

Table S1: The result of module identification by MCODE.

Group	Module	Score	Nodes	Edges	Node IDs
Vehicle	1	2.75	8	22	Carm1, Sin3a, Ncoa2, Crebbp, Ncor1, Med1, Hdac3, Ncoa3
	2	2.562	32	82	Il17a, Il2, Ptpre, H2-Eb1, Cd8a, Tnfrsf1a, Tnf, Casp1, Il18, Cxcl2, Cd14, Cd86, Tlr2, Il23a, Tbx21, Il12a, Irf5, Nfkb1, Relb, Jun, Ptgs2, Nfkbia, Ncor2, Cdk2, Myc, Stat3, Socs3, Bcl3, Cxcl10, Csf2, Il7r, Il5
	3	2.062	16	33	Egf, Mapk3, Egfr, Akt1, Dut, Mki67, Bcl2, Casp8, F5, Hrg, F13a1, Clu, F8, Sparc, Pros1, Vwf
	4	2	11	22	Il1b, Plg, Alb, Fn1, Vegfa, Ifng, Il10, Il12b, Cd40lg, Cd40, Traf6
	5	2	15	30	Nfkbib, Rel, Chuk, Cd4, Il15, Il2ra, Icam1, Il1rn, Il1a, Myd88, Irak1, Rela, Pmpcb, Nfkb2, Ikbkb
	6	1.8	5	9	Itgb2l, Fgg, Fgb, Itgb2, Itgax
	7	1.778	9	16	Bmpr1b, Bmp2, Bmp7, Id2, Smad4, Bmpr1a, Smad5, Bmpr2, Bmp4
	8	1.714	7	12	Cant1, Entpd4, Hprt, Entpd5, Atic, Entpd6, Gmps
	9	1.714	7	12	Ywhaz, Gp9, Gp1bb, Colla1, Gp5, F12, Gp1ba
	10	1.667	9	15	Mdh2, Ddo, Got2, Acly, Csl, Pck2, Pck1, Cs, Pcx
	11	1.5	8	12	Ldhb, Ldha, Tktl2, Pgm2, Tkt, Pkm2, Ldhc, Pklr
	12	1.4	5	7	Pten, Cdk4, Ccnd1, Irf1, Trp53
	13	1.4	5	7	Odc1, Acyl, Oat, Otc, Arg2
	14	1.4	5	7	Mef2c, Myod1, Srf, Myog, Mef2a
	15	1.385	13	18	Ebi3, Il27ra, Il27, Fas, Fadd, Tnfsf10, Cflar, Prdx3, Txn1, Cat, Sod1, Casp3, Irf8
	16	1.364	11	15	Igf1, Adipoq, Sirt1, Ppargc1a, Foxo1, Pparg, Ar, Gnrh1, Nr2c1, Thra, Rxrb
	17	1.333	6	8	Cyba, Mmp2, Ncf2, Mapk12, Cdc25b, Mapk14
	18	1.2	5	6	Ncf4, Nox3, Nox1, Ncf1, Rac1
	19	1.167	6	7	Pdcd1lg2, Ptpn6, Grb2, Ctla4, Yes1, Lck
	20	1.167	6	7	Pcna, Rpa3, Rad51, Rpa2, Asf1b, Chaf1b
	21	1.167	6	7	Cda, Tk2, Dtymk, Itpa, Cmpk2, Dctd

	22	1	3	3	Junb, Fosb, Fos
	23	1	3	3	Phex, Slc34a1, Fgf23
	24	1	4	4	Pbk, Nuf2, Shcbp1, Zwilch
	25	1	3	3	Nip7, Eif6, Sbds
	26	1	3	3	Map3k7ip2, Ticam1, Tlr3
	27	1	3	3	Cd3e, Nck1, Lcp2
	28	1	3	3	Rag1, Pax5, Cd79a
	29	1	4	4	Aco2, Idh3a, Aco1, Idh3g
	30	1	4	4	Med9, Med24, Med21, Med16
JA	1	4.056	18	73	Rela, Myd88, Cd40, Il5, Il2, Il1b, Il13, Tnf, Icam1, Tlr4, Traf6, Nfkb1, Cxcl10, Il6, Socs3, Stat3, Ifng, Il12b
	2	2	11	22	Shc1, Insrr, Fyn, Grb2, Tek, Ptpn11, Egf, Fn1, Vegfa, Igf1, Insr
	3	2	16	32	Got1, Got2, Mdh2, Idh3g, Ogdh, Idh1, Idh2, Idh3a, Nit2, Glud1, Glc, Asns, Glc2, Cth, Glul, Aldh4a1
	4	1.966	116	228	Crebbp, Arnt, Ep300, Arntl, Hes6, Epas1, CBF1, Ctbp1, Nfyb, Tcf3, Crem, Trrap, Wwtr1, Arnt2, Mafb, Foxd3, Pou3f1, Hoxa10, Kdmla, Spib, Tcfe3, Dmbx1, Lmo4, Barx2, Satb2, Grin1, Nr6a1, Cacna1c, Creg1, Mga, Pax1, Atf5, Meis1, Lbx1, Ecsit, Pknox1, Tfam, Tbl1x, Pus1, Deaf1, Ikzf1, Calml3, Calm5, Dach1, Taf4b, Bsx, Tdg, Pbx1, Nrfl, Pdlim1, Pou3f2, Rcor2, Npas4, Six1, Hoxb13, Lbxcor1, Helt, Onecut3, Itpr2, Calm2, Rarg, Alx4, Nfyc, Abt1, Ncoa6, Pbx3, Hand2, Crx, Alx1, Calm4, Hoxa11, Pbx2, Itpr3, Foxh1, Tfdp2, Nr2e3, Tcf12, Pou2f3, Rbl2, Atf7ip, Nobox, Pax4, Clock, Pax7, Tle1, Rbl1, Sall4, Pax8, Ptf1a, Pou4f3, Pou5f1, Zeb1, Tcfef, Gsc, Rbpjl, Hivep2, Snai3, Tead4, Sra1, Pax3, Pou1f1, Pax2, Grin2c, Grin2d, Sfpil, Hoxd12, Pax9, Kat2b, Dazap2, Tbx2, Ankrd1, Carm1, Sox6, Ets1, Tfdp1, Tcfcp2
	5	1.929	14	27	Cd40lg, Lck, Ptpn6, Lat, Cd247, Lcp2, Il10, Cd4, Tlr2, Cd14, Cd80, Cd86, Csf2, Il1a
	6	1.8	5	9	Padi2, Hspa5, Canx, Vcp, P4hb

	7	1.4	5	7	Atrx, Dnmt1, Mecp2, Mbd4, Dnmt3a
	8	1.333	6	8	Tbx21, Il17a, Il15, Irf1, Il27, Stat1
	9	1.25	4	5	Pik3ca, Egfr, Erbb2, Trp53
	10	1.25	4	5	Mki67, Cks2, Pcna, Mad211
	11	1.25	8	10	Pink1, Htra2, Aifm1, Cat, Nqo1, Keap1, Nfe2l2, Park7
	12	1.25	4	5	Bmpr1b, Bmpr2, Bmp6, Smad1
	13	1.25	4	5	Slc40a1, Slc11a2, Tfrc, Hfe
	14	1.25	4	5	Kidins220, Crk, Ywhab, Braf
	15	1.2	5	6	Brix1, Abce1, Pno1, Emg1, Taf9
	16	1.2	5	6	Cdc25b, Cdc25c, Chek1, Cdc25a, Ccnb2
	17	1	3	3	Timp1, Mmp9, Jun
	18	1	3	3	Bdnf, Ntf5, Ntrk3
	19	1	3	3	Pten, Pik3r2, Pip4k2c
	20	1	3	3	Gdf11, Acvr2a, Acvr1b
	21	1	3	3	Hspa8, Hspd1, Hsph1
	22	1	3	3	Ctgf, Apoa1, Agt
	23	1	4	4	Oprm1, Oprd1, Oprk1, Penk
	24	1	4	4	Mafg, Nfe2, Mafk, Mare
UA	1	4.55	20	91	Prc1, Spc25, Cks2, Kif20a, Kif11, Ect2, Rrm2, Cks1b, Mki67, Top2a, Cdk1, Ncaph, Mad211, Cenpn, Cdc20, Incenp, Ccna2, Ccnb1, Plk1, Ccnb2
	2	2.963	27	80	Il18, Irf5, Il12b, Cd80, Ifng, Ptprc, Cd14, Tlr2, Nfkb1a, Ikbkg, Chuk, Nfkbib, Ikbkb, Nfkb2, Il17a, Il10, Il13, Cd4, Il1r1, Casp1, Il1b, Nod2, Tnf, Cxcl10, Cxcl2, Il1rn, Il1a
	3	2.667	12	32	Traf6, Cd40, Cd86, Nfkb1, Il6, Csf2, Il5, Il23a, Tlr4, Tlr5, Irak1, Tlr9
	4	2.4	10	24	Kng2, Alb, A2m, Hrg, Serping1, Clu, Kng1, Sparc, Fn1, Klkb1
	5	2.08	25	52	Ghr, Igfbp4, Igf2, Igfbp5, Pappa, Igf1, Pitx2, Nkx2-5, Tcf4, Tcf7l2, Tcfap2a, Cebpb, Kat2a, Cops5,

				Pou2f1, Grin2d, Myst2, Crebbp, Grin2c, Grin2b, Grin1, Grin2a, Ep300, Stat5a, Prl	
6	1.709	55	94	Ikbke, Bcl2, Bcl2l11, Pik3r1, Lat, Sykb, Lcp2, Pin1, Mdk, Zhx2, Raf1, Ywhab, Map2k2, Mapk1, Eps15l1, Grb2, Eps15, Cltc, Cbl, Src, Vwf, Itgb3, Bear1, Itga2b, Ptpn1, Mlh1, Rfc1, Atf2, Gadd45a, Myst1, Pbrm1, Zwi1ch, Hmnr, Melk, Shebp1, Bub1b, Cbx5, Bub1, Trp53bp1, Brca1, Erbb2, Erbb3, Akt1, Nos3, Sirt1, Lep, Cntf, Lif, Stat1, Ifih1, Ccl5, Ddx58, Ifnb1, Tank, Irf3	
7	1.588	17	27	Relb, Icam1, Cd44, Il2ra, Shc1, Egfr, Stat3, Socs3, Stat6, Il2, Jun, Mcm4, Cdc6, Mcm3, Rb1, Ccnd1, Pmpcb	
8	1.5	6	9	Rad50, Chek2, Msh6, Msh2, Ung, Fen1	
9	1.429	7	10	Uqcrf5, Ppa1, Ppa2, Atp5b, Lhpp, Atp5j, Uqcr	
10	1.4	5	7	Irak2, Tlr3, Tlr6, Tirap, Myd88	
11	1.333	9	12	Plcb3, Plcb2, Plcb4, Mpl, Jak2, Epor, Kitl, Plcb1, Pik3ca	
12	1.25	4	5	Ckap2, Birc5, Aurkb, Pbk	
13	1.25	4	5	Ide, Mme, Psen2, App	
14	1.2	5	6	Mcm7, Rpa2, Pole2, Rpa3, Rpa1	
15	1.2	5	6	Uqcrc2, Ndufa5, Ndubf3, Uqcrh, Uqcrb	
16	1.2	5	6	Carm1, Ncoa2, Grip1, Ncoa3, Sin3a	
17	1	4	4	Atp5h, Cox6b1, Ndufs7, Ndufv2	
18	1	4	4	Spp1, Itgb1, Vtn, Itga4	
19	1	4	4	Oprm1, Oprd1, Oprk1, Penk	
JU	1	4.545	11	50	Ccnb2, Mki67, Mad2l1, Cdc20, Cdca8, Top2a, Birc5, Kif11, Pre1, Ccnb1, Ccna2
	2	4.308	13	56	Myd88, Il6, Tlr2, Tnf, Il12b, Tlr4, Il1a, Il18, Ifng, Cd80, Il10, Il23a, Il17a
	3	2.25	16	36	Il5, Socs3, Stat3, Rela, Cd14, Cd86, Cd4, Il2, Traf6, Tnfrsf1a, Il1b, Cxcl10, Stat1, Cd40, Csf2, Il13
	4	2	23	46	Alb, Vegfa, Hrg, Egf, Clu, Sparc, Myc, Rb1, Ccne1, Ccne2, Skp2, Ccnd1, Cdkn2a, Cdk4, Skp1a, Plg, Mmp9, Timp1, Lep, Igf1, Foxo3, FasL, Tgfb1
	5	1.875	8	15	Aurkb, Rrm2, Cdk1, Kif20a, Plk1, Bub1, Ect2, NcapH

6	1.8	10	18	Itgb3bp, Psen1, Ngfr, Psen2, Arntl, Per3, Timeless, Per1, Clock, Ncstn
7	1.714	7	12	Tbxa2r, Gnaq, Gna14, Rgs2, Gna11, ORP-2, Gna15
8	1.571	7	11	Fn1, Itga2b, Ibsp, Itga2, Itgb6, Nid1, Vtn
9	1.417	12	17	Ptpnc, Lck, Grb2, Erbb2, Erbb3, Akt1, Gsk3b, Fyn, Cd44, Foxp3, Il2ra, Fas
10	1.4	15	21	Map2k1, Mdk, Map2k2, Mapk1, Pxn, Itga5, Isg15, Ddx58, Tbk1, Ifnb1, Tlr8, Irf7, Spp1, Itgb1, Ptk2
11	1.333	6	8	Gen1, Lig4, Xrcc6, Xrcc4, Wrm, Xrcc5
12	1.2	5	6	Myc
13	1.2	5	6	Bcl2, Dut, Pcn, Rfc4, Rpa1
14	1.2	5	6	Nr4a2, Nr5a1, Rxrb, Nr5a2, Thra
15	1	3	3	Pten, Cdkn1b, Trp53
16	1	3	3	Ntrk2, Ntrk1, Bdnf
17	1	4	4	Cep55, Melk, Kif22, Hmnr
18	1	3	3	Ptges2, Tbxas1, Ptgs
19	1	4	4	Ppargc1a, Creb1, Ddit3, Atf2
20	1	3	3	Zfp2, Lhx9, Gata4
21	1	3	3	Ace, Gm9847, Ren1
22	1	3	3	Scg2, Scg3, Chga
23	1	4	4	Tgfbr2, Smad2, Tgfbr1, Smad7
24	1	3	3	Rps3, Eif3a, Abce1
25	1	4	4	Pik3r5, Pip4k2c, Pik3cg, Inpp5d
26	1	4	4	Irs1, Pik3r2, Itgam, Pik3cb
27	1	3	3	Uba52, Sumo1, Pias1
28	1	4	4	Oprm1, Oprd1, Oprk1, Penk
29	1	4	4	Cald1, Tpm4, Vcl, Tpm1

Table S2: The overlapping GO terms (Biological Process) of each group.

Group	GO terms (Biological Process)
JA and JU:16	regulation of cytokine biosynthetic process positive regulation of cytokine biosynthetic process positive regulation of interleukin-6 biosynthetic process regulation of immunoglobulin secretion positive regulation of isotype switching to IgG isotypes positive regulation of interleukin-12 biosynthetic process regulation of defense response regulation of transcription from RNA polymerase II promoter anatomical structure morphogenesis cell death death negative regulation of insulin receptor signaling pathway morphogenesis of a branching structure mammary gland development multicellular organismal process branching morphogenesis of a tube
JA and UA:95	regulation of interleukin-6 production positive regulation of protein kinase cascade positive regulation of lymphocyte proliferation positive regulation of mononuclear cell proliferation positive regulation of leukocyte proliferation regulation of lymphocyte activation regulation of leukocyte activation regulation of protein kinase cascade

regulation of cell activation
regulation of mononuclear cell proliferation
regulation of lymphocyte proliferation
positive regulation of signal transduction
regulation of leukocyte proliferation
positive regulation of cell communication
positive regulation of transcription factor activity
positive regulation of DNA binding
positive regulation of binding
regulation of chemokine production
positive regulation of MAPKKK cascade
regulation of transcription factor activity
positive regulation of stress-activated protein kinase signaling pathway
positive regulation of JNK cascade
positive regulation of multicellular organismal process
positive regulation of interleukin-6 production
regulation of DNA binding
positive regulation of NF-kappaB transcription factor activity
regulation of binding
regulation of MAPKKK cascade
regulation of signal transduction
positive regulation of I-kappaB kinase/NF-kappaB cascade
positive regulation of chemokine biosynthetic process
regulation of I-kappaB kinase/NF-kappaB cascade
regulation of cell communication
regulation of cellular biosynthetic process

regulation of biosynthetic process
regulation of JNK cascade
regulation of stress-activated protein kinase signaling pathway
regulation of B cell activation
regulation of adaptive immune response
regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
positive regulation of response to stimulus
positive regulation of T cell activation
regulation of cellular response to stress
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process
regulation of nitrogen compound metabolic process
activation of innate immune response
protein kinase cascade
regulation of T cell activation
defense response to bacterium
signal transduction
regulation of molecular function
positive regulation of molecular function
regulation of immunoglobulin mediated immune response
regulation of B cell mediated immunity
positive regulation of T cell proliferation
regulation of gene expression
positive regulation of innate immune response
positive regulation of protein transport
leukocyte migration

regulation of innate immune response
immune response-regulating signal transduction
positive regulation of defense response
regulation of T cell proliferation
regulation of lymphocyte mediated immunity
regulation of leukocyte mediated immunity
intracellular signaling cascade
cellular response to stimulus
hemopoietic or lymphoid organ development
adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
adaptive immune response
activation of immune response
immune system development
positive regulation of MHC class II biosynthetic process
taxis
chemotaxis
locomotion
positive regulation of transport
positive regulation of immune response
behavior
pattern recognition receptor signaling pathway
leukocyte differentiation
transmembrane receptor protein tyrosine kinase signaling pathway
enzyme linked receptor protein signaling pathway
protein amino acid phosphorylation

phosphorylation
phosphorus metabolic process
phosphate metabolic process
post-translational protein modification
protein modification process
biopolymer modification
reproductive developmental process
cellular protein metabolic process
cellular macromolecule metabolic process
peptidyl-amino acid modification
protein metabolic process

UA and JU:10

positive regulation of apoptosis
positive regulation of programmed cell death
positive regulation of cell death
regulation of apoptosis
regulation of biological quality
regulation of programmed cell death
regulation of cell death
homeostatic process
regulation of cell differentiation
cell cycle

JA, UA and JU:93

immune system process
immune response
regulation of cytokine production
positive regulation of cellular process
positive regulation of biological process

positive regulation of macromolecule metabolic process
positive regulation of cellular metabolic process
regulation of response to stimulus
positive regulation of metabolic process
positive regulation of macromolecule biosynthetic process
positive regulation of cellular biosynthetic process
positive regulation of biosynthetic process
regulation of immune response
regulation of immune system process
positive regulation of nitrogen compound metabolic process
regulation of multicellular organismal process
positive regulation of cell proliferation
defense response
positive regulation of lymphocyte activation
positive regulation of leukocyte activation
positive regulation of cell activation
positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process
regulation of interleukin-12 production
positive regulation of immune system process
inflammatory response
regulation of secretion
response to stimulus
positive regulation of cytokine production
positive regulation of transcription, DNA-dependent
positive regulation of RNA metabolic process
regulation of immunoglobulin production

regulation of cellular localization
regulation of phosphorylation
positive regulation of transcription
regulation of phosphate metabolic process
regulation of phosphorus metabolic process
positive regulation of gene expression
regulation of protein secretion
regulation of production of molecular mediator of immune response
regulation of cell proliferation
response to wounding
response to other organism
regulation of localization
regulation of protein amino acid phosphorylation
response to external stimulus
regulation of macromolecule metabolic process
cytokine-mediated signaling pathway
regulation of transport
regulation of cellular metabolic process
response to bacterium
regulation of protein transport
regulation of protein modification process
response to biotic stimulus
regulation of metabolic process
regulation of establishment of protein localization
regulation of response to stress
regulation of protein metabolic process

multi-organism process
response to stress
regulation of immune effector process
regulation of protein localization
regulation of primary metabolic process
positive regulation of cellular protein metabolic process
positive regulation of protein metabolic process
positive regulation of peptidyl-tyrosine phosphorylation
regulation of macromolecule biosynthetic process
regulation of cellular protein metabolic process
regulation of cellular process
response to molecule of bacterial origin
regulation of peptidyl-tyrosine phosphorylation
regulation of developmental process
positive regulation of protein amino acid phosphorylation
regulation of biological process
positive regulation of phosphorylation
positive regulation of transcription from RNA polymerase II promoter
positive regulation of phosphorus metabolic process
positive regulation of phosphate metabolic process
negative regulation of biological process
biological regulation
positive regulation of protein modification process
cell activation
response to organic substance
organ development

response to chemical stimulus
response to lipopolysaccharide
system development
negative regulation of cellular process
anatomical structure development
positive regulation of developmental process
leukocyte activation
negative regulation of response to stimulus
multicellular organismal development
developmental process

UA:77

regulation of interleukin-1 secretion
regulation of interleukin-1 beta secretion
positive regulation of interleukin-1 secretion
positive regulation of interleukin-1 production
positive regulation of interleukin-1 beta production
positive regulation of interleukin-1 beta secretion
immune response-activating signal transduction
positive regulation of cytokine secretion
response to peptidoglycan
innate immune response-activating signal transduction
regulation of interleukin-1 beta production
regulation of interleukin-1 production
regulation of cytokine secretion
positive regulation of tumor necrosis factor production
neutrophil chemotaxis
positive regulation of protein secretion

cell proliferation
hemopoiesis
cell chemotaxis
regulation of tumor necrosis factor production
leukocyte chemotaxis
I-kappaB kinase/NF-kappaB cascade
negative regulation of molecular function
leukocyte homeostasis
cytokine production
negative regulation of signal transduction
positive regulation of secretion
negative regulation of cell communication
I-kappaB phosphorylation
negative regulation of interleukin-12 production
nucleotide-binding oligomerization domain containing signaling pathway
regulation of vascular endothelial growth factor production
nucleotide-binding oligomerization domain containing 2 signaling pathway
fever
positive regulation vascular endothelial growth factor production
negative regulation of immune system process
T cell differentiation
locomotory behavior
cell migration
positive regulation of humoral immune response
response to lipoteichoic acid
positive regulation of humoral immune response mediated by circulating immunoglobulin

response to muramyl dipeptide
lipopolysaccharide-mediated signaling pathway
placenta development
response to peptide hormone stimulus
response to hormone stimulus
female gamete generation
response to endogenous stimulus
cell-substrate adhesion
response to insulin stimulus
organelle organization
cellular process
insulin receptor signaling pathway
cellular component organization
nerve growth factor receptor signaling pathway
cellular response to insulin stimulus
cellular response to stress
multicellular organism reproduction
reproductive process in a multicellular organism
cell-matrix adhesion
response to exogenous dsRNA
macromolecule metabolic process
B cell receptor signaling pathway
cellular response to hormone stimulus
gamete generation
reproductive structure development
negative regulation of developmental process

embryonic placenta development
T cell homeostasis
integrin-mediated signaling pathway
response to virus
sexual reproduction
response to dsRNA
peptidyl-serine phosphorylation
cell cycle process
negative regulation of cell proliferation

JU:30

regulation of cell cycle
negative regulation of apoptosis
negative regulation of programmed cell death
negative regulation of cell death
anti-apoptosis
cell development
cell differentiation
cell division
cellular developmental process
gland development
mammary gland alveolus development
myeloid cell differentiation
rhythmic process
developmental growth
positive regulation of myeloid cell differentiation
homeostasis of number of cells
G1/S transition of mitotic cell cycle

induction of programmed cell death
induction of apoptosis
tube morphogenesis
positive regulation of cell differentiation
erythrocyte differentiation
interphase of mitotic cell cycle
erythrocyte homeostasis
interphase
regulation of myeloid cell differentiation
growth
regulation of homeostatic process
regulation of epithelial cell proliferation
female sex differentiation

JA:44

regulation of chemokine biosynthetic process
regulation of interleukin-12 biosynthetic process
regulation of interleukin-6 biosynthetic process
positive regulation of B cell activation
regulation of isotype switching to IgG isotypes
positive regulation of isotype switching
positive regulation of DNA recombination
acute inflammatory response
regulation of isotype switching
regulation of transcription, DNA-dependent
regulation of RNA metabolic process
positive regulation of B cell proliferation
regulation of DNA recombination

regulation of transcription
positive regulation of DNA metabolic process
acute-phase response
regulation of B cell proliferation
apoptosis
programmed cell death
regulation of DNA metabolic process
neutrophil apoptosis
negative regulation of metabolic process
regulation of growth
negative regulation of transport
myeloid cell apoptosis
antigen processing and presentation
neutrophil homeostasis
regulation of MHC class II biosynthetic process
positive regulation of peptidyl-serine phosphorylation
epithelial cell proliferation involved in salivary gland morphogenesis
positive regulation of tyrosine phosphorylation of STAT protein
positive regulation of activated T cell proliferation
regulation of insulin receptor signaling pathway
cell surface receptor linked signal transduction
MAPKKK cascade
peptidyl-tyrosine modification
peptidyl-tyrosine phosphorylation
reproductive process
reproduction

protein amino acid autophosphorylation
chemical homeostasis
positive regulation of protein kinase activity
positive regulation of kinase activity
positive regulation of transferase activity

Table S3: Classification of GO functions of core module related to cerebral ischemia document verification

Category	Reference	Category	Reference
Metabolism	(Egi et al., 2011; Mies et al., 1991)	response to endogenous stimulus	(Mirante et al., 2013)
Biosynthesis	(Wu et al., 2012)	Growth	(Ma et al., 2011)
cell communication	(Rami et al., 2001)	Death	(Bodalia et al., 2013)
cell proliferation	(Zhang et al., 2001)	morphogenesis	(Anselmino et al., 2014)
response to external stimulus	(Speetzen et al., 2013)	reproduction	(Mitka, 2014)
protein modification	(Mirante et al., 2013)	cell cycle	(Adibhatla and Hatcher, 2010)
transport	(Andres et al., 2011)	behavior	(Noh et al., 2011)
cell differentiation	(Zhang et al., 2001; Zhang et al., 2011)	development	(Kozoriz et al., 2013)
response to stress	(Ahmad et al., 2012)		

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Table S4: The overlapping pathway of each group.

Group	KEGG Pathway
JA and JU:2	Intestinal immune network for IgA production Autoimmune thyroid disease
JA and UA:5	Acute myeloid leukemia Focal adhesion Natural killer cell mediated cytotoxicity Renal cell carcinoma ErbB signaling pathway
UA and JU:7	Small cell lung cancer Endometrial cancer Fc epsilon RI signaling pathway Non-small cell lung cancer Melanoma Bladder cancer Cell cycle
JA, UA and JU:21	Toll-like receptor signaling pathway Cytokine-cytokine receptor interaction Jak-STAT signaling pathway Allograft rejection NOD-like receptor signaling pathway RIG-I-like receptor signaling pathway Cytosolic DNA-sensing pathway T cell receptor signaling pathway Graft-versus-host disease Type I diabetes mellitus

	<p>Adipocytokine signaling pathway</p> <p>Apoptosis</p> <p>Asthma</p> <p>Hematopoietic cell lineage</p> <p>MAPK signaling pathway</p> <p>Pathways in cancer</p> <p>Chemokine signaling pathway</p> <p>Pancreatic cancer</p> <p>Glioma</p> <p>Prostate cancer</p> <p>Chronic myeloid leukemia</p>
UA:14	<p>B cell receptor signaling pathway</p> <p>Systemic lupus erythematosus</p> <p>Primary immunodeficiency</p> <p>VEGF signaling pathway</p> <p>Colorectal cancer</p> <p>Neurotrophin signaling pathway</p> <p>Insulin signaling pathway</p> <p>Fc gamma R-mediated phagocytosis</p> <p>Progesterone-mediated oocyte maturation</p> <p>Gap junction</p> <p>Regulation of actin cytoskeleton</p> <p>GnRH signaling pathway</p> <p>Adherens junction</p> <p>ECM-receptor interaction</p>
JU:2	<p>p53 signaling pathway</p>

Oocyte meiosis

Table S5: The top 10 Biological Process of GO and KEGG Pathway of core module.

Module	Nodes	Edges	GO	GO terms (Biological Process)	KEGG	KEGG Pathways
			p-value		p-value	
Vehicle-2	32	82	1.0E-13	immune system process (20)	4.2E-8	Toll-like receptor signaling pathway (10)
			5.0E-14	positive regulation of biological process (24)	3.4E-7	Cytokine-cytokine receptor interaction (12)
			1.0E-13	immune response (17)	1.5E-6	T cell receptor signaling pathway (9)
			7.3E-13	positive regulation of cellular process (22)	8.0E-6	Jak-STAT signaling pathway (9)
			5.1E-11	response to stimulus (25)	3.5E-5	Hematopoietic cell lineage (7)
			3.5E-9	positive regulation of nitrogen compound metabolic process (14)	8.6E-5	Allograft rejection (6)
			4.9E-9	positive regulation of metabolic process (15)	1.0E-4	NOD-like receptor signaling pathway (6)
			2.6E-8	positive regulation of macromolecule metabolic process (14)	1.3E-4	Adipocytokine signaling pathway (6)
			2.9E-8	positive regulation of cellular metabolic process (14)	9.8E-4	Cytosolic DNA-sensing pathway (5)
			2.7E-8	positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	1.5E-3	Type I diabetes mellitus (5)

(13)						
JA-1	18	73	1.2E-14	immune system process (16)	1.2E-12	Toll-like receptor signaling pathway (11)
			3.1E-12	immune response (13)	1.6E-7	Cytokine-cytokine receptor interaction (10)
			3.7E-12	regulation of cytokine production (10)	1.9E-6	Jak-STAT signaling pathway (8)
			6.6E-12	positive regulation of cellular process (16)	5.6E-6	Allograft rejection (6)
			3.3E-11	positive regulation of biological process (16)	6.3E-6	NOD-like receptor signaling pathway (6)
			3.5E-11	positive regulation of macromolecule metabolic process (13)	8.4E-6	RIG-I-like receptor signaling pathway (6)
			3.7E-11	positive regulation of cellular metabolic process (13)	1.1E-4	Cytosolic DNA-sensing pathway (5)
			4.8E-11	regulation of cytokine biosynthetic process (8)	9.7E-5	T cell receptor signaling pathway (6)
			5.7E-11	regulation of response to stimulus (11)	1.0E-4	Graft-versus-host disease (5)
			5.2E-11	positive regulation of metabolic process (13)	1.3E-4	Type I diabetes mellitus (5)
JA-2	11	22	4.0E-9	transmembrane receptor protein tyrosine kinase signaling pathway(8)	5.7E-6	Focal adhesion (7)
			2.4E-8	enzyme linked receptor protein signaling pathway (8)	2.5E-3	Glioma (4)
			2.3E-4	enzyme linked receptor protein signaling pathway (8)	4.6E-3	Prostate cancer (4)
					8.4E-3	Natural killer cell mediated cytotoxicity

			3.3E-4	protein amino acid phosphorylation (7)	(4)
			7.9E-4	phosphorylation (7)	9.3E-3 Pathways in cancer (5)
			7.9E-4	phosphorus metabolic process (7)	3.8E-2 Renal cell carcinoma (3)
			2.1E-3	phosphate metabolic process (7)	3.9E-2 Chronic myeloid leukemia (3)
			1.9E-3	post-translational protein modification (7)	4.4E-2 ErbB signaling pathway (3)
				cell surface receptor linked signal transduction (9)	
			1.8E-3	multicellular organismal development (9)	
			1.9E-3	anatomical structure morphogenesis(7)	
UA-2	27	80	3.1E-22	immune system process (23)	1.3E-12 NOD-like receptor signaling pathway (11)
			1.8E-17	immune response (18)	
			2.3E-11	positive regulation of cytokine production (9)	1.9E-12 Toll-like receptor signaling pathway (12)
			2.4E-10	regulation of cytokine production (10)	6.0E-10 Cytosolic DNA-sensing pathway (9)
			5.0E-10	defense response (13)	8.4E-9 T cell receptor signaling pathway (10)
			1.4E-9	response to stimulus (21)	1.6E-8 Cytokine-cytokine receptor interaction (12)
			1.2E-9	positive regulation of biological process (18)	
			7.8E-9	regulation of immune system process (11)	7.3E-8 RIG-I-like receptor signaling pathway (8)

			2.1E-8	positive regulation of multicellular organismal process (9)	3.6E-7	Apoptosis (8)
					3.4E-5	Type I diabetes mellitus (6)
			3.4E-8	positive regulation of cellular process (16)	4.1E-5	Adipocytokine signaling pathway (6)
					4.6E-5	MAPK signaling pathway (9)
UA-6	55	94	3.2E-5	transmembrane receptor protein tyrosine kinase signaling pathway (10)	6.1E-7	ErbB signaling pathway (10)
					2.6E-6	Endometrial cancer (8)
			2.6E-5	protein amino acid phosphorylation (15)	2.4E-6	Fc epsilon RI signaling pathway (9)
			1.7E-5	enzyme linked receptor protein signaling pathway (11)	1.9E-6	Focal adhesion (12)
					6.4E-6	Toll-like receptor signaling pathway (9)
			5.3E-5	phosphorylation (15)	2.0E-5	T cell receptor signaling pathway (9)
			6.5E-5	phosphate metabolic process (16)	2.2E-5	Non-small cell lung cancer (7)
			6.5E-5	phosphorus metabolic process (16)	2.0E-5	Natural killer cell mediated cytotoxicity (9)
			1.2E-4	post-translational protein modification (17)		
			4.7E-4	response to stress (17)	2.6E-5	Prostate cancer (8)
			5.4E-4	immune system process (14)	6.1E-5	RIG-I-like receptor signaling pathway (7)
			5.4E-4	cellular response to stimulus (12)		
UA-7	17	27	6.6E-3	regulation of phosphorylation (6)	1.5E-3	Jak-STAT signaling pathway (6)

			4.0E-3	regulation of phosphate metabolic process (6)	6.6E-3	Cell cycle (5)
			4.0E-3	regulation of phosphorus metabolic process (6)	9.1E-3	Glioma (4)
			8.7E-3	negative regulation of response to stimulus (4)	9.6E-3	Pancreatic cancer (4)
			2.5E-2	organ development (9)		
			2.2E-2	regulation of cellular metabolic process (11)		
			2.1E-2	regulation of cell proliferation (6)		
			2.4E-2	regulation of protein amino acid phosphorylation (4)		
			2.1E-2	positive regulation of cellular process (8)		
			1.9E-2	regulation of metabolic process (11)		
JU-3	16	36	8.9E-9	immune system process (12)	8.7E-8	Toll-like receptor signaling pathway (8)
			1.6E-7	positive regulation of biological process (13)	2.3E-5	Cytokine-cytokine receptor interaction (8)
			4.6E-7	positive regulation of macromolecule metabolic process (10)	1.8E-5	Jak-STAT signaling pathway (7)
			5.5E-7	positive regulation of cellular process (12)	5.3E-4	Hematopoietic cell lineage (5)
			5.4E-7	positive regulation of metabolic process (10)	1.6E-3	T cell receptor signaling pathway (5)
			6.5E-7	immune response (9)	2.3E-3	Intestinal immune network for IgA

			6.3E-6	positive regulation of cellular metabolic process (9)		production (4)
					2.4E-3	Allograft rejection (4)
			1.2E-5	response to stimulus (13)	3.2E-3	Adipocytokine signaling pathway (4)
			3.8E-5	regulation of response to stimulus (7)	3.5E-3	Autoimmune thyroid disease (4)
			1.4E-4	inflammatory response (6)	1.3E-3	Asthma (3)
JU-4	23	46	4.5E-9	regulation of apoptosis (13)	4.5E-12	Pathways in cancer (14)
			2.6E-9	regulation of programmed cell death (13)	3.1E-10	Bladder cancer (8)
			1.8E-9	regulation of cell death (13)	3.7E-10	Cell cycle (10)
			1.9E-9	positive regulation of biological process (17)	4.5E-7	Pancreatic cancer (7)
			9.6E-8	positive regulation of cellular process (15)	9.8E-7	Small cell lung cancer (7)
			9.6E-8	regulation of cell cycle (9)	3.0E-6	Non-small cell lung cancer (6)
			6.6E-7	regulation of multicellular organismal process (12)	6.0E-6	Glioma (6)
					7.7E-6	p53 signaling pathway (6)
			9.9E-7	negative regulation of biological process (14)	7.9E-6	Melanoma (6)
			4.9E-6	regulation of cell proliferation (10)	9.9E-6	Chronic myeloid leukemia (6)
			5.7E-6	positive regulation of apoptosis (8)		

Table S6: The degree, weighted degree and PageRank of each PMD.

Module	PMD	Degree	Average/ Degree	Weighted degree	Average/ Weighted degree	PageRank	Average/ PageRank
MJA-1	$Ifn8_{JA-1}^D$	13	8.11	12.53	7.43	0.087	0.056
	$Il6_{JA-1}^D$	17		16.01		0.111	
	$Tlr4_{JA-1}^D$	12		11.05		0.079	
MJA-2	Egf_{JA-2}^D	8	4	7.16	3.60	0.170	0.091
	$Grb2_{JA-2}^D$	7		6.32		0.152	
MUA-2	Tnf_{UA-2}^D	23	5.93	21.83	5.29	0.133	0.037
	$Cd4_{UA-2}^D$	10		9.16		0.061	
MUA-6	$Ifnb1_{UA-6}^D$	8	3.42	7.58	3.09	0.040	0.018

	<i>Grb2</i> ^D _{UA-6}	8		7.65		0.039	
	<i>Akt1</i> ^D _{UA-6}	8		7.57		0.041	
MUA-7	<i>Il2</i> ^D _{UA-7}	5	3.18	4.81	2.92	0.088	0.059
	<i>Ccnd1</i> ^D _{UA-7}	5		4.71		0.086	
MJU-3	<i>Il1b</i> ^D _{JU-3}	11	4.5	8.85	3.91	0.139	0.063
	<i>Cd4</i> ^D _{JU-3}	7		6.55		0.086	
	<i>Stat1</i> ^D _{JU-3}	4		3.64		0.072	
MJU-4	<i>Vegfa</i> ^D _{JU-4}	9	4	8.15	3.60	0.082	0.043
	<i>Igf1</i> ^D _{JU-4}	5		4.52		0.053	

Note: PMD is pharmacology module drivers, ^D on the upper right corner of gene' name means Driver, and on the lower right corner is its source.

Table S7: PMD in each group related to cerebral ischemia document verification:

Group	PMD	References
MJA-1	Il6 ^M	(Tureyen et al., 2007)
	Ifng	(Andersen et al., 2012)
	Tlr4	(Hua et al., 2009)
MJA-2	Egf	(Teramoto et al., 2003)
	Grb2	(Jin et al., 2001)
MUA-2	Tnf ^M	(Adibhatla and Hatcher, 2005)
	Cd4	(Schroeter et al., 2002)
MUA-6	Akt1	(Hui et al., 2005)
	Grb2	(Jin et al., 2001)
	Ifnb1	(Hori et al., 2015)
MUA-7	Ccnd1	(Zhao et al., 2013)
	Il2	(Zhai et al., 1997)
MJU-3	Il1b ^M	(Stroemer and Rothwell, 1997)
	Cd4	(Schroeter et al., 2002)
	Stat1	(Takagi et al., 2002)

MJU-4	Vegfa	(Nag et al., 2002)
	Igfl	(Guan et al., 1993)

Note: ^M represent the biomarker of cerebral ischemia.

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