01
GO:0090026	positive regulation of monocyte chemotaxis	2	APP, CXCL12	3.94E-02	4.48E-01

GO:0006809	nitric oxide biosynthetic process	2	NOS2, CYP1B1	4.11E-02	4.61E-01
GO:0046686	response to cadmium ion	2	TERT, CDK1	4.28E-02	4.74E-01
GO:2000773	negative regulation of cellular senescence	2	CDK6, TERT	4.44E-02	4.81E-01
GO:0051247	positive regulation of protein metabolic process	2	APP, CHRNA7	4.44E-02	4.81E-01
GO:0051262	protein tetramerization	2	APP, SNCA	4.78E-02	4.93E-01
GO:0010971	positive regulation of G2/M transition of mitotic cell cycle	2	APP, CDK1	4.78E-02	4.93E-01
GO:0051897	positive regulation of phosphatidylinositol 3-kinase/protein kinase B signal transduction	3	APP, EGFR, IGF1R	4.92E-02	4.93E-01
GO:0001774	microglial cell activation	2	APP, SNCA	4.94E-02	4.93E-01
GO:0095500	acetylcholine receptor signaling pathway	2	ACHE, CHRNA7	4.94E-02	4.93E-01
GO:0019933	cAMP-mediated signaling	2	PDE4D, PDE5A	4.94E-02	4.93E-01

GO:1905606	regulation of presynapse assembly	2	APP, SNCA	4.94E-02	4.93E-01
GO:0071549	cellular response to dexamethasone stimulus	2	EGFR, IGF1R	5.11E-02	4.99E-01
GO:1902894	negative regulation of miRNA transcription	2	APP, ESR1	5.11E-02	4.99E-01
GO:0045907	positive regulation of vasoconstriction	2	PTGS2, EGFR	5.28E-02	5.09E-01
GO:1990000	amyloid fibril formation	2	APP, SNCA	5.44E-02	5.09E-01
GO:0045740	positive regulation of DNA replication	2	CDK1, EGFR	5.44E-02	5.09E-01
GO:0010575	positive regulation of vascular endothelial growth factor production	2	CYP1B1, PTGS2	5.44E-02	5.09E-01
GO:0051968	positive regulation of synaptic transmission, glutamatergic	2	PTGS2, EGFR	5.61E-02	5.14E-01
GO:0060045	positive regulation of cardiac muscle cell proliferation	2	CDK1, MAPK14	5.61E-02	5.14E-01
GO:2000463	positive regulation of excitatory postsynaptic potential	2	APP, CHRNA7	5.77E-02	5.24E-01

GO:0008284	positive regulation of cell population proliferation	4	CSNK2A1, CHRNA7, EGFR, IGF1R	5.92E-02	5.28E-01
GO:0008306	associative learning	2	APP, CHRNA7	5.94E-02	5.28E-01
GO:0070555	response to interleukin-1	2	APP, SNCA	6.10E-02	5.37E-01
GO:0031100	animal organ regeneration	2	CXCL12, CDK1	6.27E-02	5.41E-01
GO:0046326	positive regulation of D-glucose import	2	TERT, MAPK14	6.27E-02	5.41E-01
GO:0001937	negative regulation of endothelial cell proliferation	2	ALOX5, XDH	6.59E-02	5.64E-01
GO:0018107	peptidyl-threonine phosphorylation	2	CSNK2A1, CDK1	6.76E-02	5.72E-01
GO:0048144	fibroblast proliferation	2	CDK1, ESR1	6.92E-02	5.81E-01
GO:0035094	response to nicotine	2	CHRNA7, IGF1R	7.08E-02	5.89E-01
GO:0007155	cell adhesion	4	ACHE, APP, CXCL12, CYP1B1	7.30E-02	6.02E-01
GO:0030177	positive regulation of Wnt signaling pathway	2	CSNK2A1, TERT	7.41E-02	6.05E-01

GO:0006469	negative regulation of protein kinase activity	2	GSTP1, SNCA	7.57E-02	6.09E-01
GO:0050796	regulation of insulin secretion	2	NOS2, ALOX5	7.73E-02	6.09E-01
GO:0042177	negative regulation of protein catabolic process	2	NOS2, EGFR	7.73E-02	6.09E-01
GO:0045663	positive regulation of myoblast differentiation	2	IGFBP3, MAPK14	7.73E-02	6.09E-01
GO:0001525	angiogenesis	3	CYP1B1, MAPK14, PTGS2	7.89E-02	6.11E-01
GO:1904646	cellular response to amyloid-beta	2	APP, IGF1R	7.89E-02	6.11E-01
GO:0001933	negative regulation of protein phosphorylation	2	IGFBP3, XDH	8.05E-02	6.18E-01
GO:0036323	vascular endothelial growth factor receptor-1 signaling pathway	2	EGFR, IGF1R	8.21E-02	6.18E-01
GO:0042130	negative regulation of T cell proliferation	2	ARG1, PDE5A	8.37E-02	6.18E-01
GO:0043409	negative regulation of MAPK cascade	2	GSTP1, IGF1R	8.37E-02	6.18E-01

GO:0035790	platelet-derived growth factor receptor-alpha signaling pathway	2	EGFR, IGF1R	8.37E-02	6.18E-01
GO:0038109	Kit signaling pathway	2	EGFR, IGF1R	8.54E-02	6.18E-01
GO:0038145	macrophage colony-stimulating factor signaling pathway	2	EGFR, IGF1R	8.54E-02	6.18E-01
GO:0042311	vasodilation	2	KCNMA1, EGFR	8.54E-02	6.18E-01
GO:0006468	protein phosphorylation	3	CDK6, CSNK2A1, IGFBP3	8.66E-02	6.22E-01
GO:1900087	positive regulation of G1/S transition of mitotic cell cycle	2	TERT, EGFR	8.86E-02	6.23E-01
GO:0031547	brain-derived neurotrophic factor receptor signaling pathway	2	EGFR, IGF1R	9.01E-02	6.23E-01
GO:0051592	response to calcium ion	2	KCNMA1, EGFR	9.01E-02	6.23E-01
GO:0048863	stem cell differentiation	2	MAPK14, ESR1	9.01E-02	6.23E-01
GO:0035791	platelet-derived growth factor receptor-beta signaling pathway	2	EGFR, IGF1R	9.01E-02	6.23E-01

GO:0048012	hepatocyte growth factor receptor signaling pathway	2	EGFR, IGF1R	9.33E-02	6.35E-01
GO:0031623	receptor internalization	2	ACHE, SNCA	9.33E-02	6.35E-01
GO:0071320	cellular response to cAMP	2	PDE4D, CYP1B1	9.49E-02	6.36E-01
GO:0045786	negative regulation of cell cycle	2	CDK6, PTGS2	9.49E-02	6.36E-01
GO:0050890	cognition	2	APP, CHRNA7	9.65E-02	6.37E-01
GO:0038063	collagen-activated tyrosine kinase receptor signaling pathway	2	EGFR, IGF1R	9.65E-02	6.37E-01
GO:0030282	bone mineralization	2	ALOX15, PTGS2	9.81E-02	6.38E-01
GO:0090398	cellular senescence	2	MAPK14, IGF1R	9.81E-02	6.38E-01
GO:0007612	learning	2	APP, PTGS2	9.97E-02	6.44E-01

Category	Term	Name	Count	Genes	PValue	FDR
Cell Component (27)	GO:0048471	perinuclear region of cytoplasm	8	ACHE, APP, NOS2, ALOX5, PDE4D, TYR, EGFR, SNCA	1.77E-04	2.30E-02
	GO:0005829	cytosol	20	APP, NOS2, CSNK2A1, MAOA, ARG1, GSTP1, PDE4D, ALOX15, PTGS2, MAPK14, ESR1, EGFR, CDK6, TERT, ALOX5, CDK1, NLRP3, PDE5A, XDH, SNCA	4.46E-04	2.30E-02
	GO:0016324	apical plasma membrane	6	ABCB1, CHRNA7, PDE4D, KCNMA1, EGFR, ABCG2	5.28E-04	2.30E-02
	GO:0005615	extracellular space	11	MMP12, ACHE, APP, ARG1, ALOX5, GSTP1, IGFBP3, F3, XDH, EGFR, SNCA	5.82E-04	2.30E-02
	GO:0005739	mitochondrion	10	APP, ALDH2, MAOA, GSTP1, CDK1, NLRP3, CYP1B1, MAPK14, ESR2, SNCA	1.39E-03	4.41E-02
	GO:0005576	extracellular region	11	MMP12, ACHE, APP, CXCL12, ARG1, ALOX5, GSTP1, IGFBP3, NLRP3, MAPK14, SNCA	3.01E-03	7.94E-02
	GO:0005901	caveola	3	KCNMA1, PTGS2, IGF1R	6.68E-03	1.51E-01
	GO:0098591	external side of apical plasma membrane	2	ABCB1, ABCG2	9.77E-03	1.93E-01

GO:0005634	nucleus	18	ACHE, APP, NOS2, CSNK2A1, ARG1, GSTP1, PDE4D, IGFBP3, MAPK14, ESR1, EGFR, ESR2, MMP12, CDK6, TERT, CDK1, NLRP3, SNCA	1.14E-02	2.00E-01
GO:0034774	secretory granule lumen	3	ALOX5, GSTP1, MAPK14	1.59E-02	2.19E-01
GO:0005641	nuclear envelope lumen	2	APP, ALOX5	1.62E-02	2.19E-01
GO:0016020	membrane	16	ACHE, APP, ABCB1, CHRNA7, PDE4D, ALOX15, F3, ESR1, CYP19A1, EGFR, IGF1R, KCNMA1, CDK1, CYP1B1, NLRP3, SNCA	1.69E-02	2.19E-01
GO:1904813	ficolin-1-rich granule lumen	3	ALOX5, GSTP1, MAPK14	1.80E-02	2.19E-01
GO:0009986	cell surface	5	ACHE, APP, ABCB1, F3, EGFR	2.21E-02	2.27E-01
GO:0005886	plasma membrane	16	ACHE, APP, ABCB1, NOS2, CSNK2A1, CHRNA7, PDE4D, ALOX15, F3, ESR1, EGFR, IGF1R, TERT, KCNMA1, ABCG2, SNCA	2.28E-02	2.27E-01
GO:0043231	intracellular membrane-bounded organelle	6	APP, CYP1B1, TYR, PTGS2, ESR2, IGF1R	2.42E-02	2.27E-01
GO:0032991	protein-containing complex	5	APP, PTGS2, ESR1, EGFR, SNCA	2.54E-02	2.27E-01

GO:0005798	Golgi-associated vesicle	2	APP, TYR	2.59E-02	2.27E-01
GO:0098794	postsynapse	3	APP, CHRNA7, SNCA	4.15E-02	3.29E-01
GO:0005737	cytoplasm	16	APP, ABCB1, NOS2, ARG1, GSTP1, TYR, PTGS2, MAPK14, ESR1, EGFR, MMP12, CDK6, TERT, CDK1, NLRP3, SNCA	4.17E-02	3.29E-01
GO:0045121	membrane raft	3	APP, EGFR, ABCG2	4.65E-02	3.50E-01
GO:0043235	receptor complex	3	APP, EGFR, IGF1R	4.89E-02	3.51E-01
GO:0045202	synapse	4	ACHE, APP, CHRNA7, SNCA	5.47E-02	3.76E-01
GO:0000307	cyclin-dependent protein kinase holoenzyme complex	2	CDK6, CDK1	7.26E-02	4.66E-01
GO:0031965	nuclear membrane	3	ALOX5, PDE4D, EGFR	7.37E-02	4.66E-01
GO:0005764	lysosome	3	APP, TYR, SNCA	9.50E-02	5.56E-01
GO:0005788	endoplasmic reticulum lumen	3	APP, IGFBP3, PTGS2	9.50E-02	5.56E-01

Category	Term	Name	Count	Genes	PValue	FDR
Molecular Function (63)	GO:0042803	protein homodimerization activity	9	ACHE, APP, TERT, NOS2, CHRNA7, TYR, PTGS2, XDH, ABCG2	3.88E-05	6.65E-03
	GO:0019899	enzyme binding	7	APP, PDE4D, MAPK14, PTGS2, ESR1, EGFR, ESR2	4.45E-05	6.65E-03
	GO:0005506	iron ion binding	5	ALOX5, ALOX15, CYP1B1, CYP19A1, XDH	1.20E-04	1.20E-02
	GO:0016491	oxidoreductase activity	5	MAOA, ALOX5, TYR, XDH, SNCA	6.94E-04	4.33E-02
	GO:0042802	identical protein binding	11	APP, CSNK2A1, TERT, KCNMA1, NLRP3, TYR, ESR1, EGFR, ABCG2, IGF1R, SNCA	7.24E-04	4.33E-02
	GO:0020037	heme binding	4	NOS2, CYP1B1, PTGS2, CYP19A1	2.60E-03	1.29E-01
	GO:0016701	oxidoreductase activity, acting on single donors with incorporation of molecular oxygen	2	ALOX5, PTGS2	3.53E-03	1.51E-01
	GO:0005524	ATP binding	9	ABCB1, CDK6, CSNK2A1, CDK1, NLRP3, MAPK14, EGFR, ABCG2, IGF1R	4.66E-03	1.55E-01

GO:0005515	protein binding	32	APP, ACHE, ABCB1, MAOA, GSTP1, CHRNA7, ALOX15, PTGS2, EGFR, IGF1R, TERT, ALOX5, CYP1B1, NLRP3, XDH, SNCA, NOS2, CSNK2A1, ARG1, PDE4D, IGFBP3, TYR, MAPK14, F3, ESR1, ESR2, CXCL12, CDK6, KCNMA1, CDK1, PDE5A, ABCG2	4.67E-03	1.55E-01
GO:0050660	flavin adenine dinucleotide binding	3	NOS2, MAOA, XDH	5.87E-03	1.76E-01
GO:0030284	nuclear estrogen receptor activity	2	ESR1, ESR2	7.05E-03	1.76E-01
GO:0004052	arachidonate 12(S)-lipoxygenase activity	2	ALOX5, ALOX15	7.05E-03	1.76E-01
GO:0051117	ATPase binding	3	PDE4D, ESR1, EGFR	1.01E-02	2.32E-01
GO:0101021	estrogen 2-hydroxylase activity	2	CYP1B1, CYP19A1	1.58E-02	3.26E-01
GO:0034056	estrogen response element binding	2	ESR1, ESR2	1.93E-02	3.26E-01
GO:0042166	acetylcholine binding	2	ACHE, CHRNA7	1.93E-02	3.26E-01
GO:0016702	oxidoreductase activity, acting on single donors with incorporation of molecular oxygen, incorporation of two atoms of oxygen	2	ALOX5, PTGS2	2.10E-02	3.26E-01

GO:0043565	sequence-specific DNA binding	4	MMP12, NLRP3, ESR1, ESR2	2.20E-02	3.26E-01
GO:0005520	insulin-like growth factor binding	2	IGFBP3, IGF1R	2.27E-02	3.26E-01
GO:0031994	insulin-like growth factor I binding	2	IGFBP3, IGF1R	2.27E-02	3.26E-01
GO:0015562	efflux transmembrane transporter activity	2	ABCB1, ABCG2	2.44E-02	3.26E-01
GO:0008559	ABC-type xenobiotic transporter activity	2	ABCB1, ABCG2	2.44E-02	3.26E-01
GO:0008395	steroid hydroxylase activity	2	CYP1B1, CYP19A1	2.62E-02	3.26E-01
GO:0106310	protein serine kinase activity	4	CDK6, CSNK2A1, CDK1, MAPK14	2.62E-02	3.26E-01
GO:0004114	3',5'-cyclic-nucleotide phosphodiesterase activity	2	PDE4D, PDE5A	2.79E-02	3.34E-01
GO:0005178	integrin binding	3	APP, CXCL12, EGFR	3.24E-02	3.72E-01
GO:0047555	3',5'-cyclic-GMP phosphodiesterase activity	2	PDE4D, PDE5A	3.65E-02	4.04E-01
GO:0004115	3',5'-cyclic-AMP phosphodiesterase activity	2	PDE4D, PDE5A	3.82E-02	4.07E-01

GO:0005158	insulin receptor binding	2	APP, IGF1R	3.99E-02	4.11E-01
GO:0003707	nuclear steroid receptor activity	2	ESR1, ESR2	4.16E-02	4.14E-01
GO:0042910	xenobiotic transmembrane transporter activity	2	ABCB1, ABCG2	4.33E-02	4.17E-01
GO:0004693	cyclin-dependent protein serine/threonine kinase activity	2	CDK6, CDK1	5.00E-02	4.62E-01
GO:0005496	steroid binding	2	ESR1, ESR2	5.34E-02	4.62E-01
GO:0005516	calmodulin binding	3	NOS2, ESR1, EGFR	5.38E-02	4.62E-01
GO:0003682	chromatin binding	4	APP, CDK1, ESR1, EGFR	5.51E-02	4.62E-01
GO:0030332	cyclin binding	2	CDK6, CDK1	5.84E-02	4.62E-01
GO:0046872	metal ion binding	10	TERT, NOS2, ARG1, PDE4D, IGFBP3, KCNMA1, PDE5A, TYR, PTGS2, SNCA	6.02E-02	4.62E-01
GO:0016301	kinase activity	3	CSNK2A1, CDK1, EGFR	6.07E-02	4.62E-01
GO:0016712	oxidoreductase activity, acting on paired donors, with incorporation or reduction of	2	CYP1B1, CYP19A1	6.17E-02	4.62E-01

	molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen				
GO:0042626	ATPase-coupled transmembrane transporter activity	2	ABCB1, ABCG2	6.50E-02	4.62E-01
GO:0140359	ABC-type transporter activity	2	ABCB1, ABCG2	7.49E-02	4.62E-01
GO:0001223	transcription coactivator binding	2	TERT, ESR1	8.31E-02	4.62E-01
GO:0005011	macrophage colony-stimulating factor receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0038062	protein tyrosine kinase collagen receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0005008	hepatocyte growth factor receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0005004	GPI-linked ephrin receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0060175	brain-derived neurotrophic factor receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01

GO:0005018	platelet-derived growth factor alpha-receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0008288	boss receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0036332	placental growth factor receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0005009	insulin receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0005020	stem cell factor receptor activity	2	EGFR, IGF1R	8.63E-02	4.62E-01
GO:0005019	platelet-derived growth factor beta-receptor activity	2	EGFR, IGF1R	8.79E-02	4.62E-01
GO:0005006	epidermal growth factor receptor activity	2	EGFR, IGF1R	8.79E-02	4.62E-01
GO:0030544	Hsp70 protein binding	2	CDK1, SNCA	8.79E-02	4.62E-01
GO:0005007	fibroblast growth factor receptor activity	2	EGFR, IGF1R	8.79E-02	4.62E-01
GO:0005010	insulin-like growth factor receptor activity	2	EGFR, IGF1R	8.95E-02	4.62E-01
GO:0004879	nuclear receptor activity	2	ESR1, ESR2	9.12E-02	4.62E-01

GO:0005021	vascular endothelial growth factor receptor activity	2	EGFR, IGF1R	9.12E-02	4.62E-01
GO:0005005	transmembrane-ephrin receptor activity	2	EGFR, IGF1R	9.28E-02	4.62E-01
GO:0016705	oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen	2	CYP1B1, CYP19A1	9.92E-02	4.71E-01
GO:0005507	copper ion binding	2	TYR, SNCA	9.92E-02	4.71E-01
GO:0004672	protein kinase activity	3	CDK1, MAPK14, EGFR	9.97E-02	4.71E-01

Table S3. KEGG pathway annotation of the 35 selected targets.

Term	**Name**	**Count**	**Genes**	**PValue**	**FDR**
hsa04913	Ovarian steroidogenesis	5	ALOX5, CYP1B1, PTGS2, CYP19A1, IGF1R	4.40E-05	0.008011063
hsa05200	Pathways in cancer	10	CXCL12, CDK6, TERT, NOS2, GSTP1, PTGS2, ESR1, EGFR, ESR2, IGF1R	1.35E-04	0.012254945

hsa01522	Endocrine resistance	5	MAPK14, ESR1, EGFR, ESR2, IGF1R	5.39E-04	0.032675332
hsa00330	Arginine and proline metabolism	4	ALDH2, NOS2, MAOA, ARG1	9.12E-04	0.034473305
hsa04726	Serotonergic synapse	5	APP, MAOA, ALOX5, ALOX15, PTGS2	9.47E-04	0.034473305
hsa05224	Breast cancer	5	CDK6, ESR1, EGFR, ESR2, IGF1R	2.40E-03	0.072909346
hsa04148	Efferocytosis	5	ARG1, ALOX5, ALOX15, MAPK14, PTGS2	2.98E-03	0.077411552
hsa05225	Hepatocellular carcinoma	5	CDK6, TERT, GSTP1, EGFR, IGF1R	3.96E-03	0.09015345
hsa05207	Chemical carcinogenesis - receptor activation	5	CHRNA7, CYP1B1, ESR1, EGFR, ESR2	9.04E-03	0.158705122
hsa05022	Pathways of neurodegeneration - multiple diseases	7	APP, CSNK2A1, NOS2, CHRNA7, MAPK14, PTGS2, SNCA	9.55E-03	0.158705122
hsa05163	Human cytomegalovirus infection	5	CXCL12, CDK6, MAPK14, PTGS2, EGFR	1.07E-02	0.158705122
hsa01100	Metabolic pathways	13	NOS2, MAOA, ARG1, GSTP1, PDE4D, ALOX15, TYR, PTGS2, CYP19A1, ALDH2, ALOX5, PDE5A, XDH	1.12E-02	0.158705122

hsa00380	Tryptophan metabolism	3	ALDH2, MAOA, CYP1B1	1.13E-02	0.158705122
hsa05010	Alzheimer disease	6	APP, CSNK2A1, NOS2, CHRNA7, PTGS2, SNCA	1.62E-02	0.210569611
hsa04218	Cellular senescence	4	CDK6, IGFBP3, CDK1, MAPK14	2.23E-02	0.270092258
hsa00590	Arachidonic acid metabolism	3	ALOX5, ALOX15, PTGS2	2.45E-02	0.278125729
hsa05204	Chemical carcinogenesis - DNA adducts	3	GSTP1, CYP1B1, PTGS2	3.05E-02	0.281544359
hsa04917	Prolactin signaling pathway	3	MAPK14, ESR1, ESR2	3.05E-02	0.281544359
hsa05206	MicroRNAs in cancer	5	ABCB1, CDK6, CYP1B1, PTGS2, EGFR	3.11E-02	0.281544359
hsa05218	Melanoma	3	CDK6, EGFR, IGF1R	3.21E-02	0.281544359
hsa04115	p53 signaling pathway	3	CDK6, IGFBP3, CDK1	3.38E-02	0.281544359
hsa05214	Glioma	3	CDK6, EGFR, IGF1R	3.46E-02	0.281544359
hsa05133	Pertussis	3	NOS2, NLRP3, MAPK14	3.63E-02	0.281544359

hsa05140	Leishmaniasis	3	NOS2, MAPK14, PTGS2	3.71E-02	0.281544359
hsa05205	Proteoglycans in cancer	4	MAPK14, ESR1, EGFR, IGF1R	4.34E-02	0.316093483
hsa05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	3	CSNK2A1, MAPK14, EGFR	4.70E-02	0.324102758
hsa05222	Small cell lung cancer	3	CDK6, NOS2, PTGS2	4.99E-02	0.324102758
hsa04520	Adherens junction	3	CSNK2A1, EGFR, IGF1R	4.99E-02	0.324102758
hsa05215	Prostate cancer	3	GSTP1, EGFR, IGF1R	5.47E-02	0.343569933
hsa04625	C-type lectin receptor signaling pathway	3	NLRP3, MAPK14, PTGS2	6.19E-02	0.363136938
hsa04064	NF-kappa B signaling pathway	3	CXCL12, CSNK2A1, PTGS2	6.19E-02	0.363136938
hsa04066	HIF-1 signaling pathway	3	NOS2, EGFR, IGF1R	6.71E-02	0.370747484
hsa04914	Progesterone-mediated oocyte maturation	3	CDK1, MAPK14, IGF1R	6.82E-02	0.370747484

hsa05145	Toxoplasmosis	3	NOS2, ALOX5, MAPK14	6.93E-02	0.370747484
hsa00340	Histidine metabolism	2	ALDH2, MAOA	8.18E-02	0.425367595
hsa00220	Arginine biosynthesis	2	NOS2, ARG1	8.54E-02	0.428870767
hsa00230	Purine metabolism	3	PDE4D, PDE5A, XDH	8.72E-02	0.428870767
hsa04926	Relaxin signaling pathway	3	NOS2, MAPK14, EGFR	8.95E-02	0.428870767
hsa04068	FoxO signaling pathway	3	MAPK14, EGFR, IGF1R	9.31E-02	0.434383137