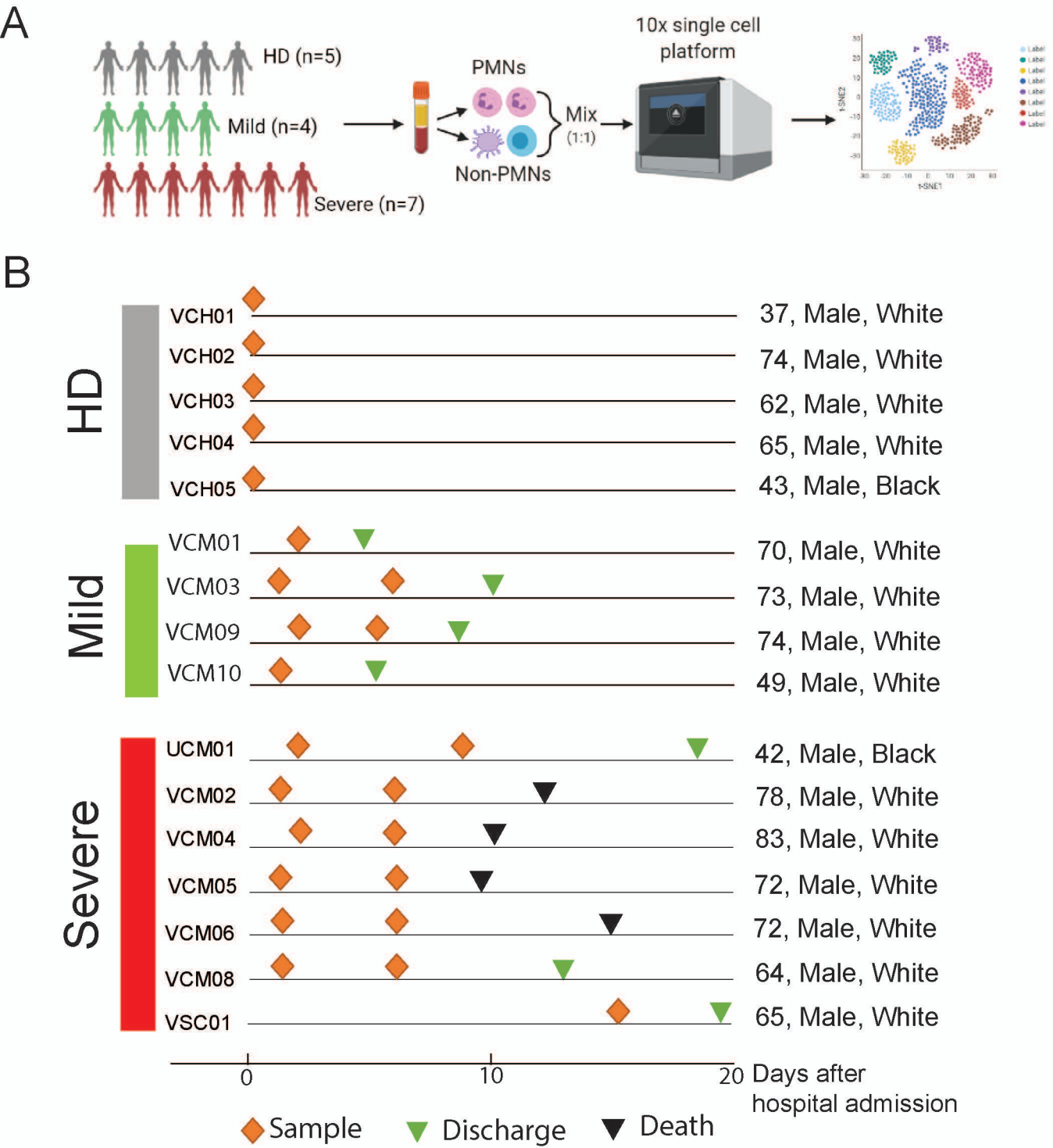
A
HD (n=5)
Mild (n=4)
Severe (n=7)
PMNs
Non-PMNs
Mix
(1:1)
10x single cell
platform
B
HD
VCH01
VCH02
VCH03
VCH04
VCH05
37, Male, White
74, Male, White
62, Male, White
65, Male, White
43, Male, Black
Mild
VCM01
VCM03
VCM09
VCM10
70, Male, White
73, Male, White
74, Male, White
49, Male, White
Severe
UCM01
VCM02
VCM04
VCM05
VCM06
VCM08
VSC01
42, Male, Black
78, Male, White
83, Male, White
72, Male, White
72, Male, White
64, Male, White
65, Male, White
0
10
20
Days after
hospital admission
Sample
Discharge
Death

Fig. S1 (A), schematic showing the overall study design. The scRNA-seq was applied to whole blood cells across three conditions and the output data were used for expression analyses. (B), Timeline of the course of disease for 11 patients infected with SARS-CoV-2 enrolled in our study.

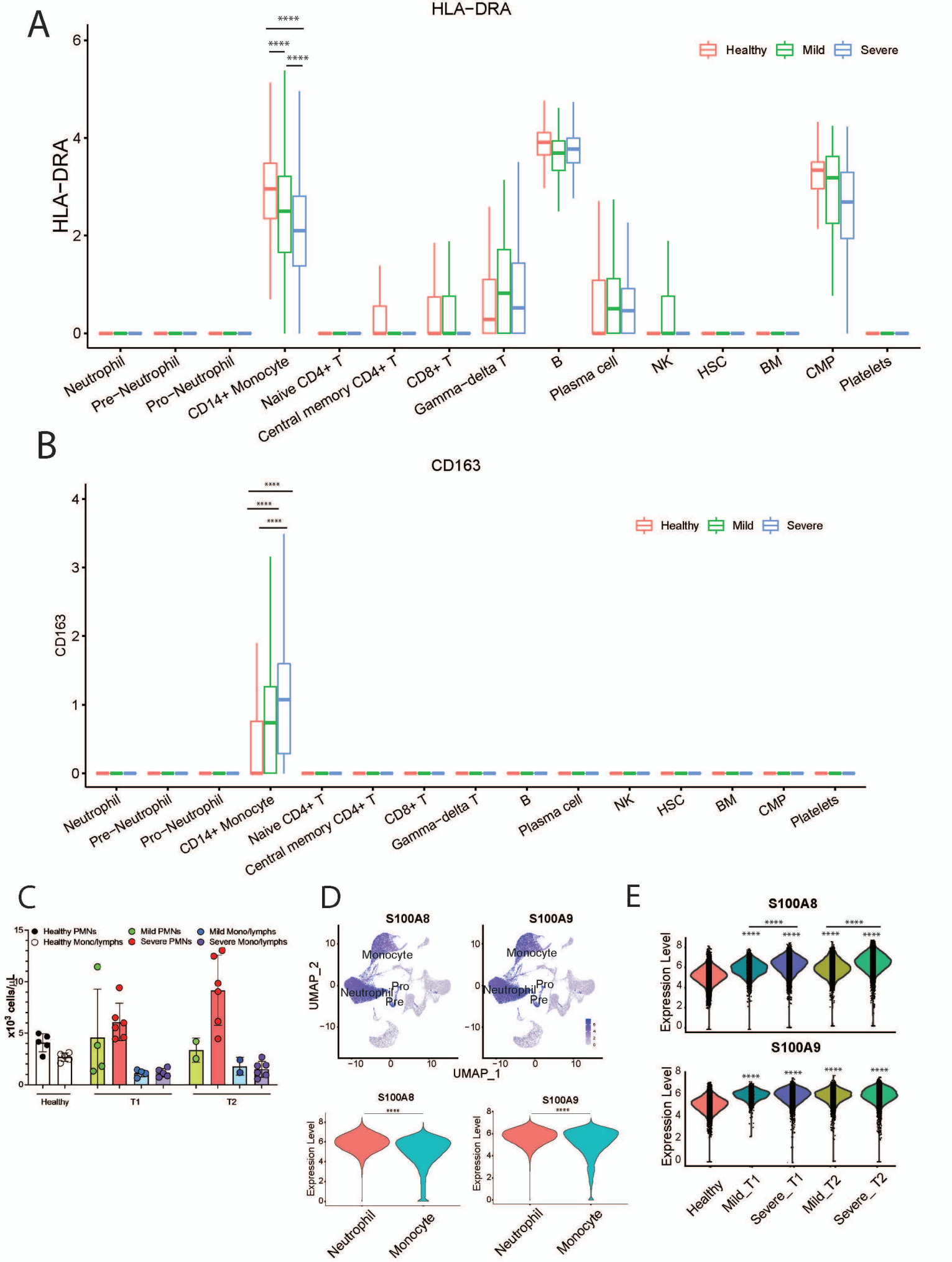
A
HLA-DRA
HLA-DRA
Healthy
Mild
Severe
****
****
****
Neutrophil
Pre-Neutrophil
Pro-Neutrophil
CD14+ Monocyte
Naive CD4+ T
Central memory CD4+ T
CD8+ T
Gamma-delta T
B
Plasma cell
NK
HSC
BM
CMP
Platelets
B
CD163
CD163
Healthy
Mild
Severe
C
Healthy PMNs
Healthy Mono/lymphs
Mild PMNs
Severe PMNs
Mild Mono/lymphs
Severe Mono/lymphs
x10^3 cells/μL
Healthy
T1
T2
D
S100A8
S100A9
Monocyte
Neutrophil
Pro
Pre
UMAP_1
UMAP_2
S100A8
S100A9
Expression Level
Neutrophil
Monocyte
E
S100A8
S100A9
Expression Level
Healthy
Mild_T1
Severe_T1
Mild_T2
Severe_T2

Fig. S2. (A) Violin plots showing expression of HLA-DRA by different cell clusters. (B) Violin plots showing the expression of CD163 by different cell clusters. (C) Absolute cell number counts in the blood from healthy, mild, and severe patients (D) UMAP plot showing the expression of S100A8 and S100A9 by neutrophils and monocytes. (E) Violin plots showing expression of S100A8 (up) and S100A9 (below) by neutrophils in different groups of patients. Asterisks on figures indicate statistical significance as follows: ****, $P < 0.0001$.

Fig. S3

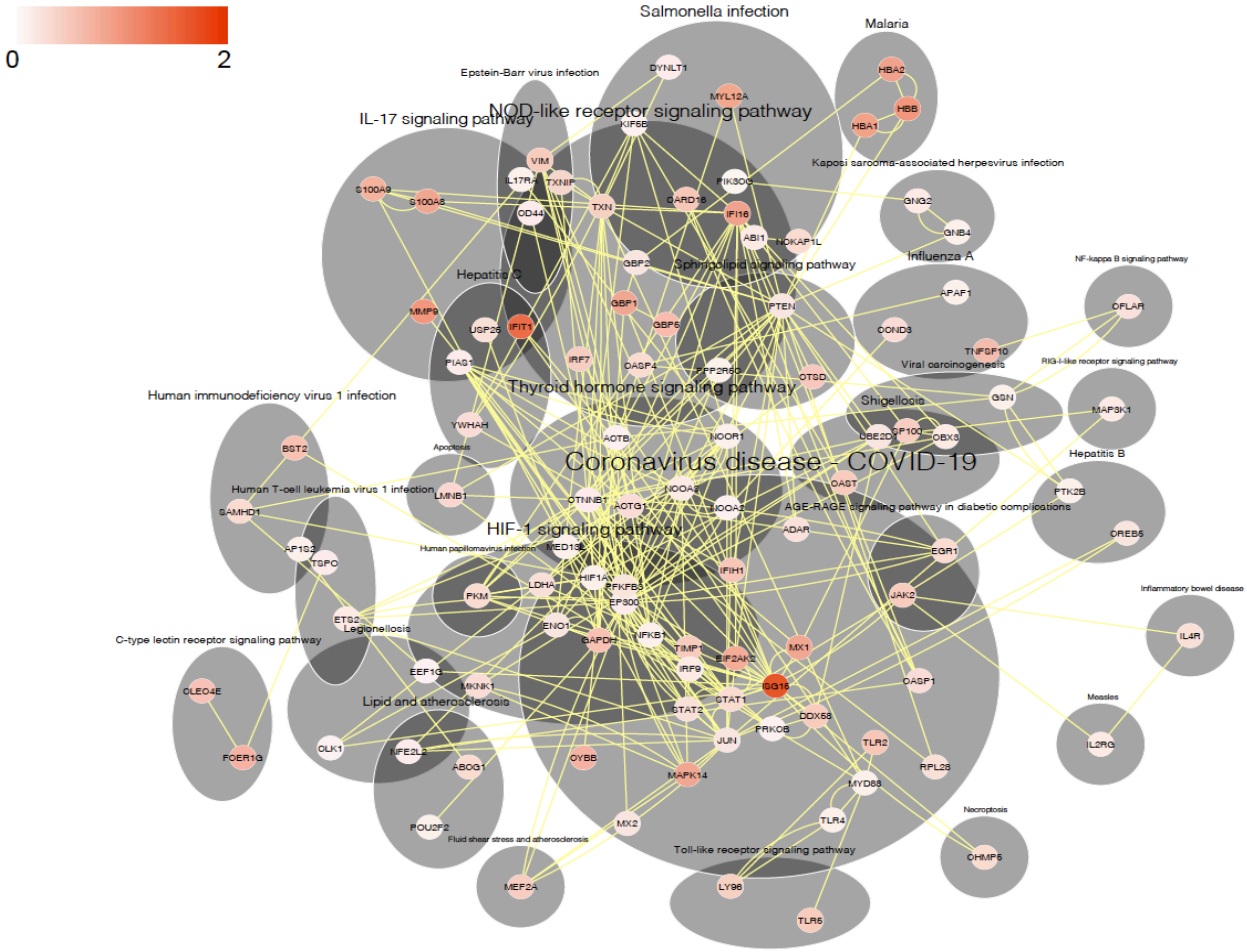
0
2
Salmonella infection
Malaria
Epstein-Barr virus infection
NOD-like receptor signaling pathway
IL-17 signaling pathway
Kaposi sarcoma-associated herpesvirus infection
Hepatitis C
Sphingolipid signaling pathway
Influenza A
NF-kappa B signaling pathway
Thyroid hormone signaling pathway
Viral carcinogenesis
RIG-I-like receptor signaling pathway
Human immunodeficiency virus 1 infection
Shigellosis
Coronavirus disease - COVID-19
Apoptosis
Hepatitis B
Human T-cell leukemia virus 1 infection
AGE-RAGE signaling pathway in diabetic complications
HIF-1 signaling pathway
Human papillomavirus infection
Inflammatory bowel disease
C-type lectin receptor signaling pathway
Legionellosis
Measles
Lipid and atherosclerosis
Fluid shear stress and atherosclerosis
Necroptosis
Toll-like receptor signaling pathway

Fig. S3 Protein-protein interaction networks of significantly up-regulated pathways (adjusted P-value <0.05) in neutrophils from mild COVID19 patients compared with that from healthy controls. Color bar indicates fold change of genes between groups.


wound healing
viral translation
viral RNA genome replication
viral process
viral life cycle
viral genome replication
viral gene expression
viral entry into host cell
vesicle organization
vesicle docking
vasoconstriction
vacuole organization
vacuolar localization
vacuolar acidification
unfolded protein binding
UMP metabolic process
ubiquitin protein ligase binding
ubiquitin protein ligase activity
ubiquitin−specific protease binding
ubiquitin−protein transferase regulator activity
ubiquitin−protein transferase activity
ubiquitin−like protein transferase activity
ubiquitin−like protein peptidase activity
ubiquitin−like protein ligase binding
ubiquitin−like protein ligase activity
ubiquitin−like protein binding
type I interferon signaling pathway
type I interferon production
type B pancreatic cell proliferation
type 2 immune response
tumor necrosis factor superfamily cytokine production
tumor necrosis factor production
tumor necrosis factor−mediated signaling pathway
tubulin binding
trivalent inorganic anion homeostasis
transmembrane transporter binding
translational initiation
translational elongation
translation regulator activity, nucleic acid binding
translation initiation factor activity
translation factor activity, RNA binding
transition metal ion homeostasis
transcription coregulator activity
transcription coactivator activity
TRAIL−activated apoptotic signaling pathway
toll−like receptor signaling pathway
toll−like receptor 4 signaling pathway
toll−like receptor 2 signaling pathway
tolerance induction
tissue migration
threonine−type peptidase activity
threonine−type endopeptidase activity
temperature homeostasis
telomere maintenance
T cell receptor signaling pathway
T cell proliferation
T cell migration
T cell mediated immunity
T cell homeostasis
T cell differentiation involved in immune response
T cell differentiation
T cell chemotaxis
T cell activation involved in immune response
T−helper cell differentiation
T−helper 2 cell differentiation
T−helper 1 type immune response
superoxide metabolic process
superoxide anion generation
substrate adhesion−dependent cell spreading
substantia nigra development
structural constituent of ribosome
structural constituent of cytoskeleton
stress−activated protein kinase signaling cascade
stress−activated MAPK cascade
stimulatory C−type lectin receptor signaling pathway
spliceosomal snRNP assembly
spliceosomal complex assembly
spindle organization
snRNA binding
smooth muscle cell proliferation
smooth muscle cell migration
small GTPase binding
sister chromatid segregation
sister chromatid cohesion
single stranded viral RNA replication via double stranded DNA intermediate
single−stranded DNA binding
signal transduction by p53 class mediator
SH3 domain binding
sequence−specific mRNA binding
secretory granule organization
rRNA processing
rRNA metabolic process
rRNA binding
RNA transport
RNA stabilization
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile
RNA splicing, via transesterification reactions
RNA splicing
RNA polymerase II−specific DNA−binding transcription factor binding
RNA polyadenylation
RNA localization
RNA export from nucleus
RNA catabolic process
RIG−I signaling pathway
ribosome biogenesis
ribosome assembly
ribosomal small subunit biogenesis
ribosomal small subunit binding
ribosomal small subunit assembly
ribosomal large subunit biogenesis
ribosomal large subunit binding
ribosomal large subunit assembly
ribose phosphate metabolic process
ribonucleotide metabolic process
ribonucleoside triphosphate metabolic process
ribonucleoside triphosphate biosynthetic process
ribonucleoprotein complex subunit organization
ribonucleoprotein complex biogenesis
ribonucleoprotein complex binding
ribonucleoprotein complex assembly
retrograde protein transport, ER to cytosol
response to vitamin E
response to vitamin D
response to vitamin
response to virus
response to UV
response to type I interferon
response to tumor necrosis factor
response to tumor cell
response to topologically incorrect protein
response to temperature stimulus
response to steroid hormone
response to starvation
response to reactive oxygen species
response to protozoan
response to progesterone
response to peptide hormone
response to peptide
response to oxygen levels
response to oxidative stress
response to nutrient levels
response to nutrient
response to muramyl dipeptide
response to monosaccharide
response to molecule of bacterial origin
response to metal ion
response to mechanical stimulus
response to lipopolysaccharide
response to lectin
response to interleukin−4
response to interleukin−1
response to interferon−gamma
response to interferon−beta
response to interferon−alpha
response to immobilization stress
response to hypoxia
response to hydrogen peroxide
response to fungus
response to fatty acid
response to extracellular stimulus
response to endoplasmic reticulum stress
response to decreased oxygen levels
response to corticosterone
response to carbohydrate
response to cadmium ion
response to angiotensin
response to amyloid−beta
response to amphetamine
respiratory electron transport chain
respiratory burst involved in defense response
respiratory burst
replication fork processing
renal sodium ion transport


renal absorption
regulatory T cell differentiation
regulation of viral process
regulation of viral life cycle
regulation of viral genome replication
regulation of viral entry into host cell
regulation of vasoconstriction
regulation of vacuole organization
regulation of ubiquitin protein ligase activity
regulation of ubiquitin−protein transferase activity
regulation of ubiquitin−dependent protein catabolic process
regulation of type I interferon production
regulation of type I interferon−mediated signaling pathway
regulation of type B pancreatic cell proliferation
regulation of type 2 immune response
regulation of tumor necrosis factor superfamily cytokine production
regulation of tumor necrosis factor production
regulation of tumor necrosis factor−mediated signaling pathway
regulation of tube size
regulation of tube diameter
regulation of translational initiation
regulation of translation in response to stress
regulation of translation
regulation of transcription from RNA polymerase II promoter in response to stress
regulation of toll−like receptor signaling pathway
regulation of T cell receptor signaling pathway
regulation of T cell proliferation
regulation of T cell migration
regulation of T cell mediated cytotoxicity
regulation of T cell differentiation
regulation of T cell chemotaxis
regulation of T cell activation
regulation of T−helper 2 cell differentiation
regulation of syncytium formation by plasma membrane fusion
regulation of supramolecular fiber organization
regulation of superoxide metabolic process
regulation of superoxide anion generation
regulation of substrate adhesion−dependent cell spreading
regulation of stress fiber assembly
regulation of stress−activated protein kinase signaling cascade
regulation of smooth muscle contraction
regulation of smooth muscle cell proliferation
regulation of smooth muscle cell migration
regulation of small GTPase mediated signal transduction
regulation of sister chromatid segregation
regulation of single stranded viral RNA replication via double stranded DNA intermediate
regulation of signal transduction by p53 class mediator
regulation of RNA stability
regulation of RNA splicing
regulation of Rho protein signal transduction
regulation of response to cytokine stimulus
regulation of response to biotic stimulus
regulation of respiratory burst
regulation of release of sequestered calcium ion into cytosol
regulation of release of cytochrome c from mitochondria
regulation of regulatory T cell differentiation
regulation of regulated secretory pathway
regulation of reactive oxygen species metabolic process
regulation of Rac protein signal transduction
regulation of proton transport
regulation of proteolysis involved in cellular protein catabolic process
regulation of protein ubiquitination
regulation of protein transport
regulation of protein stability
regulation of protein serine/threonine kinase activity
regulation of protein polymerization
regulation of protein modification by small protein conjugation or removal
regulation of protein import into nucleus
regulation of protein import
regulation of protein dephosphorylation
regulation of protein catabolic process
regulation of protein binding
regulation of protein acetylation
regulation of protein−containing complex assembly
regulation of proteasomal ubiquitin−dependent protein catabolic process
regulation of proteasomal protein catabolic process
regulation of programmed necrotic cell death
regulation of production of molecular mediator of immune response
regulation of podosome assembly
regulation of platelet−derived growth factor receptor signaling pathway
regulation of plasma membrane organization
regulation of phosphoprotein phosphatase activity
regulation of phagocytosis
regulation of peptidase activity
regulation of pattern recognition receptor signaling pathway
regulation of oxidative stress−induced cell death
regulation of osteoclast differentiation
regulation of osteoblast differentiation
regulation of organelle assembly
regulation of nucleotide−binding oligomerization domain containing signaling pathway
regulation of nucleocytoplasmic transport
regulation of nuclease activity
regulation of nuclear division
regulation of nuclear−transcribed mRNA catabolic process, deadenylation−dependent decay
regulation of NLRP3 inflammasome complex assembly
regulation of nitric oxide metabolic process
regulation of nitric oxide biosynthetic process
regulation of nitric−oxide synthase biosynthetic process
regulation of NIK/NF−kappaB signaling
regulation of neutrophil migration
regulation of neutrophil chemotaxis
regulation of neutrophil activation
regulation of neuron projection development
regulation of neuron death
regulation of necrotic cell death
regulation of necroptotic process
regulation of natural killer cell proliferation
regulation of natural killer cell mediated immunity
regulation of natural killer cell mediated cytotoxicity
regulation of natural killer cell activation
regulation of myoblast fusion
regulation of myoblast differentiation
regulation of myeloid leukocyte mediated immunity
regulation of myeloid leukocyte differentiation
regulation of myeloid cell differentiation
regulation of muscle system process
regulation of mRNA stability
regulation of mRNA splicing, via spliceosome
regulation of mRNA processing
regulation of mRNA polyadenylation
regulation of mRNA metabolic process
regulation of mRNA catabolic process
regulation of mRNA 3'−end processing
regulation of mononuclear cell proliferation
regulation of mononuclear cell migration
regulation of monocyte chemotactic protein−1 production
regulation of mitotic sister chromatid separation
regulation of mitotic nuclear division
regulation of mitotic metaphase/anaphase transition
regulation of mitotic cell cycle phase transition
regulation of mitotic cell cycle
regulation of metaphase/anaphase transition of cell cycle
regulation of metallopeptidase activity
regulation of metalloendopeptidase activity
regulation of metal ion transport
regulation of MAP kinase activity
regulation of macroautophagy
regulation of lymphocyte proliferation
regulation of lymphocyte migration
regulation of lymphocyte mediated immunity
regulation of lymphocyte differentiation
regulation of lymphocyte chemotaxis
regulation of lymphocyte apoptotic process
regulation of lipid metabolic process
regulation of leukocyte proliferation
regulation of leukocyte migration
regulation of leukocyte mediated immunity
regulation of leukocyte mediated cytotoxicity
regulation of leukocyte differentiation
regulation of leukocyte degranulation
regulation of leukocyte chemotaxis
regulation of leukocyte cell−cell adhesion
regulation of lamellipodium organization
regulation of lamellipodium assembly
regulation of ketone biosynthetic process
regulation of keratinocyte migration
regulation of intrinsic apoptotic signaling pathway in response to DNA damage
regulation of intrinsic apoptotic signaling pathway by p53 class mediator
regulation of intrinsic apoptotic signaling pathway
regulation of intracellular transport
regulation of intracellular protein transport
regulation of interleukin−8 production
regulation of interleukin−6 production
regulation of interleukin−4 production
regulation of interleukin−12 production
regulation of interleukin−10 production
regulation of interleukin−1 production
regulation of interleukin−1 beta production
regulation of interferon−gamma production
regulation of interferon−beta production
regulation of interferon−alpha production
regulation of innate immune response
regulation of inflammatory response
regulation of immunoglobulin mediated immune response
regulation of immune effector process
regulation of I−kappaB kinase/NF−kappaB signaling
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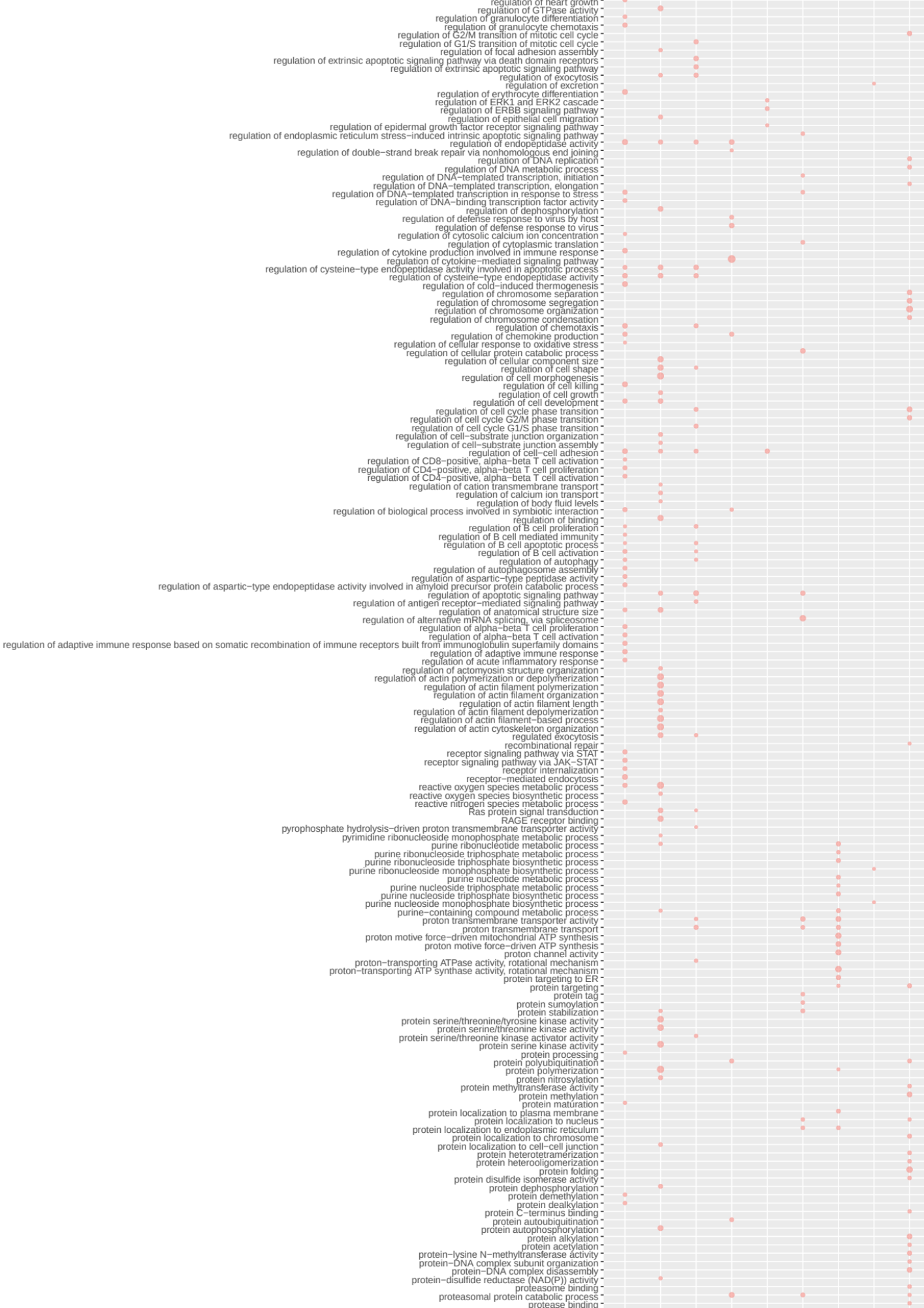
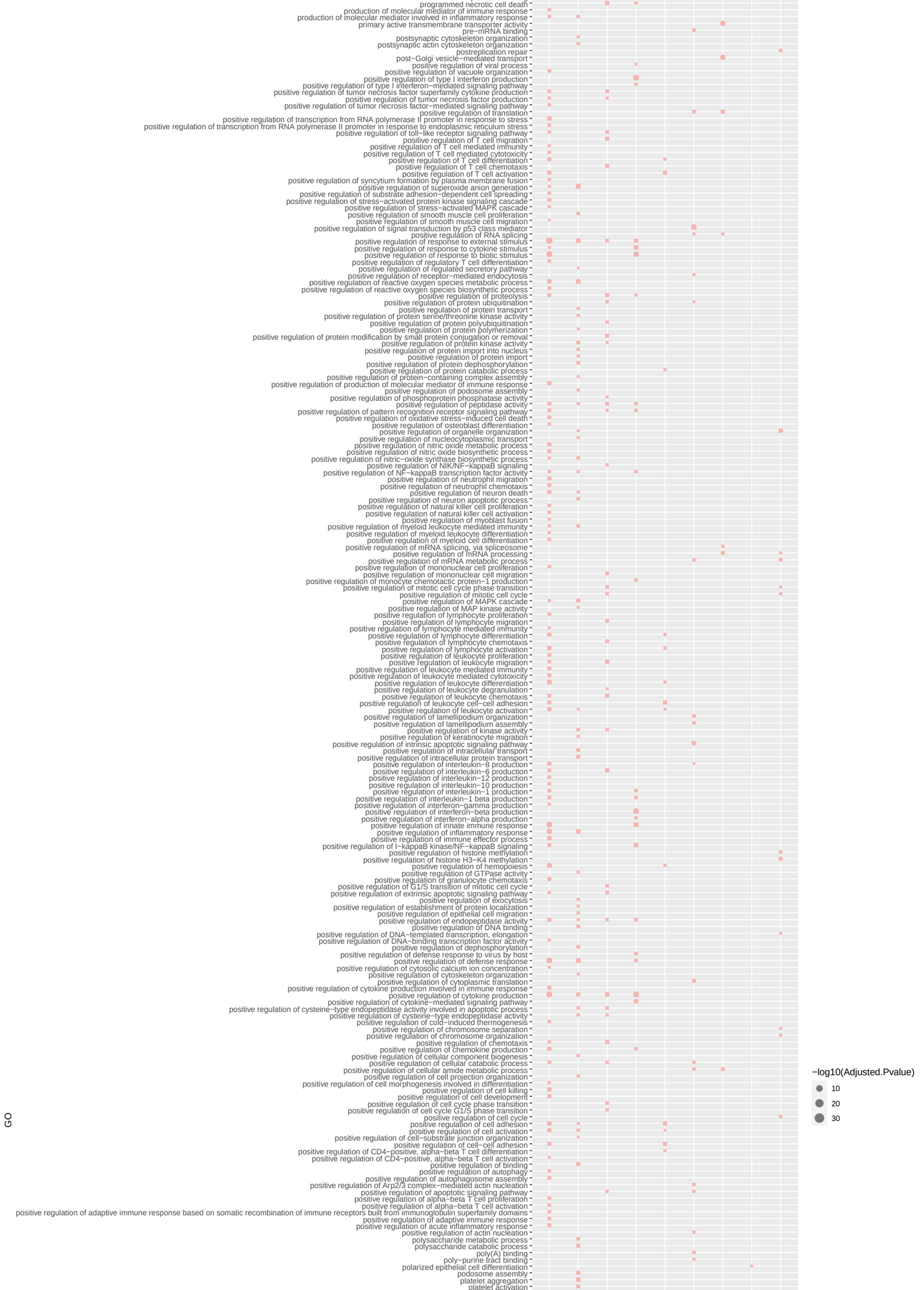
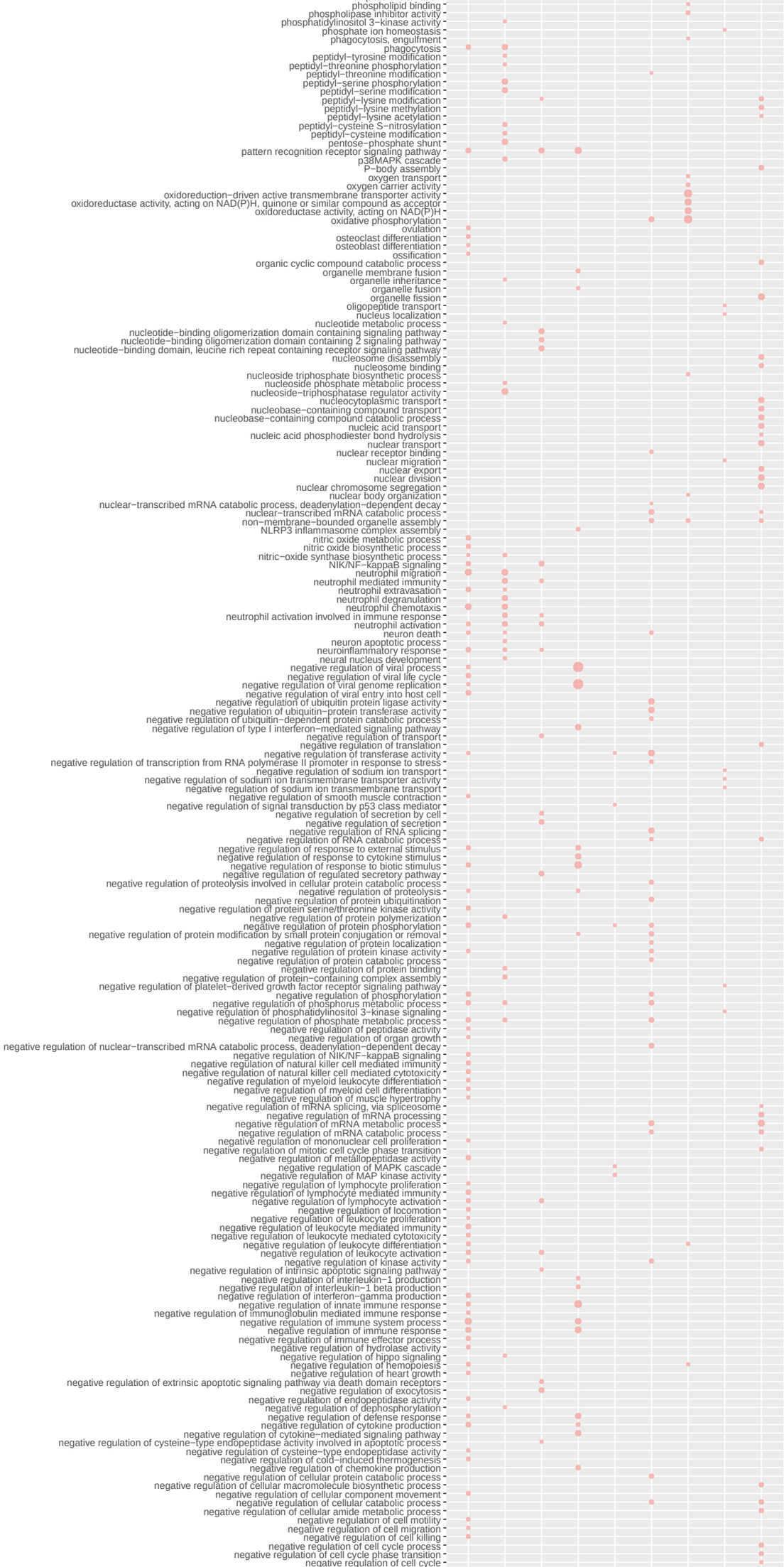
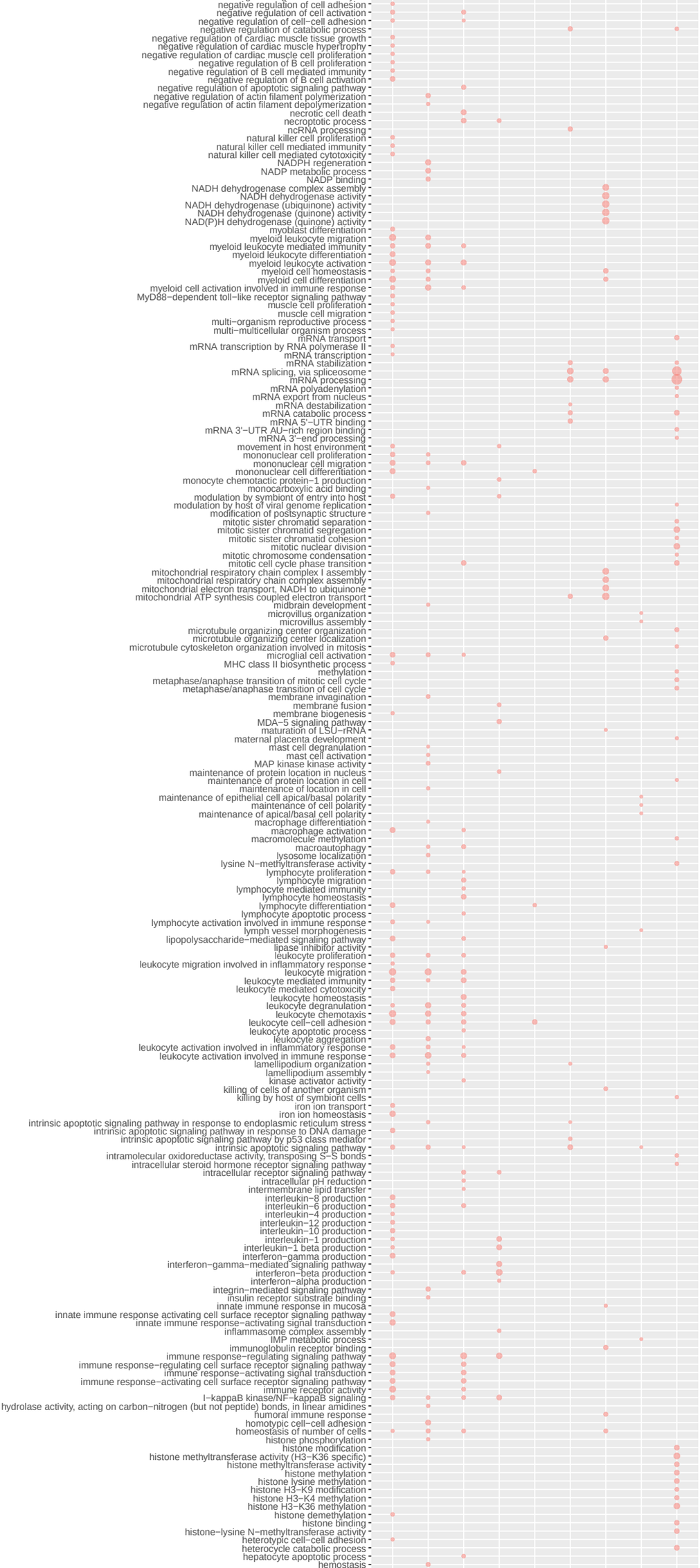
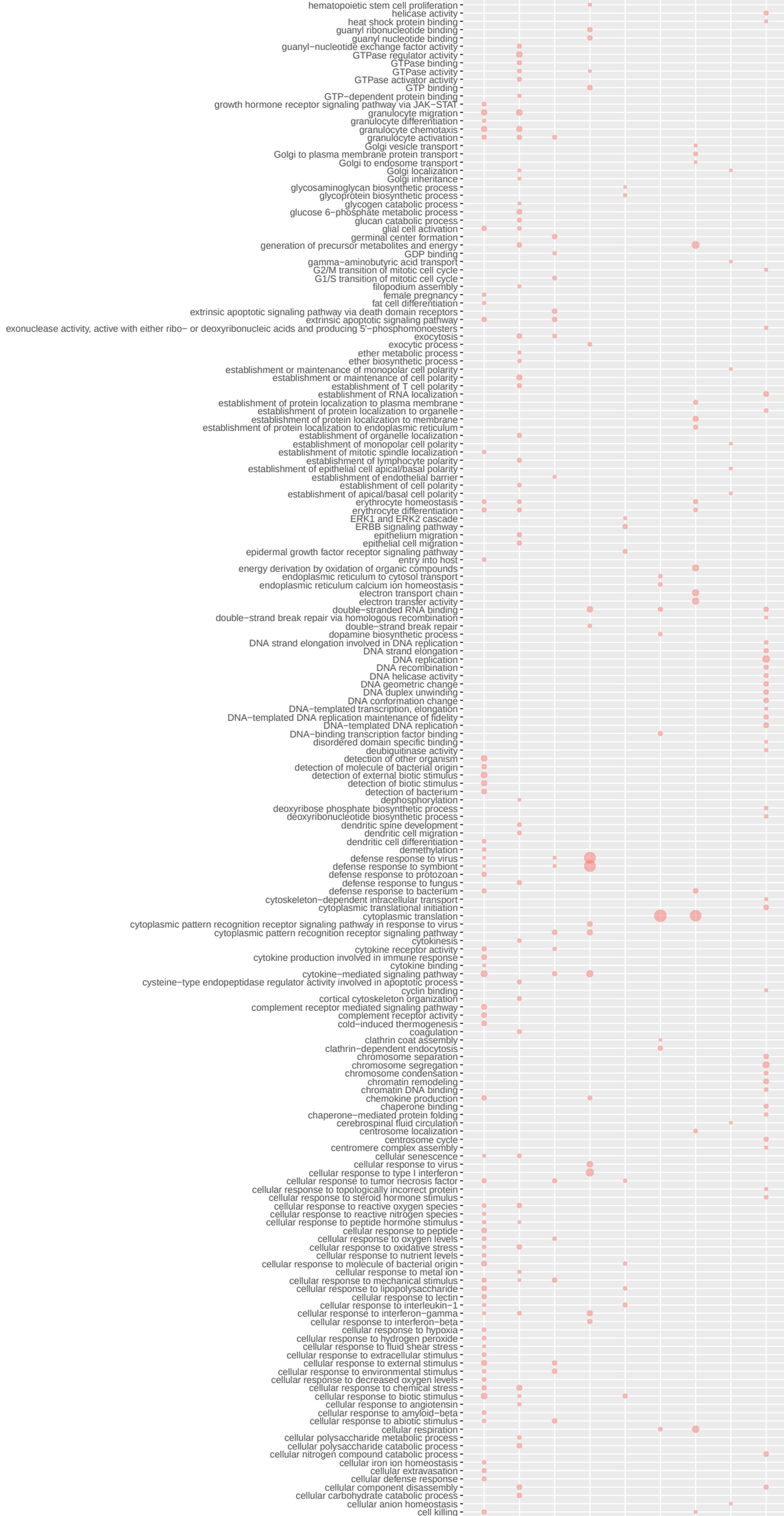
regulation of histone modification
regulation of histone methylation
regulation of histone H3−K4 methylation
regulation of hemopoiesis
regulation of hematopoietic stem cell differentiation
regulation of hematopoietic progenitor cell differentiation


regulation of heart growth
regulation of GTPase activity
regulation of granulocyte differentiation
regulation of granulocyte chemotaxis
regulation of G2/M transition of mitotic cell cycle
regulation of G1/S transition of mitotic cell cycle
regulation of focal adhesion assembly
regulation of extrinsic apoptotic signaling pathway via death domain receptors
regulation of extrinsic apoptotic signaling pathway
regulation of exocytosis
regulation of excretion
regulation of erythrocyte differentiation
regulation of ERK1 and ERK2 cascade
regulation of ERBB signaling pathway
regulation of epithelial cell migration
regulation of epidermal growth factor receptor signaling pathway
regulation of endoplasmic reticulum stress−induced intrinsic apoptotic signaling pathway
regulation of endopeptidase activity
regulation of double−strand break repair via nonhomologous end joining
regulation of DNA replication
regulation of DNA metabolic process
regulation of DNA−templated transcription, initiation
regulation of DNA−templated transcription, elongation
regulation of DNA−templated transcription in response to stress
regulation of DNA−binding transcription factor activity
regulation of dephosphorylation
regulation of defense response to virus by host
regulation of defense response to virus
regulation of cytosolic calcium ion concentration
regulation of cytoplasmic translation
regulation of cytokine production involved in immune response
regulation of cytokine−mediated signaling pathway
regulation of cysteine−type endopeptidase activity involved in apoptotic process
regulation of cysteine−type endopeptidase activity
regulation of cold−induced thermogenesis
regulation of chromosome separation
regulation of chromosome segregation
regulation of chromosome organization
regulation of chromosome condensation
regulation of chemotaxis
regulation of chemokine production
regulation of cellular response to oxidative stress
regulation of cellular protein catabolic process
regulation of cellular component size
regulation of cell shape
regulation of cell morphogenesis
regulation of cell killing
regulation of cell growth
regulation of cell development
regulation of cell cycle phase transition
regulation of cell cycle G2/M phase transition
regulation of cell cycle G1/S phase transition
regulation of cell−substrate junction organization
regulation of cell−substrate junction assembly
regulation of cell−cell adhesion
regulation of CD8−positive, alpha−beta T cell activation
regulation of CD4−positive, alpha−beta T cell proliferation
regulation of CD4−positive, alpha−beta T cell activation
regulation of cation transmembrane transport
regulation of calcium ion transport
regulation of body fluid levels
regulation of biological process involved in symbiotic interaction
regulation of binding
regulation of B cell proliferation
regulation of B cell mediated immunity
regulation of B cell apoptotic process
regulation of B cell activation
regulation of autophagy
regulation of autophagosome assembly
regulation of aspartic−type peptidase activity
regulation of aspartic−type endopeptidase activity involved in amyloid precursor protein catabolic process
regulation of apoptotic signaling pathway
regulation of antigen receptor−mediated signaling pathway
regulation of anatomical structure size
regulation of alternative mRNA splicing, via spliceosome
regulation of alpha−beta T cell proliferation
regulation of alpha−beta T cell activation
regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
regulation of adaptive immune response
regulation of acute inflammatory response
regulation of actomyosin structure organization
regulation of actin polymerization or depolymerization
regulation of actin filament polymerization
regulation of actin filament organization
regulation of actin filament length
regulation of actin filament depolymerization
regulation of actin filament−based process
regulation of actin cytoskeleton organization
regulated exocytosis
recombinational repair
receptor signaling pathway via STAT
receptor signaling pathway via JAK−STAT
receptor internalization
receptor−mediated endocytosis
reactive oxygen species metabolic process
reactive oxygen species biosynthetic process
reactive nitrogen species metabolic process
Ras protein signal transduction
RAGE receptor binding
pyrophosphate hydrolysis−driven proton transmembrane transporter activity
pyrimidine ribonucleoside monophosphate metabolic process
purine ribonucleotide metabolic process
purine ribonucleoside triphosphate metabolic process
purine ribonucleoside triphosphate biosynthetic process
purine ribonucleoside monophosphate biosynthetic process
purine nucleotide metabolic process
purine nucleoside triphosphate metabolic process
purine nucleoside triphosphate biosynthetic process
purine nucleoside monophosphate biosynthetic process
purine−containing compound metabolic process
proton transmembrane transporter activity
proton transmembrane transport
proton motive force−driven mitochondrial ATP synthesis
proton motive force−driven ATP synthesis
proton channel activity
proton−transporting ATPase activity, rotational mechanism
proton−transporting ATP synthase activity, rotational mechanism
protein targeting to ER
protein targeting
protein tag
protein sumoylation
protein stabilization
protein serine/threonine/tyrosine kinase activity
protein serine/threonine kinase activity
protein serine/threonine kinase activator activity
protein serine kinase activity
protein processing
protein polyubiquitination
protein polymerization
protein nitrosylation
protein methyltransferase activity
protein methylation
protein maturation
protein localization to plasma membrane
protein localization to nucleus
protein localization to endoplasmic reticulum
protein localization to chromosome
protein localization to cell−cell junction
protein heterotetramerization
protein heterooligomerization
protein folding
protein disulfide isomerase activity
protein dephosphorylation
protein demethylation
protein dealkylation
protein C−terminus binding
protein autoubiquitination
protein autophosphorylation
protein alkylation
protein acetylation
protein−lysine N−methyltransferase activity
protein−DNA complex subunit organization
protein−DNA complex disassembly
protein−disulfide reductase (NAD(P)) activity
proteasome binding
proteasomal protein catabolic process
protease binding


GO
programmed necrotic cell death
production of molecular mediator of immune response
production of molecular mediator involved in inflammatory response
primary active transmembrane transporter activity
pre−mRNA binding
postsynaptic cytoskeleton organization
postsynaptic actin cytoskeleton organization
postreplication repair
post−Golgi vesicle−mediated transport
positive regulation of viral process
positive regulation of vacuole organization
positive regulation of type I interferon production
positive regulation of type I interferon−mediated signaling pathway
positive regulation of tumor necrosis factor superfamily cytokine production
positive regulation of tumor necrosis factor production
positive regulation of tumor necrosis factor−mediated signaling pathway
positive regulation of translation
positive regulation of transcription from RNA polymerase II promoter in response to stress
positive regulation of transcription from RNA polymerase II promoter in response to endoplasmic reticulum stress
positive regulation of toll−like receptor signaling pathway
positive regulation of T cell migration
positive regulation of T cell mediated immunity
positive regulation of T cell mediated cytotoxicity
positive regulation of T cell differentiation
positive regulation of T cell chemotaxis
positive regulation of T cell activation
positive regulation of syncytium formation by plasma membrane fusion
positive regulation of superoxide anion generation
positive regulation of substrate adhesion−dependent cell spreading
positive regulation of stress−activated protein kinase signaling cascade
positive regulation of stress−activated MAPK cascade
positive regulation of smooth muscle cell proliferation
positive regulation of smooth muscle cell migration
positive regulation of signal transduction by p53 class mediator
positive regulation of RNA splicing
positive regulation of response to external stimulus
positive regulation of response to cytokine stimulus
positive regulation of response to biotic stimulus
positive regulation of regulatory T cell differentiation
positive regulation of regulated secretory pathway
positive regulation of receptor−mediated endocytosis
positive regulation of reactive oxygen species metabolic process
positive regulation of reactive oxygen species biosynthetic process
positive regulation of proteolysis
positive regulation of protein ubiquitination
positive regulation of protein transport
positive regulation of protein serine/threonine kinase activity
positive regulation of protein polyubiquitination
positive regulation of protein polymerization
positive regulation of protein modification by small protein conjugation or removal
positive regulation of protein kinase activity
positive regulation of protein import into nucleus
positive regulation of protein import
positive regulation of protein dephosphorylation
positive regulation of protein catabolic process
positive regulation of protein−containing complex assembly
positive regulation of production of molecular mediator of immune response
positive regulation of podosome assembly
positive regulation of phosphoprotein phosphatase activity
positive regulation of peptidase activity
positive regulation of pattern recognition receptor signaling pathway
positive regulation of oxidative stress−induced cell death
positive regulation of osteoblast differentiation
positive regulation of organelle organization
positive regulation of nucleocytoplasmic transport
positive regulation of nitric oxide metabolic process
positive regulation of nitric oxide biosynthetic process
positive regulation of nitric−oxide synthase biosynthetic process
positive regulation of NIK/NF−kappaB signaling
positive regulation of NF−kappaB transcription factor activity
positive regulation of neutrophil migration
positive regulation of neutrophil chemotaxis
positive regulation of neuron death
positive regulation of neuron apoptotic process
positive regulation of natural killer cell proliferation
positive regulation of natural killer cell activation
positive regulation of myoblast fusion
positive regulation of myeloid leukocyte mediated immunity
positive regulation of myeloid leukocyte differentiation
positive regulation of myeloid cell differentiation
positive regulation of mRNA splicing, via spliceosome
positive regulation of mRNA processing
positive regulation of mRNA metabolic process
positive regulation of mononuclear cell proliferation
positive regulation of mononuclear cell migration
positive regulation of monocyte chemotactic protein−1 production
positive regulation of mitotic cell cycle phase transition
positive regulation of mitotic cell cycle
positive regulation of MAPK cascade
positive regulation of MAP kinase activity
positive regulation of lymphocyte proliferation
positive regulation of lymphocyte migration
positive regulation of lymphocyte mediated immunity
positive regulation of lymphocyte differentiation
positive regulation of lymphocyte chemotaxis
positive regulation of lymphocyte activation
positive regulation of leukocyte proliferation
positive regulation of leukocyte migration
positive regulation of leukocyte mediated immunity
positive regulation of leukocyte mediated cytotoxicity
positive regulation of leukocyte differentiation
positive regulation of leukocyte degranulation
positive regulation of leukocyte chemotaxis
positive regulation of leukocyte cell−cell adhesion
positive regulation of leukocyte activation
positive regulation of lamellipodium organization
positive regulation of lamellipodium assembly
positive regulation of kinase activity
positive regulation of keratinocyte migration
positive regulation of intrinsic apoptotic signaling pathway
positive regulation of intracellular transport
positive regulation of intracellular protein transport
positive regulation of interleukin−8 production
positive regulation of interleukin−6 production
positive regulation of interleukin−12 production
positive regulation of interleukin−10 production
positive regulation of interleukin−1 production
positive regulation of interleukin−1 beta production
positive regulation of interferon−gamma production
positive regulation of interferon−beta production
positive regulation of interferon−alpha production
positive regulation of innate immune response
positive regulation of inflammatory response
positive regulation of immune effector process
positive regulation of I−kappaB kinase/NF−kappaB signaling
positive regulation of histone methylation
positive regulation of histone H3−K4 methylation
positive regulation of hemopoiesis
positive regulation of GTPase activity
positive regulation of granulocyte chemotaxis
positive regulation of G1/S transition of mitotic cell cycle
positive regulation of extrinsic apoptotic signaling pathway
positive regulation of exocytosis
positive regulation of establishment of protein localization
positive regulation of epithelial cell migration
positive regulation of endopeptidase activity
positive regulation of DNA binding
positive regulation of DNA−templated transcription, elongation
positive regulation of DNA−binding transcription factor activity
positive regulation of dephosphorylation
positive regulation of defense response to virus by host
positive regulation of defense response
positive regulation of cytosolic calcium ion concentration
positive regulation of cytoskeleton organization
positive regulation of cytoplasmic translation
positive regulation of cytokine production involved in immune response
positive regulation of cytokine production
positive regulation of cytokine−mediated signaling pathway
positive regulation of cysteine−type endopeptidase activity involved in apoptotic process
positive regulation of cysteine−type endopeptidase activity
positive regulation of cold−induced thermogenesis
positive regulation of chromosome separation
positive regulation of chromosome organization
positive regulation of chemotaxis
positive regulation of chemokine production
positive regulation of cellular component biogenesis
positive regulation of cellular catabolic process
positive regulation of cellular amide metabolic process
positive regulation of cell projection organization
positive regulation of cell morphogenesis involved in differentiation
positive regulation of cell killing
positive regulation of cell development
positive regulation of cell cycle phase transition
positive regulation of cell cycle G1/S phase transition
positive regulation of cell cycle
positive regulation of cell adhesion
positive regulation of cell activation
positive regulation of cell−substrate junction organization
positive regulation of cell−cell adhesion
positive regulation of CD4−positive, alpha−beta T cell differentiation
positive regulation of CD4−positive, alpha−beta T cell activation
positive regulation of binding
positive regulation of autophagy
positive regulation of autophagosome assembly
positive regulation of Arp2/3 complex−mediated actin nucleation
positive regulation of apoptotic signaling pathway
positive regulation of alpha−beta T cell proliferation
positive regulation of alpha−beta T cell activation
positive regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
positive regulation of adaptive immune response
positive regulation of acute inflammatory response
positive regulation of actin nucleation
polysaccharide metabolic process
polysaccharide catabolic process
poly(A) binding
poly−purine tract binding
polarized epithelial cell differentiation
podosome assembly
platelet aggregation
platelet activation
−log10(Adjusted.Pvalue)
10
20
30


phospholipid binding
phospholipase inhibitor activity
phosphatidylinositol 3−kinase activity
phosphate ion homeostasis
phagocytosis, engulfment
phagocytosis
peptidyl−tyrosine modification
peptidyl−threonine phosphorylation
peptidyl−threonine modification
peptidyl−serine phosphorylation
peptidyl−serine modification
peptidyl−lysine modification
peptidyl−lysine methylation
peptidyl−lysine acetylation
peptidyl−cysteine S−nitrosylation
peptidyl−cysteine modification
pentose−phosphate shunt
pattern recognition receptor signaling pathway
p38MAPK cascade
P−body assembly
oxygen transport
oxygen carrier activity
oxidoreduction−driven active transmembrane transporter activity
oxidoreductase activity, acting on NAD(P)H, quinone or similar compound as acceptor
oxidoreductase activity, acting on NAD(P)H
oxidative phosphorylation
ovulation
osteoclast differentiation
osteoblast differentiation
ossification
organic cyclic compound catabolic process
organelle membrane fusion
organelle inheritance
organelle fusion
organelle fission
oligopeptide transport
nucleus localization
nucleotide metabolic process
nucleotide−binding oligomerization domain containing signaling pathway
nucleotide−binding oligomerization domain containing 2 signaling pathway
nucleotide−binding domain, leucine rich repeat containing receptor signaling pathway
nucleosome disassembly
nucleosome binding
nucleoside triphosphate biosynthetic process
nucleoside phosphate metabolic process
nucleoside−triphosphatase regulator activity
nucleocytoplasmic transport
nucleobase−containing compound transport
nucleobase−containing compound catabolic process
nucleic acid transport
nucleic acid phosphodiester bond hydrolysis
nuclear transport
nuclear receptor binding
nuclear migration
nuclear export
nuclear division
nuclear chromosome segregation
nuclear body organization
nuclear−transcribed mRNA catabolic process, deadenylation−dependent decay
nuclear−transcribed mRNA catabolic process
non−membrane−bounded organelle assembly
NLRP3 inflammasome complex assembly
nitric oxide metabolic process
nitric oxide biosynthetic process
nitric−oxide synthase biosynthetic process
NIK/NF−kappaB signaling
neutrophil migration
neutrophil mediated immunity
neutrophil extravasation
neutrophil degranulation
neutrophil chemotaxis
neutrophil activation involved in immune response
neutrophil activation
neuron death
neuron apoptotic process
neuroinflammatory response
neural nucleus development
negative regulation of viral process
negative regulation of viral life cycle
negative regulation of viral genome replication
negative regulation of viral entry into host cell
negative regulation of ubiquitin protein ligase activity
negative regulation of ubiquitin−protein transferase activity
negative regulation of ubiquitin−dependent protein catabolic process
negative regulation of type I interferon−mediated signaling pathway
negative regulation of transport
negative regulation of translation
negative regulation of transferase activity
negative regulation of transcription from RNA polymerase II promoter in response to stress
negative regulation of sodium ion transport
negative regulation of sodium ion transmembrane transporter activity
negative regulation of sodium ion transmembrane transport
negative regulation of smooth muscle contraction
negative regulation of signal transduction by p53 class mediator
negative regulation of secretion by cell
negative regulation of secretion
negative regulation of RNA splicing
negative regulation of RNA catabolic process
negative regulation of response to external stimulus
negative regulation of response to cytokine stimulus
negative regulation of response to biotic stimulus
negative regulation of regulated secretory pathway
negative regulation of proteolysis involved in cellular protein catabolic process
negative regulation of proteolysis
negative regulation of protein ubiquitination
negative regulation of protein serine/threonine kinase activity
negative regulation of protein polymerization
negative regulation of protein phosphorylation
negative regulation of protein modification by small protein conjugation or removal
negative regulation of protein localization
negative regulation of protein kinase activity
negative regulation of protein catabolic process
negative regulation of protein binding
negative regulation of protein−containing complex assembly
negative regulation of platelet−derived growth factor receptor signaling pathway
negative regulation of phosphorylation
negative regulation of phosphorus metabolic process
negative regulation of phosphatidylinositol 3−kinase signaling
negative regulation of phosphate metabolic process
negative regulation of peptidase activity
negative regulation of organ growth
negative regulation of nuclear−transcribed mRNA catabolic process, deadenylation−dependent decay
negative regulation of NIK/NF−kappaB signaling
negative regulation of natural killer cell mediated immunity
negative regulation of natural killer cell mediated cytotoxicity
negative regulation of myeloid leukocyte differentiation
negative regulation of myeloid cell differentiation
negative regulation of muscle hypertrophy
negative regulation of mRNA splicing, via spliceosome
negative regulation of mRNA processing
negative regulation of mRNA metabolic process
negative regulation of mRNA catabolic process
negative regulation of mononuclear cell proliferation
negative regulation of mitotic cell cycle phase transition
negative regulation of metallopeptidase activity
negative regulation of MAPK cascade
negative regulation of MAP kinase activity
negative regulation of lymphocyte proliferation
negative regulation of lymphocyte mediated immunity
negative regulation of lymphocyte activation
negative regulation of locomotion
negative regulation of leukocyte proliferation
negative regulation of leukocyte mediated immunity
negative regulation of leukocyte mediated cytotoxicity
negative regulation of leukocyte differentiation
negative regulation of leukocyte activation
negative regulation of kinase activity
negative regulation of intrinsic apoptotic signaling pathway
negative regulation of interleukin−1 production
negative regulation of interleukin−1 beta production
negative regulation of interferon−gamma production
negative regulation of innate immune response
negative regulation of immunoglobulin mediated immune response
negative regulation of immune system process
negative regulation of immune response
negative regulation of immune effector process
negative regulation of hydrolase activity
negative regulation of hippo signaling
negative regulation of hemopoiesis
negative regulation of heart growth
negative regulation of extrinsic apoptotic signaling pathway via death domain receptors
negative regulation of exocytosis
negative regulation of endopeptidase activity
negative regulation of dephosphorylation
negative regulation of defense response
negative regulation of cytokine production
negative regulation of cytokine−mediated signaling pathway
negative regulation of cysteine−type endopeptidase activity involved in apoptotic process
negative regulation of cysteine−type endopeptidase activity
negative regulation of cold−induced thermogenesis
negative regulation of chemokine production
negative regulation of cellular protein catabolic process
negative regulation of cellular macromolecule biosynthetic process
negative regulation of cellular component movement
negative regulation of cellular catabolic process
negative regulation of cellular amide metabolic process
negative regulation of cell motility
negative regulation of cell migration
negative regulation of cell killing
negative regulation of cell cycle process
negative regulation of cell cycle phase transition
negative regulation of cell cycle


negative regulation of cell adhesion
negative regulation of cell activation
negative regulation of cell−cell adhesion
negative regulation of catabolic process
negative regulation of cardiac muscle tissue growth
negative regulation of cardiac muscle hypertrophy
negative regulation of cardiac muscle cell proliferation
negative regulation of B cell proliferation
negative regulation of B cell mediated immunity
negative regulation of B cell activation
negative regulation of apoptotic signaling pathway
negative regulation of actin filament polymerization
negative regulation of actin filament depolymerization
necrotic cell death
necroptotic process
ncRNA processing
natural killer cell proliferation
natural killer cell mediated immunity
natural killer cell mediated cytotoxicity
NADPH regeneration
NADP metabolic process
NADP binding
NADH dehydrogenase complex assembly
NADH dehydrogenase activity
NADH dehydrogenase (ubiquinone) activity
NADH dehydrogenase (quinone) activity
NAD(P)H dehydrogenase (quinone) activity
myoblast differentiation
myeloid leukocyte migration
myeloid leukocyte mediated immunity
myeloid leukocyte differentiation
myeloid leukocyte activation
myeloid cell homeostasis
myeloid cell differentiation
myeloid cell activation involved in immune response
MyD88−dependent toll−like receptor signaling pathway
muscle cell proliferation
muscle cell migration
multi−organism reproductive process
multi−multicellular organism process
mRNA transport
mRNA transcription by RNA polymerase II
mRNA transcription
mRNA stabilization
mRNA splicing, via spliceosome
mRNA processing
mRNA polyadenylation
mRNA export from nucleus
mRNA destabilization
mRNA catabolic process
mRNA 5'−UTR binding
mRNA 3'−UTR AU−rich region binding
mRNA 3'−end processing
movement in host environment
mononuclear cell proliferation
mononuclear cell migration
mononuclear cell differentiation
monocyte chemotactic protein−1 production
monocarboxylic acid binding
modulation by symbiont of entry into host
modulation by host of viral genome replication
modification of postsynaptic structure
mitotic sister chromatid separation
mitotic sister chromatid segregation
mitotic sister chromatid cohesion
mitotic nuclear division
mitotic chromosome condensation
mitotic cell cycle phase transition
mitochondrial respiratory chain complex I assembly
mitochondrial respiratory chain complex assembly
mitochondrial electron transport, NADH to ubiquinone
mitochondrial ATP synthesis coupled electron transport
midbrain development
microvillus organization
microvillus assembly
microtubule organizing center organization
microtubule organizing center localization
microtubule cytoskeleton organization involved in mitosis
microglial cell activation
MHC class II biosynthetic process
methylation
metaphase/anaphase transition of mitotic cell cycle
metaphase/anaphase transition of cell cycle
membrane invagination
membrane fusion
membrane biogenesis
MDA−5 signaling pathway
maturation of LSU−rRNA
maternal placenta development
mast cell degranulation
mast cell activation
MAP kinase kinase activity
maintenance of protein location in nucleus
maintenance of protein location in cell
maintenance of location in cell
maintenance of epithelial cell apical/basal polarity
maintenance of cell polarity
maintenance of apical/basal cell polarity
macrophage differentiation
macrophage activation
macromolecule methylation
macroautophagy
lysosome localization
lysine N−methyltransferase activity
lymphocyte proliferation
lymphocyte migration
lymphocyte mediated immunity
lymphocyte homeostasis
lymphocyte differentiation
lymphocyte apoptotic process
lymphocyte activation involved in immune response
lymph vessel morphogenesis
lipopolysaccharide−mediated signaling pathway
lipase inhibitor activity
leukocyte proliferation
leukocyte migration involved in inflammatory response
leukocyte migration
leukocyte mediated immunity
leukocyte mediated cytotoxicity
leukocyte homeostasis
leukocyte degranulation
leukocyte chemotaxis
leukocyte cell−cell adhesion
leukocyte apoptotic process
leukocyte aggregation
leukocyte activation involved in inflammatory response
leukocyte activation involved in immune response
lamellipodium organization
lamellipodium assembly
kinase activator activity
killing of cells of another organism
killing by host of symbiont cells
iron ion transport
iron ion homeostasis
intrinsic apoptotic signaling pathway in response to endoplasmic reticulum stress
intrinsic apoptotic signaling pathway in response to DNA damage
intrinsic apoptotic signaling pathway by p53 class mediator
intrinsic apoptotic signaling pathway
intramolecular oxidoreductase activity, transposing S−S bonds
intracellular steroid hormone receptor signaling pathway
intracellular receptor signaling pathway
intracellular pH reduction
intermembrane lipid transfer
interleukin−8 production
interleukin−6 production
interleukin−4 production
interleukin−12 production
interleukin−10 production
interleukin−1 production
interleukin−1 beta production
interferon−gamma production
interferon−gamma−mediated signaling pathway
interferon−beta production
interferon−alpha production
integrin−mediated signaling pathway
insulin receptor substrate binding
innate immune response in mucosa
innate immune response activating cell surface receptor signaling pathway
innate immune response−activating signal transduction
inflammasome complex assembly
IMP metabolic process
immunoglobulin receptor binding
immune response−regulating signaling pathway
immune response−regulating cell surface receptor signaling pathway
immune response−activating signal transduction
immune response−activating cell surface receptor signaling pathway
immune receptor activity
I−kappaB kinase/NF−kappaB signaling
hydrolase activity, acting on carbon−nitrogen (but not peptide) bonds, in linear amidines
humoral immune response
homotypic cell−cell adhesion
homeostasis of number of cells
histone phosphorylation
histone modification
histone methyltransferase activity (H3−K36 specific)
histone methyltransferase activity
histone methylation
histone lysine methylation
histone H3−K9 modification
histone H3−K4 methylation
histone H3−K36 methylation
histone demethylation
histone binding
histone−lysine N−methyltransferase activity
heterotypic cell−cell adhesion
heterocycle catabolic process
hepatocyte apoptotic process
hemostasis


hematopoietic stem cell proliferation
helicase activity
heat shock protein binding
guanyl ribonucleotide binding
guanyl nucleotide binding
guanyl−nucleotide exchange factor activity
GTPase regulator activity
GTPase binding
GTPase activity
GTPase activator activity
GTP binding
GTP−dependent protein binding
growth hormone receptor signaling pathway via JAK−STAT
granulocyte migration
granulocyte differentiation
granulocyte chemotaxis
granulocyte activation
Golgi vesicle transport
Golgi to plasma membrane protein transport
Golgi to endosome transport
Golgi localization
Golgi inheritance
glycosaminoglycan biosynthetic process
glycoprotein biosynthetic process
glycogen catabolic process
glucose 6−phosphate metabolic process
glucan catabolic process
glial cell activation
germinal center formation
generation of precursor metabolites and energy
GDP binding
gamma−aminobutyric acid transport
G2/M transition of mitotic cell cycle
G1/S transition of mitotic cell cycle
filopodium assembly
female pregnancy
fat cell differentiation
extrinsic apoptotic signaling pathway via death domain receptors
extrinsic apoptotic signaling pathway
exonuclease activity, active with either ribo− or deoxyribonucleic acids and producing 5'−phosphomonoesters
exocytosis
exocytic process
ether metabolic process
ether biosynthetic process
establishment or maintenance of monopolar cell polarity
establishment or maintenance of cell polarity
establishment of T cell polarity
establishment of RNA localization
establishment of protein localization to plasma membrane
establishment of protein localization to organelle
establishment of protein localization to membrane
establishment of protein localization to endoplasmic reticulum
establishment of organelle localization
establishment of monopolar cell polarity
establishment of mitotic spindle localization
establishment of lymphocyte polarity
establishment of epithelial cell apical/basal polarity
establishment of endothelial barrier
establishment of cell polarity
establishment of apical/basal cell polarity
erythrocyte homeostasis
erythrocyte differentiation
ERK1 and ERK2 cascade
ERBB signaling pathway
epithelium migration
epithelial cell migration
epidermal growth factor receptor signaling pathway
entry into host
energy derivation by oxidation of organic compounds
endoplasmic reticulum to cytosol transport
endoplasmic reticulum calcium ion homeostasis
electron transport chain
electron transfer activity
double−stranded RNA binding
double−strand break repair via homologous recombination
double−strand break repair
dopamine biosynthetic process
DNA strand elongation involved in DNA replication
DNA strand elongation
DNA replication
DNA recombination
DNA helicase activity
DNA geometric change
DNA duplex unwinding
DNA conformation change
DNA−templated transcription, elongation
DNA−templated DNA replication maintenance of fidelity
DNA−templated DNA replication
DNA−binding transcription factor binding
disordered domain specific binding
deubiquitinase activity
detection of other organism
detection of molecule of bacterial origin
detection of external biotic stimulus
detection of biotic stimulus
detection of bacterium
dephosphorylation
deoxyribose phosphate biosynthetic process
deoxyribonucleotide biosynthetic process
dendritic spine development
dendritic cell migration
dendritic cell differentiation
demethylation
defense response to virus
defense response to symbiont
defense response to protozoan
defense response to fungus
defense response to bacterium
cytoskeleton−dependent intracellular transport
cytoplasmic translational initiation
cytoplasmic translation
cytoplasmic pattern recognition receptor signaling pathway in response to virus
cytoplasmic pattern recognition receptor signaling pathway
cytokinesis
cytokine receptor activity
cytokine production involved in immune response
cytokine binding
cytokine−mediated signaling pathway
cysteine−type endopeptidase regulator activity involved in apoptotic process
cyclin binding
cortical cytoskeleton organization
complement receptor mediated signaling pathway
complement receptor activity
cold−induced thermogenesis
coagulation
clathrin coat assembly
clathrin−dependent endocytosis
chromosome separation
chromosome segregation
chromosome condensation
chromatin remodeling
chromatin DNA binding
chemokine production
chaperone binding
chaperone−mediated protein folding
cerebrospinal fluid circulation
centrosome localization
centrosome cycle
centromere complex assembly
cellular senescence
cellular response to virus
cellular response to type I interferon
cellular response to tumor necrosis factor
cellular response to topologically incorrect protein
cellular response to steroid hormone stimulus
cellular response to reactive oxygen species
cellular response to reactive nitrogen species
cellular response to peptide hormone stimulus
cellular response to peptide
cellular response to oxygen levels
cellular response to oxidative stress
cellular response to nutrient levels
cellular response to molecule of bacterial origin
cellular response to metal ion
cellular response to mechanical stimulus
cellular response to lipopolysaccharide
cellular response to lectin
cellular response to interleukin−1
cellular response to interferon−gamma
cellular response to interferon−beta
cellular response to hypoxia
cellular response to hydrogen peroxide
cellular response to fluid shear stress
cellular response to extracellular stimulus
cellular response to external stimulus
cellular response to environmental stimulus
cellular response to decreased oxygen levels
cellular response to chemical stress
cellular response to biotic stimulus
cellular response to angiotensin
cellular response to amyloid−beta
cellular response to abiotic stimulus
cellular respiration
cellular polysaccharide metabolic process
cellular polysaccharide catabolic process
cellular nitrogen compound catabolic process
cellular iron ion homeostasis
cellular extravasation
cellular defense response
cellular component disassembly
cellular carbohydrate catabolic process
cellular anion homeostasis
cell killing

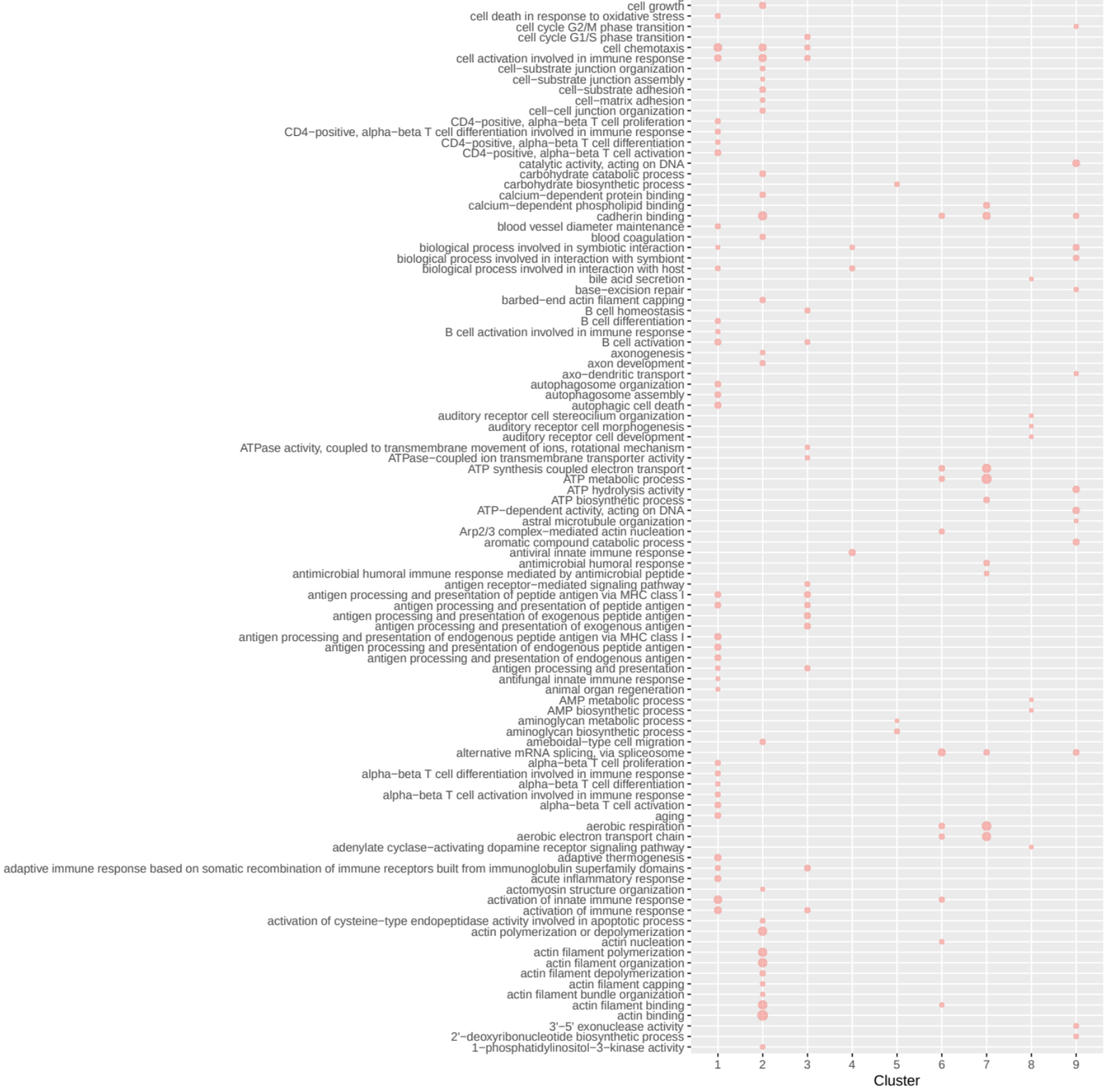

cell growth
cell death in response to oxidative stress
cell cycle G2/M phase transition
cell cycle G1/S phase transition
cell chemotaxis
cell activation involved in immune response
cell−substrate junction organization
cell−substrate junction assembly
cell−substrate adhesion
cell−matrix adhesion
cell−cell junction organization
CD4−positive, alpha−beta T cell proliferation
CD4−positive, alpha−beta T cell differentiation involved in immune response
CD4−positive, alpha−beta T cell differentiation
CD4−positive, alpha−beta T cell activation
catalytic activity, acting on DNA
carbohydrate catabolic process
carbohydrate biosynthetic process
calcium−dependent protein binding
calcium−dependent phospholipid binding
cadherin binding
blood vessel diameter maintenance
blood coagulation
biological process involved in symbiotic interaction
biological process involved in interaction with symbiont
biological process involved in interaction with host
bile acid secretion
base−excision repair
barbed−end actin filament capping
B cell homeostasis
B cell differentiation
B cell activation involved in immune response
B cell activation
axonogenesis
axon development
axo−dendritic transport
autophagosome organization
autophagosome assembly
autophagic cell death
auditory receptor cell stereocilium organization
auditory receptor cell morphogenesis
auditory receptor cell development
ATPase activity, coupled to transmembrane movement of ions, rotational mechanism
ATPase−coupled ion transmembrane transporter activity
ATP synthesis coupled electron transport
ATP metabolic process
ATP hydrolysis activity
ATP biosynthetic process
ATP−dependent activity, acting on DNA
astral microtubule organization
Arp2/3 complex−mediated actin nucleation
aromatic compound catabolic process
antiviral innate immune response
antimicrobial humoral response
antimicrobial humoral immune response mediated by antimicrobial peptide
antigen receptor−mediated signaling pathway
antigen processing and presentation of peptide antigen via MHC class I
antigen processing and presentation of peptide antigen
antigen processing and presentation of exogenous peptide antigen
antigen processing and presentation of exogenous antigen
antigen processing and presentation of endogenous peptide antigen via MHC class I
antigen processing and presentation of endogenous peptide antigen
antigen processing and presentation of endogenous antigen
antigen processing and presentation
antifungal innate immune response
animal organ regeneration
AMP metabolic process
AMP biosynthetic process
aminoglycan metabolic process
aminoglycan biosynthetic process
ameboidal−type cell migration
alternative mRNA splicing, via spliceosome
alpha−beta T cell proliferation
alpha−beta T cell differentiation involved in immune response
alpha−beta T cell differentiation
alpha−beta T cell activation involved in immune response
alpha−beta T cell activation
aging
aerobic respiration
aerobic electron transport chain
adenylate cyclase−activating dopamine receptor signaling pathway
adaptive thermogenesis
adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
acute inflammatory response
actomyosin structure organization
activation of innate immune response
activation of immune response
activation of cysteine−type endopeptidase activity involved in apoptotic process
actin polymerization or depolymerization
actin nucleation
actin filament polymerization
actin filament organization
actin filament depolymerization
actin filament capping
actin filament bundle organization
actin filament binding
actin binding
3'−5' exonuclease activity
2'−deoxyribonucleotide biosynthetic process
1−phosphatidylinositol−3−kinase activity
1
2
3
4
5
6
7
8
9
Cluster

Fig. S4 GO pathways significantly enriched in up-regulated genes in every neutrophil cluster.

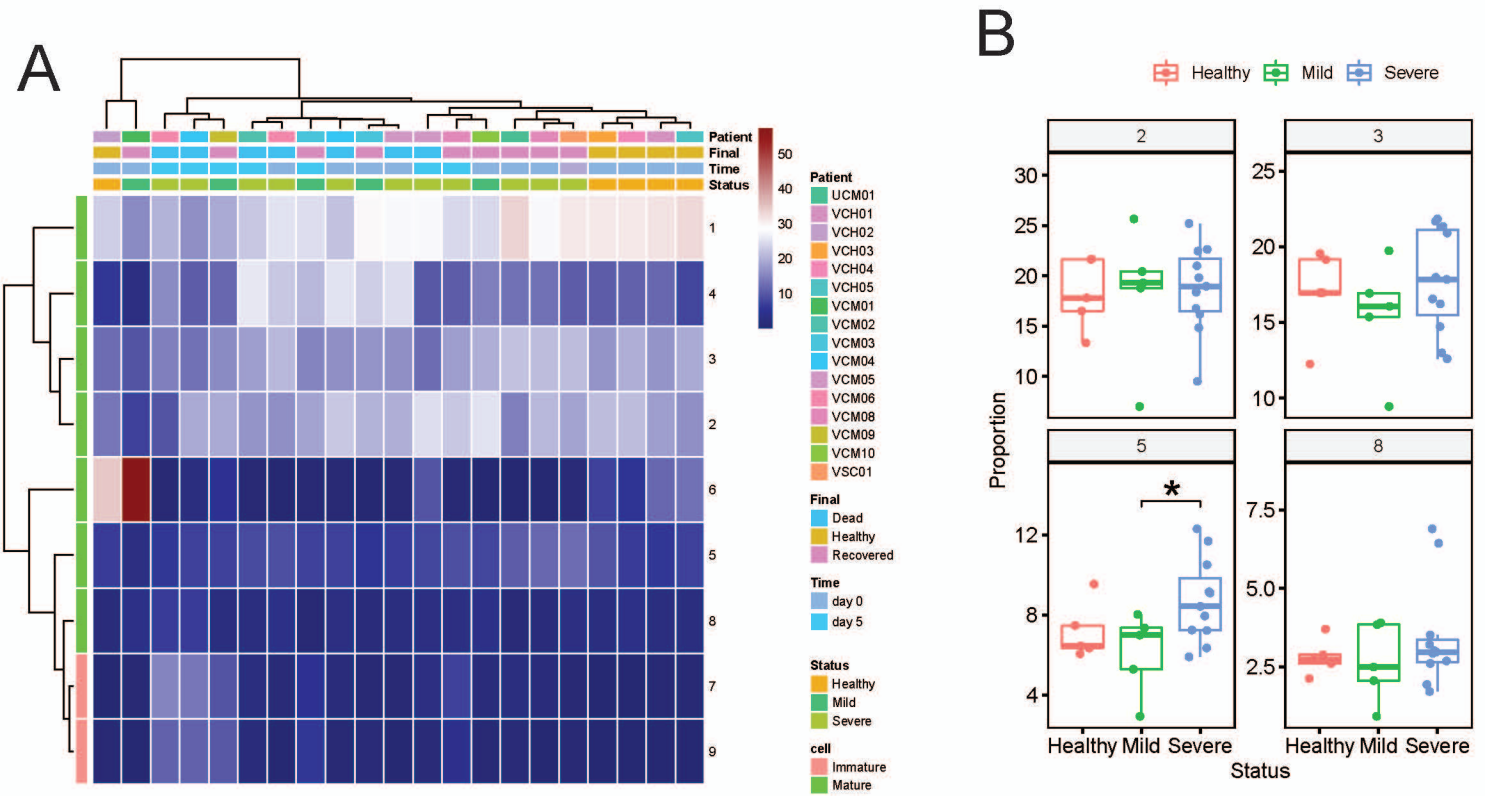

A
Patient
Final
Time
Status
50
40
30
20
10
1
4
3
2
6
5
8
7
9
Patient
UCM01
VCH01
VCH02
VCH03
VCH04
VCH05
VCM01
VCM02
VCM03
VCM04
VCM05
VCM06
VCM08
VCM09
VCM10
VSC01
Final
Dead
Healthy
Recovered
Time
day 0
day 5
Status
Healthy
Mild
Severe
cell
Immature
Mature
B
Healthy
Mild
Severe
2
3
5
8
Proportion
*
Healthy Mild Severe
Healthy Mild Severe
Status

Fig. S5 (A) Heatmap of neutrophil cluster size in every sample. (B) Proportional change of neutrophil clusters during COVID19 progression. * $p < 0.05$


GO
cell adhesion molecule binding
protein−containing complex binding
cadherin binding
oxidoreductase activity
double−stranded DNA binding
sequence−specific DNA binding
DNA binding
lipid binding
transcription regulatory region nucleic acid binding
sequence−specific double−stranded DNA binding
RNA polymerase II transcription regulatory region sequence−specific DNA binding
transcription cis−regulatory region binding
cis−regulatory region sequence−specific DNA binding
RNA polymerase II cis−regulatory region sequence−specific DNA binding
transcription regulator activity
DNA−binding transcription factor activity, RNA polymerase II−specific
DNA−binding transcription factor activity
mRNA processing
positive regulation of macromolecule biosynthetic process
negative regulation of RNA metabolic process
negative regulation of intracellular signal transduction
carbohydrate derivative metabolic process
histone modification
negative regulation of biosynthetic process
positive regulation of nucleic acid−templated transcription
positive regulation of RNA biosynthetic process
positive regulation of transcription, DNA−templated
negative regulation of cell population proliferation
negative regulation of transcription by RNA polymerase II
negative regulation of nucleic acid−templated transcription
negative regulation of RNA biosynthetic process
negative regulation of transcription, DNA−templated
negative regulation of cellular biosynthetic process
negative regulation of macromolecule biosynthetic process
positive regulation of transcription by RNA polymerase II
generation of precursor metabolites and energy
endocytosis
regulation of lymphocyte activation
chromatin organization
transcription by RNA polymerase II
regulation of transcription by RNA polymerase II
regulation of biosynthetic process
vesicle−mediated transport
regulation of cellular biosynthetic process
circulatory system development
phosphorylation
regulation of macromolecule biosynthetic process
negative regulation of nitrogen compound metabolic process
system development
positive regulation of macromolecule metabolic process
negative regulation of macromolecule metabolic process
regulation of RNA metabolic process
positive regulation of protein modification process
positive regulation of phosphorylation
negative regulation of metabolic process
regulation of nucleobase−containing compound metabolic process
protein modification process
cellular protein modification process
animal organ development
positive regulation of phosphate metabolic process
positive regulation of phosphorus metabolic process
negative regulation of cellular metabolic process
locomotion
cellular response to oxygen−containing compound
cellular response to stress
cell population proliferation
response to endogenous stimulus
positive regulation of nitrogen compound metabolic process
chromosome organization
macromolecule modification
positive regulation of nucleobase−containing compound metabolic process
RNA metabolic process
regulation of kinase activity
regulation of protein kinase activity
positive regulation of protein phosphorylation
positive regulation of RNA metabolic process
cell cycle
regulation of transferase activity
intracellular signal transduction
protein phosphorylation
regulation of protein modification process
regulation of cell population proliferation
regulation of phosphorylation
response to lipid
regulation of cell cycle
cellular response to endogenous stimulus
regulation of phosphorus metabolic process
regulation of phosphate metabolic process
mRNA metabolic process
reproduction
nucleic acid metabolic process
reproductive process
regulation of protein phosphorylation
positive regulation of immune response
negative regulation of molecular function
homeostatic process
regulation of hydrolase activity
negative regulation of cellular protein metabolic process
negative regulation of catalytic activity
negative regulation of protein metabolic process
positive regulation of transport
cell−cell adhesion
membrane organization
regulation of proteolysis
regulation of leukocyte activation
regulation of cell activation
positive regulation of cytokine production
immune response−regulating signaling pathway
metal ion binding
ion binding
nucleic acid binding
cation binding
signaling receptor binding
RNA binding
structural molecule activity
positive regulation of multicellular organismal process
cellular response to organic substance
inflammatory response
lymphocyte activation
response to organic substance
regulation of response to stress
cellular response to chemical stimulus
regulation of cytokine production
response to chemical
cytokine production
leukocyte activation
positive regulation of response to stimulus
RNA processing
cell activation
regulation of response to external stimulus
positive regulation of immune system process
regulation of defense response
immune effector process
regulation of response to stimulus
cell surface receptor signaling pathway
macromolecule biosynthetic process
cellular response to cytokine stimulus
regulation of immune system process
cellular nitrogen compound biosynthetic process
response to cytokine
response to bacterium
response to stress
immune system process
response to external stimulus
regulation of immune response
immune response
defense response
biological process involved in interspecies interaction between organisms
response to biotic stimulus
organonitrogen compound biosynthetic process
response to other organism
response to external biotic stimulus
defense response to other organism
cellular macromolecule biosynthetic process
cellular amide metabolic process
innate immune response
amide biosynthetic process
peptide metabolic process
peptide biosynthetic process
translation
1 4 6 7 9
Cluster
−log10(Adjusted.Pvalue)
3
5
7
NES
3
2
1
0
−1
−2

Fig. S6 GSEA analysis of significantly different GO pathway gene sets in selected neutrophil clusters from COVID19 patients compared with that from healthy controls. NES, normalized enrichment score.

regulation of cell death
regulation of response to stimulus
catabolic process
cellular catabolic process
cation binding
metal ion binding
response to chemical
heterocycle biosynthetic process
homeostatic process
cell surface receptor signaling pathway
vesicle−mediated transport
positive regulation of macromolecule biosynthetic process
positive regulation of RNA metabolic process
positive regulation of nucleobase−containing compound metabolic process
nucleobase−containing compound biosynthetic process
positive regulation of nucleic acid−templated transcription
positive regulation of RNA biosynthetic process
positive regulation of transcription, DNA−templated
nucleic acid metabolic process
RNA metabolic process
regulation of macromolecule biosynthetic process
regulation of nucleobase−containing compound metabolic process
regulation of RNA biosynthetic process
regulation of nucleic acid−templated transcription
transcription, DNA−templated
regulation of transcription, DNA−templated
regulation of RNA metabolic process
nucleic acid−templated transcription
RNA biosynthetic process
regulation of biosynthetic process
regulation of cellular biosynthetic process
RNA binding
signaling receptor binding
structural molecule activity
cellular developmental process
cell development
cellular response to oxygen−containing compound
animal organ development
cellular response to stress
movement of cell or subcellular component
response to growth factor
positive regulation of biosynthetic process
regulation of locomotion
localization of cell
cell motility
neurogenesis
cell cycle
regulation of cellular component movement
cell projection organization
regulation of cell motility
positive regulation of nitrogen compound metabolic process
plasma membrane bounded cell projection organization
response to hormone
positive regulation of cellular biosynthetic process
regulation of cell migration
regulation of cell cycle
negative regulation of cell population proliferation
cellular response to organic substance
neuron differentiation
reproductive process
reproduction
response to nitrogen compound
endocytosis
generation of neurons
locomotion
nervous system development
response to organonitrogen compound
positive regulation of transcription by RNA polymerase II
positive regulation of response to stimulus
head development
membrane organization
cellular response to endogenous stimulus
response to oxygen−containing compound
cellular response to organic cyclic compound
cell activation
regulation of lymphocyte activation
transcription by RNA polymerase II
regulation of immune system process
immune response−regulating signaling pathway
regulation of transcription by RNA polymerase II
regulation of leukocyte activation
cell population proliferation
regulation of cell population proliferation
positive regulation of immune system process
regulation of cell activation
response to endogenous stimulus
response to lipid
response to bacterium
response to abiotic stimulus
response to organic cyclic compound
positive regulation of immune response
immune effector process
regulation of immune response
innate immune response
hydrolase activity
transcription regulator activity
adenyl ribonucleotide binding
adenyl nucleotide binding
ATP binding
catalytic activity
anion binding
ion binding
purine nucleotide binding
purine ribonucleotide binding
ribonucleotide binding
small molecule binding
purine ribonucleoside triphosphate binding
nucleoside phosphate binding
nucleotide binding
carbohydrate derivative binding
regulation of response to external stimulus
gene expression
lymphocyte activation
response to stress
immune response
leukocyte activation
response to external stimulus
immune system process
response to organic substance
biosynthetic process
organic substance biosynthetic process
protein metabolic process
cellular nitrogen compound biosynthetic process
cellular biosynthetic process
macromolecule biosynthetic process
defense response
inflammatory response
response to cytokine
cellular macromolecule metabolic process
defense response to other organism
cellular protein metabolic process
biological process involved in interspecies interaction between organisms
response to other organism
response to external biotic stimulus
response to biotic stimulus
organonitrogen compound biosynthetic process
cellular amide metabolic process
peptide metabolic process
cellular macromolecule biosynthetic process
amide biosynthetic process
peptide biosynthetic process
translation

GO

1 4 6 7 9

Cluster

NES

2
1
0
−1

−log10(Adjusted.Pvalue)

2
4
6
8

Fig. S7 GSEA analysis of significantly different GO gene sets in selected neutrophil clusters from severe COVID19 patients compared with that from mild COVID19 patients.